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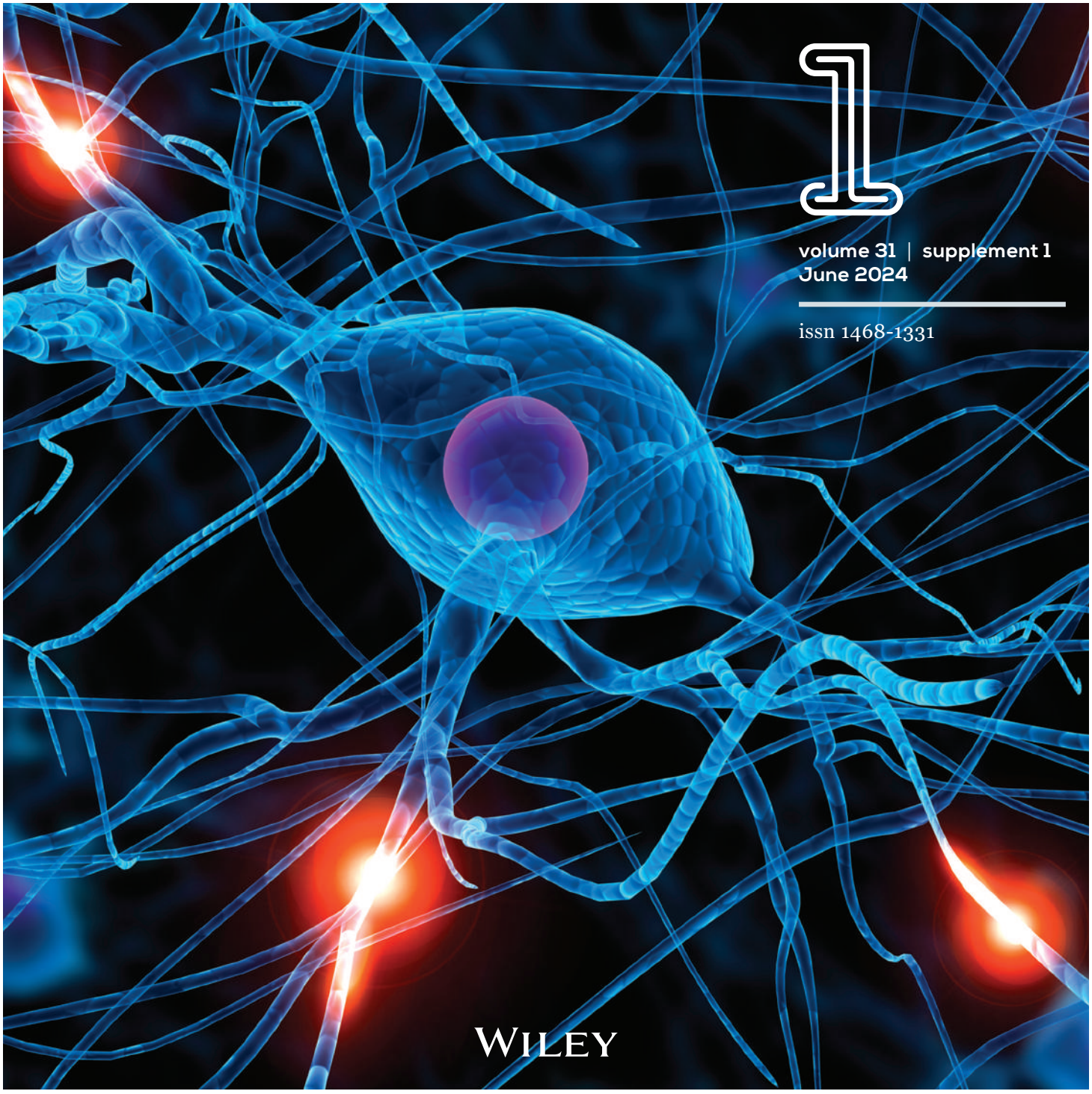

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Contents

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ABSTRACT

Plenary Sessions

Sunday, June 30 2024

Presidential Symposium

PLEN02_1 | How nature and nurture conspire to regulate brain development and plasticity

M. Greenberg
Harvard Medical School, Boston, MA, USA

Experience-dependent neuronal activity plays a critical role in shaping the connectivity and function of the central nervous system. These actions are mediated in part by the action of a program of neuronal activity-driven gene expression. Investigation of these gene expression programs has uncovered important roles in dendritic growth, the development of excitatory and inhibitory synapses, the composition of protein complexes at pre- and post-synaptic sites, and the production of neuropeptides that control neural circuit development. Moreover, defects in the activity-dependent gene program contribute to disorders of human cognition. Thus, study of this transcriptional response promises new insights into neuronal plasticity and disease.
Disclosure: Nothing to disclose.

PLEN02_2 | How the brain barriers ensure CNS immune privilege

B. Engelhardt
University of Bern, Theodor Kocher Institute, Switzerland

Proper communication of central nervous system (CNS) neurons requires a homeostatic environment, which does not tolerate uncontrolled entry of blood components including immune cells into the CNS parenchyma. The CNS has thus developed a unique relationship with the immune system known as CNS immune privilege. CNS immune privilege is established by endothelial, epithelial, glial and fibroblasts composed brain barriers. The brain barriers establish compartments in the CNS that differ with regard to their accessibility to immune cells and immune mediators. We have developed reporter mice allowing to image the brain barriers and immune cell and immune mediator movement in the CNS by in vivo live cell imaging. This allows to determine the barrier functions of the different brain barriers and how their disturbance affects CNS immunity during neuroinflammatory conditions. Based on our studies we propose that CNS immune privilege relies on the proper function of the brain barriers, which allow for CNS immune surveillance but prohibit activation of immune responses from the CNS parenchyma unless it is directly injured.
Disclosure: Nothing to disclose.

PLEN02_3 | How clinical observations challenge neuroscience

M. Vidailhet
Groupe Hospitalier de la Pitié Salpêtrière, Paris, France

PLEN02_4 | Myasthenia gravis; Individualized treatment based on a well-defined disease pathogenesis

N. E. Gilhus
Department of Neurology, Haukeland University Hospital and Department of Clinical Medicine, University of Bergen, Bergen, Norway

Background: Myasthenia gravis (MG) and MG subgroup is diagnosed by clinical history and examination, autoantibody testing, and electrophysiological tests.
Pathogenesis: Autoantibodies binding to the postsynaptic membrane at the neuromuscular junction cause MG. IgG antibodies to acetylcholine receptor (AChR), MuSK, or LRP4 impair AChRs by receptor cross-linking, complement activation, AChR blockade, or impaired AChR clustering. IgG subclass varies. Thymus hyperplasia and thymoma can both induce AChR autoantibody production and MG. Active synthesis of new AChRs is ongoing in MG, and the structural postsynaptic changes are reversible.
Treatment: MG treatment should be in accordance with international guidelines and at the same time adapted to the individual patient. Treatment decisions should be taken by neurologist and patient together. The treatment should be based on autoantibody status, MG generalization and severity, and thymus pathology. Symptomatic drug therapy with acetylcholine-esterase inhibition represents a primary therapy. Immunotherapy should be offered to all patients who have not met their treatment goals. The combination of prednisolone and azathioprine represents first-line immunotherapy. Rituximab is an alternative, especially in MuSK-MG and in newly-onset AChR-MG. Mycophenolate, tacrolimus, and methotrexate represent other commonly used immunosuppressants. Thymectomy should be undertaken with a thymoma and in generalized MG with AChR antibodies and debut below 50 (65) years. Complement inhibitors and

FcRn blockers have a proven and clinically meaningful effect in most MG patients. They improve symptoms already after 1-2 weeks. Due to very high drug costs their use is restricted to difficult-to-treat and severe MG, and depends on local availability, formal approval, and refunding policies. New and experimental therapies may be considered in refractory cases. Physical activity is safe and beneficial in MG. At least 150 minutes per week is recommended.

Conclusions: Successful MG treatment depends on the timely combination of interventions. Most patients do well, but there is room for further improvement.

Disclosure: Nothing to disclose.

Monday, July 01 2024

Invasive neuromodulation: Hot topics and future directions

PLEN03_1 | Deep brain stimulation for the treatment of movement disorders

E. Moro
CHU de Grenoble, France

PLEN03_2 | Focused ultrasound for the treatment of tremor and Parkinson's disease

R. Martínez-Fernández
HM CINAC, University Hospital HM Puerta del Sur, Móstoles, Madrid, Spain

Over nearly a decade, MR-guided focused ultrasound technology has fully integrated into clinical practice. Utilized in its high-intensity modality for brain thermoablation, it has generated abundant high-quality scientific evidence and has become a standard treatment, particularly for Essential Tremor and Parkinson's Disease, its primary indications. While the number of sites offering the therapy and the yearly number of interventions increase exponentially, indications expand to other movement disorders such as dystonia or psychiatric conditions. Further broadening the tool's applications and unlocking its full potential will partially depend on advancements in the technology itself, along with increased clinical experience. In addition to its use for therapeutic brain ablation, focused ultrasound can also be applied in the low-intensity modality. In this mode, it enables focal and transient Blood-Brain Barrier opening, liquid biopsy, or neuromodulation. These approaches, which have already been preliminarily explored, may allow us to move beyond the symptomatic effects and impact disease pathogenesis, facilitate early and specific diagnosis, or achieve non-invasive modulation of brain activity. This presentation aims to provide an overview of the current state-of-the-art and future prospects for FUS technology in clinical neurology

Disclosure: I have received speaker honoraria form Insightec and Palex outside the context of this presentation.

PLEN03_3 | Vagal nerve and deep brain stimulation for the treatment of refractory epilepsy

P. Boon
Ghent University Hospital, Belgium

PLEN03_4 | Spinal cord stimulation for the treatment of chronic pain

C. de Vos
Center for Pain Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands

Spinal Cord Stimulation is an innovative invasive therapy, which is applied in chronic pain patients who are otherwise therapy resistant. The very first implantation was already in 1967. Although over 50 years have passed, the quality of evidence of its efficacy is still debated. This is partly due to the fact that until recently no paresthesia-free stimulation modes were available, and therefore sham controlled studies were not possible. It is also partly a due to a lack of understanding of its mechanisms of action and a lack of more objective patient related outcome measures. Fortunately, times are changing rapidly. Since the introduction of paresthesia-free stimulation modes, sham controlled studies are conducted. In addition, are we starting to better understand the mechanisms of action of Spinal Cord Stimulation, based on both animal research and more objective measures to characterize physiological effects in chronic pain patients.

Disclosure: Nothing to disclose.

Tuesday, July 02 2024

Highlights and breaking news

PLEN04_8 | EJoN: Long-term risk of recurrent vascular events and mortality in young stroke patients: Insights from a multicenter study

J. Broman[1]; S. Fandler-Höfler[2]
[1]*Department of Neurology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland;* [2]*Department of Neurology, Medical University of Graz, Graz, Austria*

Introduction: Although the incidence of stroke in the young is rising, data on long-term outcomes in these patients are scarce. We thus aimed to investigate the long-term risk of recurrent vascular events and mortality in a multicenter study.

Methods: We followed 396 consecutive patients aged 18–55 years with ischemic stroke (IS) or transient ischemic attack (TIA) enrolled in three European centers during the period 2007–2010. A detailed outpatient clinical follow-up assessment was performed between 2018 and 2020. When an in-person follow-up visit was not possible, outcome events were assessed using electronic records and registry data.

Results: During a median follow-up of 11.8 (IQR 10.4–12.7) years, 89 (22.5%) patients experienced any recurrent vascular event, 62 (15.7%) had any cerebrovascular event, 34 (8.6%) had other vascular events, and 27 (6.8%) patients died. Cumulative 10-year incidence rate per 1000 person-years was 21.6 (95% CI 17.1–26.9) for any recurrent vascular event and 14.9 (95% CI 11.3–19.3) for any cerebrovascular event (Table 1). The prevalence of cardiovascular risk factors increased over time, and 22 (13.5%) patients lacked any secondary preventive medication at the in-person follow-up. After adjustment for demographics and comorbidities, atrial fibrillation at baseline was found to be significantly associated with recurrent vascular events.

Conclusion: This multicenter study shows a considerable risk of recurrent vascular events in young IS and TIA patients. Further studies should investigate whether detailed individual risk assessment, modern secondary preventive strategies, and better patient adherence may reduce recurrence risk.

Disclosure: Nothing to disclose.

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ABSTRACT

Symposia

Saturday, June 29 2024

What will change the neurologist's care for persons of child-bearing age with epilepsy and migraine?

SYMP01_1 | Planning pregnancy in women with epilepsy and migraine using antiseizure medications

T. Tomson
Dept of Clinical Neuroscience, Karolinska Institutet, Solna, Sweden

Use of medication during pregnancy requires consideration of potential risks to the fetus due to medication exposure and risks to the fetus as well as the pregnant woman associated with sub-optimally treated condition. The outcome of such risk-benefit analyses will vary depending on the maternal condition under treatment. Poorly controlled epilepsy can cause serious harm to the mother and the fetus, which rarely is the case in migraine. In recent years new data have emerged on the risks to the fetus with exposure to different ASMs and on differences between ASMs in this regard. This has led regulators such as FDA and EMA to issue restrictions on the use of some ASMs (contraindications for valproic acid and topiramate, both also used in prophylactic treatment for migraine) in female patients of childbearing potential. In the case of active epilepsy, it is usually necessary to replace these medications with other ASMs. Finding a suitable alternative can take time, sometimes a year or more. Therefore, ideally young girls or women should not be started on these medications unless absolutely necessary. Recent data indicate that lamotrigine, levetiracetam and oxcarbazepine are among the safest ASMs. These have become preferred first-line medications for the treatment of epilepsy in patients of child-bearing potential. Pre-pregnancy optimization also includes establishing the lowest effective dose of the selected medication and documentation of the corresponding plasma concentration to serve as individual base-line for follow-up monitoring during pregnancy. Folate supplementation should also be initiated well in advance of conception.

Disclosure: Funding from Accord, Glenmark, GSK, UCB, Eisai, Ecu Pharma, Bial, Teva, Sanofi, SF Group, GW Pharma, Zentiva, and Angelini as donations to the EURAP pregnancy registry; Speaker honoraria from Eisai, Angelini, GSK and UCB.

SYMP01_2 | Care for persons with epilepsy and migraine in pregnancy, delivery and postpartum

B. Schmitz
Department of Neurology, Stroke Unit and Center for Epilepsy, Vivantes Humboldt-Klinikum Berlin, Germany

Both epilepsy (prevalence 1%) and migraine (prevalence 40%) are common disorders in women of childbearing age. Therefore, neurologists should be familiar with respect to 1. Interactions between prophylactic treatments and oral contraceptives 2. Pregnancy related changes with respect to disease severity 3. Safe acute and prophylactic treatments during pregnancy and lactation. The lecture will discuss praxis-relevant actual data with respect to pregnancy, delivery and the postpartum period in women with migraine and / or epilepsy. Clinical recommendations for counseling of patients are presented.

Disclosure: Bettina Schmitz received Honoraria Angelini / Arvelle, Bial, Desitin, Eisai, Precisis, Sanofi, UCB-Pharma Memberships and Commissions DGN, DGfE, DEGUM, DSG, BGPN Michael Foundation Chair of board of trustees EURAP Coordination Germany

SYMP01_3 | Antiseizure medication in men

M. Bjork
Haukeland University Hospital - Helse Vest, Bergen, Norway

SYMP01_4 | Clinical care of children exposed to antiseizure medications in utero

R. Bromley
University of Manchester/Royal Manchester Children's Hospital, UK

Prenatal exposure to certain antiseizure medications is associated with higher rates of congenital anomalies and altered neurodevelopmental outcomes. Offspring with such symptoms therefore become patients themselves, with a constellation of lifelong health conditions which require clinical review, diagnosis and care management plans. This talk will summarise current evidence regarding the physical and neurodevelopmental outcomes of children exposed to

antiseizure medications. It will demonstrate how, in some instances, these altered fetal and child outcomes fit together as a constellation of symptoms which form a diagnosable fetal exposure syndrome. Based on experience with fetal valproate syndrome/fetal valproate spectrum disorder (ICD 11 LD2F.03) current international guidelines suggest that clinical diagnosis for fetal exposure syndromes should be multidisciplinary in nature and include health, dysmorphology, speech therapy, physiotherapy, neuropsychological/ neurodevelopmental assessments and genetic investigations. Health service utilisation over the course of development can be high due to wide ranging physical and neurodevelopmental symptoms and key recommendations are made regarding multidisciplinary clinical care across the lifespan. The need to collaborate with educational and social services to reduce secondary impacts (e.g., poorer mental health) and to maximise educational and future occupational achievements is outlined. Finally, the role of an optimised healthcare service for children exposed to medications within the pharmacovigilance framework for antiseizure medications is discussed.

Disclosure: Dr Bromley's institution has received consultancy fees from UCB Pharma for her participation in a women's health initiative.

EAN/MDS-ES: Towards a biological classification of Parkinson's disease

SYMP02_1 | Genetic status defining Parkinson's disease

C. Klein
University of Lübeck, Germany

SYMP02_2 | Synuclein status defining Parkinson's disease

L. Parkkinen
Nuffield Department of Clinical Neurosciences, Oxford Parkinson's Disease Centre, University of Oxford, UK

Introduction: Technological advances have made it possible to define the presence of Parkinson's disease (PD) well before the onset of symptoms, and thus, we are moving away from the clinical to molecular diagnosis, similarly to Alzheimer's disease. This molecular definition of PD depends on alpha-synuclein (aSyn) seed amplification assay (SAA) that detects pathological aSyn in the CSF or other biosamples of PD and at risk-patients.

Methods: We examined the diagnostic value of the SAA quantitative parameters and whether they could be used to stratify between different synucleinopathies, monitor disease progression and predict disease conversion in patients with idiopathic REM sleep behaviour disorder (iRBD).

Results: aSyn SAA was performed in CSF samples from 74 PD, 24 multiple system atrophy (MSA) and 45 iRBD patients alongside 55 healthy controls. aSyn SAA showed 89% sensitivity and 96% specificity for PD; there was no correlation between SAA quantitative parameters and severity of clinical symptoms (e.g. UPDRS) but the different PD phenotype clusters differed in their SAA positivity. The sensitivity in MSA was 75%, and some SAA quantitative parameters were able to stratify between PD and MSA patients. Finally, we were able to detect CSF aSyn aggregation in 64% of RBD patients at baseline before they converted to synucleinopathy.

Conclusions: Our results show that aSyn SAA classifies people with PD with high sensitivity and specificity. It also provides information about molecular heterogeneity by stratifying between PD and MSA and different phenotypic clusters of PD. Importantly, aSyn SAA detects prodromal iRBD participants before diagnosis.

Disclosure: Nothing to disclose.

SYMP02_3 | Neurodegeneration and clinical status defining Parkinson's disease

J. Corvol
Sorbonne University, Pitié-Salpêtrière Hospital, Paris Brain Institute, Paris, France

Parkinson's disease is characterized by the presence of cardinal motor symptoms - akinesia, rigidity and rest tremor - related to the degeneration of dopaminergic neurons in the substantia nigra. Clinical diagnosis criteria currently rely on detecting these motor signs and excluding differential diagnosis. The denervation can be demonstrated through SPECT or PET imaging marking dopaminergic terminals. However, it is now clearly shown that denervation begins several years before the onset of motor symptoms, defining the premotor phase of the disease. In addition, the denervation also involves non-dopaminergic area responsible for non-motor symptoms, which may occur before the diagnosis during a prodromal phase in some patients. Novel imaging markers such as brain MRI neuromelanine, MIBG SPECT or FDG PET have shown good accuracy in detecting dopaminergic and non-dopaminergic denervation at the different stages of the disease. Future definitions and staging systems of Parkinson's disease must therefore incorporate both motor and non-motor features, along with dopaminergic and non-dopaminergic denervation, to comprehensively address the continuum of the disease, from its presymptomatic to its symptomatic stage.

Disclosure: J.C.C. has served in advisory boards for Alzprotect, Bayer, Biogen, Denali, Ferrer, Idorsia, iRegene, Prevail Therapeutic, Servier, Theranexus, UCB; and received grants from Sanofi and the Michael J Fox Foundation outside of this work.

SYMP02_4 | Integrative biological Parkinson's disease definitions

G. Höglinger
Ludwig-Maximilian University Hospital, Munich, Germany

EAN/EFAS: Through the looking glass: Towards autonomic markers, a raising awareness in common neurological diseases

SYMP03_1 | Autonomic dysfunction in stroke

M. Hilz
Depts. of Neurology, University of Erlangen-Nuremberg, Erlangen, Germany & Icahn School of Medicine at Mount Sinai, New York, NY, USA

Autonomic dysfunction increases the risk of stroke, e.g. in patients with diabetic autonomic neuropathy or any patient with cardiovascular autonomic dysfunction. Vice versa, stroke frequently causes autonomic nervous system dysfunction which adds to post-stroke mortality. Stroke-induced lesions of the central autonomic network cause multiple autonomic disorders, such as bladder dysfunction which is a common cause of post-stroke nursing home admission, but also post-stroke hyperglycemia, sleep disturbances, or cardiac events, including atrial fibrillation, congestive heart failure, myocardial infarctions, Takotsubo cardiomyopathy, and sudden death. Particularly insular lesions but also frontal, temporal, or parietal lobe lesions can be associated with autonomic dysregulation or increased mortality rates. Stroke severity seems to correlate with the degree of cardiovascular autonomic dysregulation. Increasing stroke severity is associated with a decrease in the overall autonomic cardiovascular modulation, particularly in cardiovagal modulation and baroreflex sensitivity, and results in a relative predominance of sympathetic activity. These changes worsen the prognosis of stroke patients and increase their risk of mortality. Psychological stress associated with the onset of stroke and the subsequent emergency situation very likely contributes to and worsens autonomic dysregulation and must be mitigated. Early initiation of cardiovascular and antihypertensive treatment might promote recovery of post-stroke cardiovascular autonomic dysregulation.

Disclosure: I received travel support and lecturing honoraria from Amicus Therapeutics and Sanofi and grant support from Sanofi. None of the support is related to my presentation.

SYMP03_2 | Autonomic manifestations of epilepsy

R. Thijs
Stichting Epilepsie Instellingen Nederland, Heemstede, The Netherlands

Autonomic manifestations of seizures are frequent; they are generally more prominent in focal seizures that originate from the temporal lobe and are particularly pronounced in focal- to- bilateral and generalized tonic–clonic seizures (TCSs). Ictal autonomic manifestations tend to be underreported because they might not be recognized as seizure- related, or might be too subtle or not remembered. Autonomic seizure manifestations can provide clues to the localization or lateralization of the ictal onset zone but should always be considered in the context of a complete diagnostic epilepsy evaluation. Ictal asystole is the most frequent clinically relevant seizure- related arrhythmia. The key clinical expressions include flaccid falls with injuries and other signs of syncope (for example, intense pallor, jerks, stiffening and gasping) during the course of a temporal lobe seizure. SUDEP contrasts with self- limiting autonomic features because it typically occurs in the aftermath of a TCS, whereas ictal apnoea and ictal asystole are associated with focal — mostly temporal lobe — seizures. SUDEP has a spectrum of heterogeneous causes but is predominantly attributable to TCS- triggered postictal apnoea–asystole.

Disclosure: RDT's s salary is supported by the Christelijke Vereniging voor de Verpleging van Lijders aan Epilepsie. RDT has received personal compensation for serving on the Advisory Boards or Speaker's Bureau for Xenon, Theravance, Novartis, Eisai, Angelini Pharma, LivAssured and UCB Pharma.

SYMP03_3 | Cardiovascular autonomic dysfunction in sleep disorders

G. Calandra-Buonaura
University of Bologna, Bologna, Italy

The autonomic nervous system and sleep are closely related. Neuronal populations involved in the transition from wakefulness to sleep and the subsequent development of sleep stages are located near central areas involved in autonomic functions, including cardiovascular autonomic control, and are mutually interconnected with them. Thus, it is not surprising that sleep dysfunction can result in altered cardiovascular autonomic control and that, similarly, several general medical and neurological disorders can cause both cardiovascular autonomic dysfunction and sleep disorders. The presentation describes the clinical features, presumed pathogenetic mechanisms, and diagnostic and prognostic implications of the impairment of cardiovascular autonomic control associated with sleep disorders such as primary insomnia, restless legs syndrome, obstructive sleep apnea, and REM sleep behavior disorder. Most of the available data suggest that the association between sleep disorders and altered autonomic control of the cardiovascular system needs to be systematically evaluated for its important clinical implications. Understanding the mechanism of this association may also provide insights into the interaction between the autonomic nervous system and sleep.

Disclosure: Nothing to disclose.

SYMP03_4 | Autonomic dysfunction in movement disorders

A. Fanciulli
Innsbruck Medical University Department of Neurology, Innsbruck, Austria

Dysautonomia is a frequent non-motor feature in both frequent and rare movement disorders and its occurrence has diagnostic,

therapeutic and prognostic implications. While autonomic referral centers are not widely available, there are several bedside screenings and first line therapeutic measures, which can be applied to improve the diagnostic accuracy and functional outcome of individuals living with movement disorders. This lecture will provide an overview on such measures for the most important autonomic domains and discuss the clinical red flags, when second line interventions and shared care approaches with allied specialties (i.e., urologists, gastroenterologists, ENT doctors) and healthcare professionals are recommended.

Disclosure: Nothing to disclose.

Stroke in women: Specific risk factors and optimal management

SYMP04_1 | Pathophysiological mechanisms of sex differences in stroke

A. Fonseca
Department of Neurology, Hospital de Santa Maria, Faculdade de Medicina, Universidade de Lisboa, Portugal

Differences in physiology between females and males underlie some of the differences between the sexes seen in stroke. Women go through specific development stages throughout their lives, which are associated with physiological and hormonal changes that can, at specific time points, influence the risk of cerebrovascular diseases. These life stages included the reproductive years, including pregnancy, and adulthood after menopause. Experimental studies conducted in recent years have also demonstrated intrinsic sex differences in animal models that may have relevance to our understanding of stroke in clinical populations.

Disclosure: Nothing to disclose.

SYMP04_2 | Stroke in pregnancy and puerperium

A. Arsovska
University Clinic of Neurology, University "Ss. Cyril and Methodius"- Faculty of Medicine, Skopje, North Macedonia

Introduction Most strokes in the general population are ischaemic (80–85%), but in pregnancy, ischaemia, haemorrhage and venous thrombosis have a similar contribution to aetiology. Pregnancy-associated stroke occurs in 18% of strokes in women younger than 35 years. The stroke incidence is 25–34 cases / 100,000 deliveries (which is three times the incidence in nonpregnant female individuals aged 15–44 years). Methods The risk is increased 9 times at the time of delivery and 3 times in the early postpartum period. During pregnancy, the female body undergoes significant physiological changes that may predispose women to thromboembolism and cardiovascular events. Associated risk factors are hematological disorders, preeclampsia and eclampsia, gestational diabetes, post-partum period, race, age older than 35 years and other. In pregnancy, imaging should be done promptly to allow early treatment and optimise outcomes. MRI is the preferred first-line imaging modality in pregnancy because it does not expose the pregnant woman to radiation. Results Regarding management of stroke during pregnancy and postpartum, the European Stroke Organization has recently published guidelines on stroke in women. Pregnant and postpartum women with acute disabling ischaemic stroke (occurring at least 10 days after delivery), who otherwise meet eligibility criteria, can be treated with intravenous thrombolysis or mechanical thrombectomy after appropriately assessing the benefit/risk profile on an individual basis. Conclusion Team approach is essential, planning is important, and management of these cases should be individualized.

Disclosure: Nothing to disclose.

SYMP04_3 | Migraine and risk of stroke in women

D. Mitsikostas
Aeginition Hospital, Athens, Greece

SYMP04_4 | Hormonal therapy and risk of stroke

H. Budinčević
Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia

Hormonal therapy is supplementing women with hormones lost during the menopausal transition to relieve symptoms associated with menopause. Conventional hormonal therapy includes estrogen alone or with a progesterone component to mimic hormones created by the human ovary. Women appear to be protected from stroke before menopause, which might be related to ovarian hormones (endogenous estrogen). The stroke risk factors specifically associated with women include oral contraceptive use and the use of exogenous hormonal therapy for menopausal symptoms. Recent European Stroke Organisation guidelines do not recommend the usage of hormonal therapy in postmenopausal women to reduce stroke risk. However, prior hormonal therapy has no impact on mortality in postmenopausal women with acute stroke. Similarly, American Heart Association guidelines recommend avoiding the use of oral contraceptive agents with exogenous estrogen in women with migraine with aura and prior ischemic stroke. Timing and route of administration may play an essential role in reducing stroke risk. The time of initiation of hormonal therapy, with initiation at <60 years of age or within ten years of menopause, appears to be associated with reduced cardiovascular risk (which includes stroke). Iatrogenically induced menopause during the premenopausal period is associated with higher cardiovascular risk, too.

Disclosure: Nothing to disclose.

Therapeutic advances in neuromuscular disorders

SYMP05_1 | From gene to RNA therapies: New treatment horizons for genetic neuromuscular disorders

S. Sacconi
CHU NICE PASTEUR 2, Nice, France

SYMP05_2 | Novel treatments in hereditary neuropathies

S. Peric
University of Belgrade – Faculty of Medicine, University Clinical Center of Serbia – Neurology Clinic, Belgrade, Serbia

Peripheral neuropathy may be the primary feature of inherited disease, or a part of the complex diseases. Only several drugs have been tested in humans for hereditary diseases where neuropathy is a primary feature. Phase 3 study was conducted to evaluate a combination of baclofen, naltrexone, and sorbitol in CMT1A. Clinical improvements were observed, but crystal formation in formulation caused a significant discontinuation. Aldose reductase inhibitor is temporarily investigated in patients with SORD neuropathy. Hereditary transthyretin amyloidosis (hATTR) is a disease where neuropathy is a part of the complex phenotype. Safety and efficacy of tafamidis, TTR stabilizer, in early-stage polyneuropathy have been demonstrated. Inotersen is an antisense oligonucleotide that proved its efficacy in a phase 3 trial conducted on patients hATTR polyneuropathy. Eplontersen is an antisense oligonucleotide conjugated to N-acetylgalactosamine which improves its distribution. Patisiran is an intravenous small interfering RNA (siRNA). Positive effects of the drug were registered in a phase 3 trial in adult patients with a hATTR polyneuropathy. Vutrisiran is a subcutaneous siRNA that was more efficacious than patisiran in a phase 3 open-label study. Another siRNA, givosiran, that silences the expression of the gene ALAS1, has been approved for the treatment of acute hepatic porphyrias. Givosiran treatment resulted in sustained reduction of annualized attack rate. Two approved enzyme replacement therapies for Fabry disease have shown favourable effects on peripheral neuropathy. Idebenone has been approved for treatment of Leber neuropathy. In conclusion, hereditary neuropathies have recently entered a therapeutic era.

Disclosure: Nothing to disclose related to this presentation.

SYMP05_3 | The landscape of new treatments in hereditary myopathies

A. Toscano
AOU G. Martino, Messina, Italy

SYMP05_4 | Advances of treatments in myasthenia gravis

K. Claeys[1,2]
[1]*Department of Neurology, University Hospitals Leuven, Leuven, Belgium;* [2]*Laboratory for Muscle Diseases and Neuropathies, Department of Neurosciences, KU Leuven, and Leuven Brain Institute (LBI), Leuven, Belgium*

Myasthenia gravis (MG) is a chronic autoimmune disease of the postsynaptic neuromuscular junction characterized by fluctuating muscle weakness and fatigability. Despite adequate dosing and longer duration of treatment, standard immunomodulatory treatment often does not achieve sufficient improvement of symptoms, leading to considerable morbidity in MG patients. Furthermore, conventional immunotherapy often is associated with severe and invalidating side effects and intolerance. This is a challenge for patients and treating neurologists, and clearly illustrates the need for new therapeutic possibilities. Newer immunotherapies more specifically address distinct targets of the main immunological pathways in MG. They include terminal complement C5 inhibitors, monoclonal antibodies against fragment crystallizable neonatal receptor (FcRn), B-cell depleting agents (anti-CD19 and 20, and B cell activating factor (BAFF) inhibitors), T-cells and cytokine-based therapies (chimeric antigen receptor T-cell (CART-T) therapy), and proteosome inhibitors. The new agents may have advantages over conventional immunosuppressive therapies for MG in terms of more favorable side effect profile, faster onset of action and the potential for a sustained and long-term remission. In my presentation, I will give an overview of the novel therapeutic agents that are already available or will become available in the following years. Also, the challenges associated with the new therapeutic options will be discussed.

Disclosure: KGC received speaker and/or advisory board honoraria from Alexion, Alnylam, Amicus Therapeutics, argenX, Biogen, Ipsen, Janssen Pharmaceuticals, Lupin, Pfizer, Roche, Sanofi-Genzyme, UCB. KGC is Chairholder of the Emil von Behring Chair for Neuromuscular and Neurodegenerative Disorders by CSL Behring.

EAN/ECTRIMS/EPNS: Paediatric- and late-onset multiple sclerosis: The extremes of the disease

SYMP06_1 | Clinical and neuroimaging features of paediatric multiple sclerosis

M. Rocca
Neuroimaging Research Unit, Division of Neuroscience, and Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy; Vita-Salute San Raffaele University, Milan, Italy

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating, and neurodegenerative disease of the central nervous system (CNS), mostly affecting young adults. Approximately 3% to 10% of MS patients experience their first attack during childhood;

onset under 10 years old is probably less than 1% of all MS cases. Despite a relatively higher relapse rate and the tendency to form larger brain lesions compared to their adult counterparts, patients with paediatric-onset (PO) MS take longer to accrue similar levels of disability and to evolve to secondary progressive (SP) disease course, although they tend to reach a certain level of disability at a younger age. More than 30% of POMS patients experience cognitive impairment, with a prominent involvement of attention, memory, processing speed, expressive language, and visuomotor integration. Longitudinal clinical studies have shown that more than half of children with MS show cognitive impairment after 10 years of follow-up. Overall, these impairments may cause significant functional impact on daily life activities and may negatively influence the subject's academic achievements. Magnetic resonance imaging (MRI) plays a crucial role in the diagnosis of MS, monitoring disease progression and treatment response, both in children and adult patients with MS. Considering MRI findings, conceptually, there are many possible reasons why the MRI features (lesions, NAWM and GM damage) in children with MS may differ from that of adults: (1) the subclinical phase of the disease process is inherently brief in young patients by virtue of their young age; (2) although the majority of developmental modifications in myelin biochemistry take place during the first 24 months of life, full myelin maturation proceeds in a caudal-rostral pattern until early adulthood, and thus, myelin maturity may influence the regional proclivity for MS related damage, particularly in the very young MS patients; and (3) children may differ from adults in their innate capacity for myelin repair, leading to fundamental differences in the MRI aspects. All of these mechanisms may clearly contribute to explain differences of clinical and cognitive outcomes between paediatric and adult patients. In line with this, multiple studies have shown that MRI features in POMS patients are different from those of adults. Both POMS and adult-onset (AO) MS patients experience partial lesion recovery; however, the extent of lesional recovery is greater in POMS patients. On the other hand, maturation of the frontal lobe white matter during the second decade of life has been suggested as a possible mechanism which confers a sort of protection from MS-related damage in paediatric patients. Maturation effects might also influence a different functional reorganization in AOMS vs POMS, since the long-range connections between the posterior cingulate cortex and the anterior prefrontal cortex have been shown to mature with age and to be associated with the development of cognitive abilities. Juvenile MS patients have also an impaired age-expected brain growth, which results in abnormally small brain volumes. Additionally, a progressive loss of volume, consistent with brain atrophy, was detected in adolescent patients, likely to indicate a failure of the anticipated resiliency of the maturing CNS to the brain injury.

Disclosure: Nothing to disclose.

SYMP06_2 | Clinical and neuroimaging features of late-onset multiple sclerosis

C. Louapre
Hôpital Pitié Salpêtrière, Paris, France

SYMP06_3 | Escalation and de-escalation of treatments in pediatric multiple sclerosis

L. Kappos
Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), Basel, Switzerland

With the increasing number of available approved and off-label treatments and the increasing experience with these treatments in pediatric MS populations the questions around their differential indication become more relevant. In addition to the known considerations in adult-onset MS, which most of us would consider as roughly applicable to pediatric MS, decisions in pediatric MS need to be based on the consideration of several questions more relevant or even specific to pediatric populations. On the side of efficacy, the more prominent role of acute inflammation, the part of MS pathogenesis best addressed by currently available treatments invites the use of the most effective treatments and not to escalate. On the side of adverse events, we need to address the concern about possible adverse impact on the immature / maturing immune system. Generally accepted and evidence-based criteria for escalation and de-escalation are not available yet. After a short review about comparable efficacy of DMTs in pediatric MS emerging – more "eminence based" – algorithms will be discussed as well as paths towards generating the necessary evidence with pragmatic trials based on well curated high quality pediatric MS cohorts.

Disclosure: No disclosure.

SYMP06_4 | Escalation and de-escalation of treatments in late-onset multiple sclerosis

F. Piehl
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Relapsing-remitting multiple sclerosis (RRMS), an inflammatory and neurodegenerative disease of the central nervous system, is usually diagnosed in early mid-life, but presentation at older ages is not uncommon. Large natural cohort studies demonstrate that while inflammatory disease manifestations with MS relapses decrease

with ageing, the risk of progressive worsening of disability instead increases. As the benefit of existing disease-modulatory therapies (DMTs) mainly concerns their capacity to suppress risk of MS relapse, the relative benefit may be different at higher ages. In fact, sub-group analyses from randomized controlled trials (RCTs) in RRMS generally indicate a reduced relative benefit regarding reducing risk of relapse and disability accrual in people aged above 40 years of age. Furthermore, there is only scarce information on if also safety aspects are impacted by age, especially since RCTs apply age limits and restrictions on comorbidities. However, the fact that comorbidities, including susceptibility to infections, increases at older ages may translate into greater treatment risks compared with younger individuals, at least regarding DMTs requiring continuous administration over extended periods of time. This also implies that treatment de-escalation or stopping should be considered in older individuals with stable disease, in particular if emerging comorbidities may impact the benefit-risk balance negatively. Until recently, the risk of disease reactivation upon stopping a DMT has been addressed only by observational studies, but recently a first RCT was completed. The evidence base for treatment decisions in people with late-onset MS will be discussed in this presentation.

Disclosure: FP has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

Tuesday, July 02 2024

Secondary prevention of cognitive impairment and dementia: Practical interventions to foster the European Brain Health Strategy

SYMP07_1 | Lifestyle and vascular multi-domain interventions: FINGERS in the era of monoclonal antibodies

M. Kivipelto
Karolinska Institutet, Solna, Sweden

SYMP07_2 | Multi-domain interventions in brain health services

G. Frisoni
Centre de la mémoire, Geneva University and University Hospitals, Geneva, Switzerland

The concepts of Brain Health, preventive neurology, and secondary prevention of neurological disorders are lately attracting great interest. However, a mismatch is evident in the literature and clinical practice, with sparse and mostly weakly effective prevention programs. A protocol for non-lifestyle non-vascular preventive interventions will be presented that might be integrated in Brain Health Services for dementia prevention. Its conceptual model will be that of the FINGER trial, which demonstrated a significant clinical impact in older persons at high vascular risk thanks to the additive effect of a number of small-impact individual interventions. The non-lifestyle non-vascular protocol will be a multi-domain intervention that will not require lifestyle changes ("biological interventions"), i.e. transcranial electrical stimulation, nutritional supplements with synaptogenetic and ketogenic efficacy, gamma sensory stimulation, and small molecules with anti-amyloid or anti-tau effects. The scenarios will be discussed of the positioning of biological multi-domain interventions in the era of anti-amyloid MABs.

Disclosure: Nothing to disclose.

SYMP07_3 | Pharmacological interventions

S. Tomic
University Hospital Center Osijek, Croatia

Secondary prevention in, at-risk persons for dementia, is among priority task of health care community due to deleterious consequence of dementia. Trials with antihypertensive drugs showed controversial results. Syst-Eur trial showed reduced risk for dementia, while SPRINT MIND study, besides its influence on overall morbidity and mortality, did not show positive effect on prevention of dementia. Same was with ramipril study or study with discontinuation of antihypertensive drugs. In the A4 study, solanezumab, which targets monomeric amyloid, did not manage to slow cognitive decline. Studies with BACE-1 inhibitor drug atabecestat was prematurely finished due to hepatic-related side effects while studies with umibecestat were stopped following an interim analysis showing worsening cognitive function with umibecestat treatment. SKYLINE study with gantenerumab was terminated following results of a pre-planned analysis of the safety and efficacy. Nonsteroid anti-inflammatory drugs (naproxen and aspirin) did not show improvement of cognition with severe side effects like major hemorrhage and all-cause mortality. Trials with hormone treatment (testosterone, estrogens or estradiol) fail to improve cognitive decline also. Hypoglicemic drugs pioglitazone and linagliptin fail to delay the onset of mild cognitive impairment or to influence on an incident accelerated cognitive decline. There was also no effect of a casein-derived angiotensin-converting enzyme inhibitory peptide (Met-Lys-Pro) on cognitive function. Still ongoing many trails that evaluate gene therapies targeting APOE4, APOE2, and NGF in addition to beta-amyloid and tau, anti-hypertensive treatment (IMPACTS-MIND and IPAT trial), semaglutid, SGLT2 inhibitors, DPP-4 inhibitors, metformin, intranasal insulin, lecanemab, donanemab, atorvastatin and lithium carbonate.

Disclosure: Svetlana Tomic has been sponsored from AbbVie and Medis Adria and received honoraria from AbbVie, Stada, Medis Adria and Pliva Teva.

EAN/ESRS: Lights off, brain still on: Sleep as a pillar of brain health

SYMP08_1 | Protein misfolding and aggregation in neurodegenerative disease: From why to how

T. Outeiro
University Medical Center Goettingen, Germany

The maintenance of the complex three-dimensional structure of all proteins is vital for their function. From the instant proteins are produced, they start facing tremendous challenges due to the highly crowded environment of the cellular milieu. Cells evolved sophisticated quality control systems that maintain protein homeostasis, and these include the protein folding and protein degradation systems. Oftentimes, as a consequence of environmental stress, genetic mutation, and/or infection, the folded structure of a protein gets altered rendering them sticky. In some instances, proteins escape the quality control systems, fall out of solution, and form protein aggregates which are pathological hallmarks in many diseases, known as protein aggregation diseases. When misfolded proteins accumulate, cells face serious problems, which may result in the activation of cell death pathways. This suicidal option is highly regulated and is, in many instances, associated with disease states, such as those found in cancer or neurodegenerative disorders, such as the prion diseases, Alzheimer's disease, Parkinson's disease, or Huntington's disease. The precise molecular mechanisms involved in protein folding and misfolding are still elusive, but it is highly likely that understanding why proteins misfold, and how we can interfere with their misfolding, and aggregation may lead to the identification of novel therapeutic targets in many of these disorders.
Disclosure: Nothing to disclose.

SYMP08_2 | How sleep maintains and improves brain health

A. Stefani
Medical University Innsbruck, Department of Neurology, Austria

Current data supporting a key role of sleep in maintaining and improving brain health will be presented and discussed.
The first talk will focus on mechanisms underlying proteins aggregation and amyloid formation in neurodegenerative diseases. Basic science studies showing a relationship between sleep and amyloid formation will be presented and discussed.
The second talk will provide the link between basic and clinical research, underlying how sleep can be a biomarker of brain health. Sleep is involved in regulation of processes like inflammation and brain waste clearance, which are fundamental in preserving brain health, and play a crucial role in the balance between healthy aging and development of neurodegeneration.
The third talk will highlight the bidirectional relationship between sleep and Alzheimer's disease. Potential mechanisms underlying the relationship between sleep changes and the development of Alzheimer's disease will be discussed. The last part of the talk will focus on future directions, e.g. novel methods to detect early sleep changes related to Alzheimer's disease, and the potential role of sleep improvement in Alzheimer's disease prevention and management.
The fourth talk will focus on the link between sleep and alpha-synucleinopathies. It is well recognized that isolated REM sleep behavior disorder is an early alpha-synucleinopathy, and more recently it has been hypothesized that isolated REM sleep without atonia may represent even an earlier stage of alpha-synucleinopathies. Current knowledge on this topic will be presented, as well as different hypothesis on spreading of alpha-synuclein pathology and their potential relation with different outcomes.
Disclosure: Nothing to disclose.

SYMP08_3 | Sleep changes and Alzheimer's disease: What comes first?

C. Liguori
2nd University of Rome Tor Vergata, Rome, Italy

SYMP08_4 | Detection of prodromal synucleinopathy through sleep

F. Dijkstra
Antwerp University Hospital, Belgium

This talk will focus on the link between sleep and alpha-synucleinopathies. It is well recognized that isolated REM sleep behavior disorder is an early alpha-synucleinopathy, and more recently it has been hypothesized that isolated REM sleep without atonia (the neurophysiological hallmark of REM sleep behavior disorder, in the absence of dream enactment behaviors) may represent even an earlier stage of alpha-synucleinopathies. Current knowledge on this topic will be presented, as well as different hypothesis on spreading of alpha-synuclein pathology and their potential relation with different outcomes (e.g. Parkinson's disease, Parkinson's dementia, dementia with Lewy bodies, or multiple system atrophy). The last part of the talk will focus on future directions, in particular addressing the role of isolated REM sleep behavior disorder and isolated REM sleep without atonia as early stages of alpha-synucleinopathies in the light of upcoming clinical trials of neuroprotection and neuromodulation. Related to this, novel methods to identify isolated REM sleep behavior disorder and isolated REM sleep without atonia, including wearables and nearables, will be discussed as potential screening or early diagnosis methods. In summary, this symposium on the basis of basic, translational and clinical neuroscience will position sleep as a window into brain health, and as an essential brain health pillar.
Disclosure: Nothing to disclose.

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ABSTRACT

Focused Workshops

Saturday, June 29 2024

Non-invasive brain stimulation: Current state of the art

FW01_1 | Which techniques are available as diagnostic or therapeutic interventions?

J. Lefaucheur
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Techniques of non-invasive brain stimulation mainly include transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). While the first technique includes diagnostic and therapeutic aspects, the second has purely therapeutic use. Most TMS measurements rely on stimulation of the motor cortex and recording of motor evoked potentials to study the pyramidal tract or radicular lesions. Advanced techniques, such as the triple stimulation technique, make it possible to detect the involvement of upper motor neurons, or, like TMS combined with an MRI-guided navigation system, make it possible to perform functional mapping of the motor cortex, for example during preoperative evaluation of brain tumor surgery. TMS can also be combined with electroencephalography to study cortical connectivity. Finally, various protocols based on single-pulse or paired-pulse TMS techniques can be applied to study various pathways or neurotransmitter systems involved in the modulation of cortical excitability under pathological conditions. From a therapeutic point of view, repetitive trains of TMS (rTMS) pulses applied during repeated daily sessions can provide clinical benefit in a number of neurological or psychiatric disorders. Various rTMS paradigms have demonstrated the ability to improve patients suffering from chronic pain or major depressive disorder, for example, with stimulation protocols delivered to various cortical targets (primary motor cortex or dorsolateral prefrontal cortex) with various parameters of frequency, pattern or duration of stimulation. Although it provides an entirely different type of stimulation (much lower current intensity delivered to the brain but of much longer duration and larger diffusion), tDCS has also shown evidence of being able to modulate clinical symptoms in various domains.
Disclosure: Nothing to disclose.

FW01_2 | Targeting deep brain structures for neurological disorders

F. Hummel
Swiss Federal Institute of Technology Lausanne (EPFL), Neuro-X Institute, Geneva, Switzerland

Deep brain structures like the basal ganglia, the thalamus or the hippocampus are core brain areas involved in the pathophysiology of neurological and psychiatric disorders, such as dementia, Parkinson's disease (PD), anxiety disorders, stroke or traumatic brain injury (TBI) as well as for transdiagnostic symptoms such as memory deficits, apathy or fatigue appearing in multiple neurological and psychiatric disorders despite the fact of their different underlying pathophysiology. Therefore, these brain areas are important and promising targets for interventional treatment strategies based on neuromodulation. However, due to their location deep in the brain they were so far only accessible by invasive deep brain stimulation (DBS). Novel non-invasive deep brain stimulation methods have the large potential to target deep brain structures with sufficient focal specificity and show particular promise for non-invasive neuromodulation-based treatment strategies for neuropsychiatric disorders in which deep brain structures play critical roles in the pathophysiology or in mediating recovery. An introduction in this novel field will be provided based on first human applications and the potential of them critically discussed.
Disclosure: Nothing to disclose.

FW01_3 | Treatment of cognitive impairment

I. Rektorova
Mararyk University, Brno Teaching Hospital Svata Anna, Brno, Czechia

EAN/MDS-ES: Tremor syndromes: From pathophysiology to diagnosis and treatment

FW02_1 | Essential tremor

M. Bologna
Department of Human Neurosciences, Sapienza University of Rome, Italy and Neuromed Institute IRCCS, Pozzilli (IS), Italy

Essential tremor (ET) is one of the most common syndromes in movement disorders. This presentation will initially discuss the pathophysiological mechanisms of tremor in patients with ET, with particular reference to the role of the cerebellum and interconnected brain areas as evidenced by neurophysiological and neuroimaging studies. The most relevant aspects concerning the diagnosis of essential tremor will then be discussed, with particular reference to areas overlapping with other pathological conditions, that is, parkinsonism, dystonia, and ataxia. In this regard, the significance of the ET plus concept will be discussed. In the final part of the presentation, the main therapeutic approaches in the field of ET will be mentioned, including the use of innovative medications, surgical options, that is, deep brain stimulation (DBS), Magnetic resonance-guided focused ultrasound (MRgFUS), as well as possible innovative interventions based on non-invasive brain stimulation techniques.
Disclosure: Nothing to disclose.

FW02_2 | Dystonic tremor

P. Schwingenschuh
Department of Neurology, Medical University of Graz, Graz, Austria

Dystonic tremor is defined as a tremor syndrome in which dystonia and tremor are the main neurological signs. The overall prevalence of tremor in dystonia is 53% and two subtypes of tremor are distinguished. Patients with dystonic tremor have a tremor in the dystonic body part, such as tremulous cervical dystonia, while patients with tremor associated with dystonia have dystonia and tremor elsewhere, such as upper limb tremor in cervical dystonia. Dystonic tremors are clinically characterized by coarse, jerky, irregular, directional, asymmetrical tremors, sometimes with sensory tricks, a null point, and overflow. A growing body of evidence suggests that the two subtypes of dystonic tremor also differ pathophysiologically. Dystonic tremor shares some mechanisms with nontremulous dystonia, while tremor associated with dystonia shows overlaps with essential tremor, which might imply different therapeutic strategies for the two subtypes of dystonic tremor.
Disclosure: Nothing to disclose.

FW02_3 | Parkinsonian tremor

R. Helmich
Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Neurology Department, Centre of Expertise for Parkinson & Movement Disorders, Nijmegen, The Netherlands

Parkinson's disease is a common neurodegenerative disorder characterized by bradykinesia, tremor, and rigidity. Parkinsonian tremor has unique clinical characteristics, as compared to other motor symptoms: it occurs early in the disease and may disappear with disease progression, in some patients it does not respond to even high doses of levodopa, it worsens considerably during stress, and tremor-dominant PD has been associated with a milder clinical course. The pathophysiology of parkinsonian tremor has been associated with abnormal activity in both the basal ganglia and the cerebello-thalamo-cortical circuit. According to the "dimmer-switch model", which is based on neuroimaging (fMRI) data, the basal ganglia trigger tremor (analogous to a light switch), while the cerebello-thalamo-cortical circuit amplifies the tremor (analogous to a light dimmer). In this lecture, I will discuss new research findings that may explain why parkinsonian tremor reduces over time, why it waxes and wanes spontaneously, why it responds variably to dopaminergic medication, and why different types of tremor (e.g. postural tremor and rest tremor) respond differently to treatment. I will also discuss, with videos, how to recognize parkinsonian tremor and how to treat it.
Disclosure: Nothing to disclose.

EAN/EFIC: Brain neurostimulation techniques to relieve pain

FW03_1 | How to treat pharmacoresistant pain. When should I recommend neuromodulation?

A. Truini
Department of Human Neuroscience, University of Rome "La Sapienza", Roma, Italy

FW03_2 | rTMS and tDCS for treating neuropathic pain

S. Jääskeläinen
Division for Medical Imaging, Turku University Hospital and University of Turku, Finland

Guidelines on therapeutic use of noninvasive brain stimulation (NIBS) with repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) support their efficacy for chronic pain. There is level A (definite efficacy) recommendation for analgesic effect of high frequency (HF) rTMS at primary motor cortex (M1) contralateral to neuropathic pain distribution, and level B (probable efficacy) for HF-rTMS at left M1 or dorsolateral prefrontal cortex for improving quality of life or pain in fibromyalgia

(FM). tDCS with anodal stimulation of M1 contralateral to pain has been suggested to be probably effective (level B) for neuropathic pain with different aetiologies, and FM. The beneficial effects of NIBS techniques arise from either excitation (HF-rTMS, iTBS, anodal tDCS) or inhibition (LF-rTMS, cTBS, cathodal tDCS) of activity within targeted neural networks leading to neuroplastic alterations that outlast stimulation and accumulate with repeated sessions. NIBS induces the release of endogenous neurotransmitters, for example, dopamine and opioids, important in the analgesic actions in structures processing and modulating pain. The parietal opercular cortex ("S2"), and M1-S1 area near midline represent promising novel options for the treatment of neuropathic and post stroke pain. Multisite stimulation protocols illustrate a practical way to enhance treatment efficacy in pain patients with comorbid disorders (e.g. depression, anxiety). Clinically useful maintenance protocols include rTMS with decreasing, individually adjusted session frequency or tDCS treatment at home. Future studies should optimize therapeutic NIBS with properly controlled large trials, evaluating the best protocols for maintenance therapy, and searching novel targets to improve efficacy in clinical practice.

Disclosure: Nothing to disclose.

FW03_3 | Neuromodulation for (cluster) headache

S. Evers
University of Münster, Germany

Neuromodulation has become an additive procedure in the acute and the prophylactic treatment of cluster headache in the last decades. It started around the year 2000 when deep brain stimulation of the inferior hypothalamus was performed with initially very successful efficacy; however, the procedure is nowadays rarely performed due to the risk of the operation and probable recurrence of attacks. According to the recent EAN guideline, noninvasive vagal nerve stimulation was more effective than sham stimulation in the abortion of acute attacks in episodic but not in chronic cluster headache (difference: 27% of patients). The same procedure showed also efficacy in the prevention of cluster headache attacks as compared to standard of care. Greater occipital nerve stimulation showed some effect in the prevention of cluster headache, which however cannot be finally calculated due to poor data. Invasive neurostimulation of the sphenopalatine ganglion (SPG) showed a significant odds ratio of 2.6 for the abortion of acute attacks after 15 min. Also, prevention of cluster headache was successful by SPG in two studies. In summary, neurostimulation in cluster headache is possible both for acute (vagal nerve) and preventive (vagal nerve and SPG) in those patients not responding to drug treatment. In most patients, neurostimulation is used as add-on therapy. In migraine, neurostimulation procedures have been studied as well. In general, the treatment effects were lower than for cluster headaches. The published evidence for all neurostimulation procedures in all headache disorders studied is very low.

Disclosure: SE received honoraria for advising and for lectures from the following companies in the last three years: Abbvie; Lilly; Lundbeck; Novartis; Perfodd; Rehaler; Teva.

Precision diagnosis for rare neurological diseases

FW04_1 | Improving diagnosis rates in rare neurological disorders requires precision medicine and research: The Solve-RD project

H. Graessner
University Hospital Tübingen, Germany

FW04_2 | Ontology-based deep phenotyping: A starting point for accurate diagnosis and classification of rare neurological diseases

C. Lucano
Orphanet – INSERM US14, Paris, France

FW04_3 | European genome data sharing, enabling collaborative analysis and expert knowledge curation to diagnose and treat rare neurological diseases

S. Beltran
Centre Nacional d'Anàlisi Genòmica, Barcelona, Spain

Introduction Collaboration in rare disease (RD) research and diagnostics is essential since affected individuals, and hence experts and data relating to any specific rare disease, are sparse and patchy. While the adoption of NGS as a primary line of investigation over the last decade has proven invaluable in identifying the molecular basis of many rare diseases, leading to diagnosis in approximately 50% of individuals affected by a RD, the other half typically remain undiagnosed even after exome sequencing or genome sequencing analysis. A key objective of the H2020 Solve-RD project is to contribute to the diagnosis of thousands of patients affected by RDs across Europe, the majority of which have previously undergone exhaustive analysis of exome sequencing (ES) data, without resolution. Solve-RD relies on the expertise from 6 European Reference Networks (ERNs), including ERN-RND, and two Spanish and Italian undiagnosed disease programs. Their experts have shared pseudonymised data from unconclusive exomes and genomes and have submitted samples to conduct multi-omics experiments. Analysis and interpretation have been done in collaboration with the consortium. Methods Analysis and interpretation at this scale requires efficiency in terms of data generation, transfer, management, storage, analysis, interpretation, and communication. The Solve-RD data infrastructure relies on the European Genome Phenome Archive (EGA), the RD-Connect Genome-Phenome Analysis Platform (GPAP), the RD3 database

(powered by Molgenis), RD-Nexus (powered by Café Variome), and local and cloud computing resources. The data workflow has been organized in a two-level expert review framework, with a main Data Analysis Task Force (DATF), a Data Interpretation Tak Force (DITF) per ERN and several cross-cutting Working Groups (WGs). Results The Solve-RD consortium experts re-analysed and interpreted integrated phenotypic and genomic data from over 22,000 individuals from 12,800 families, who had previously been analysed at local and national centres of expertise without a diagnosis being reached. This resulted in a diagnostic uplift to date of 13% of these most challenging RD cases. Furthermore, 883 families underwent short-read genome sequencing (GS). Although clinical interpretation of identified variants is still ongoing, a further 4.5% of cases have already been confirmed resolved through the analysis of GS data versus that of the original ES data reanalysis. Finally, approximately 10% of the cases underwent analysis through some of the most recent omics technologies. These technologies include one or more of the following: long read GS, high coverage ES, Optical Genome Mapping, long and short read RNA-Seq, epigenetic and metabolomics. Some of these multi-omics approaches have already proved fruitful, resulting in the closure of further diagnostic odysseys. Conclusion Systematic analysis of short-read GS data, accompanied by detailed patient descriptions, and additional omics analyses can elevate the diagnostic rate in RD cases markedly, even where prior comprehensive analysis of genetic data proved inconclusive.

Disclosure: The Solve-RD project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 779257.

EAN/ISNI: Liquid biomarkers in autoimmune central nervous system diseases

FW05_1 | Serological correlations of disease progression in Multiple Sclerosis (MS)

M. Comabella

Servei de Neurologia, Centre d´Esclerosi Múltiple de Catalunya (Cemcat), Institut de Recerca Vall d´Hebron (VHIR), Hospital Universitari Vall d´Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain

In patients with relapsing multiple sclerosis (MS), the prognostic role of biomarkers to predict disease activity and/or treatment response has been thoroughly investigated. However, in patients with progressive MS, the prognostic role of biomarkers to predict future disease progression remains more elusive. This talk will summarize the current evidence existing about the role of biomarkers to predict disease progression in MS. The presentation will mainly focus on studies measuring the serum levels of neurofilament light chain, GFAP, and chitinase 3-like 1 in patients with progressive MS. Other promising biomarkers with a potential role in disease progression will also be discussed.

Disclosure: I have received compensation for consulting services and speaking honoraria from Bayer Schering Pharma, Merk Serono, Biogen-Idec, Teva Pharmaceuticals, Sanofi-Aventis, Genzyme, BMS, ROCHE, and Novartis.

FW05_2 | Humoral signatures of myelin oligodendrocyte glycoprotein antibody associated disorder (MOGAD)

J. Lünemann

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Myelin oligodendrocyte glycoprotein (MOG)-antibody (Ab)-associated disease (MOGAD) is an inflammatory demyelinating disease of the CNS. Clinical manifestations and the course of MOGAD are heterogeneous. While the detection of MOG-IgG by cell-based assays is an essential criterion in MOGAD diagnosis, biomarkers that aid in disease prognostication, treatment monitoring, and the development of new interventions are lacking. Recent studies indicate that the combined analysis of functional MOG-Ab features can potentially provide clinically useful information on disease activity and future risk for relapse. MOG-Ab specificities for epitopes other than the immunodominant proline 42 epitope is reported to be associated with relapsing disease while enhanced MOG-Ab effector functions mediated by the IgG Fc-domain and increased serum levels of canonical biomarkers for neuro-axonal damage such as neurofilament light chain track with clinically active disease. Early identification and targeted management of patients with chronic disease and higher disease severity could improve long-term clinical outcomes for patients with MOGAD.

Disclosure: JDL received speaker fees, research support, travel support, and/or served on advisory boards by the EU Framework Programme Horizon Europe (BEHIND-MS), The German Research Foundation (LU 9001-1; LU 900-4; and the Collaborative Research Centre SFB-TRR128 'Initiating/Effector versus Regulatory Mechanisms in Multiple Sclerosis – Progress towards Tackling the Disease'), Abbvie, Alexion, Argenx, Biogen, Merck, Novartis, Roche, Sanofi, Takeda.

FW05_3 | Emerging biomarkers in antibody-mediated autoimmune encephalitides (AE)

M. Spatola

IDIBAPS Research Institute, Barcelona, Spain

Targeting molecular pathways in gliomas: A promising approach

FW06_1 | Interactions between normal brain and tumor cells are leading to new treatment paradigms

W. Wick
Department of Neurooncology, Universitätsklinikum Heidelberg, Heidelberg, Germany

FW06_2 | Targeting IDH mutations: Biological rationale and clinical applications

R. Rudà
Division of Neuro-Oncology, Department of Neuroscience, University of Turin and City of Health and Science Hospital, Turin, Italy

Isocitrate dehydrogenase (IDH) 1 and 2 mutations are driver molecular alterations for glioma growth. IDH 1/2-mutant gliomas grade 2 and 3 (according to WHO Classification 2021) typically occur in a young, otherwise healthy population. In up to 80% of patients seizures, often pharmacoresistant, are the sole symptom. These tumors are slowly growing but with a high risk of malignant evolution over time and, overall, the majority is not curable. Standard of care consists of maximal safe resection, followed in grade 3 and high-risk grade 2 tumors by radiotherapy and chemotherapy with alkylating agents, while observation with MRI is reserved to young patients with grade 2 tumors after a large surgical resection. Importantly, although long-term tumor remissions can be obtained with available treatments, survivors carry a non-negligible risk of delayed treatment-induced adverse events. Vorasidenib, a brain-penetrant pan-IDH mutant inhibitor, has demonstrated in early clinical trials the ability to significantly reduce the concentration of D-2-hydroxyglutarate (2-HG), which is the product of mutant IDH enzyme and acts as an oncometabolite. Phase III INDIGO trial has shown that the inhibition of the mutant IDH neomorphic function with vorasidenib in the setting of residual or recurrent predominantly non-enhancing, chemo- and radiotherapy naive grade 2 gliomas after surgery, is able to significantly improve both imaging-based progression-free survival and time to next intervention as compared to placebo. Adverse effects were mild with only transitory elevation of liver enzymes. Trials are ongoing on novel IDH inhibitors, vaccination strategies and combinations of IDH inhibitors with other molecular compounds.
Disclosure: Bayer, Novocure, Servier, CureVac.

FW06_3 | How to best monitor molecular pathways with advanced neuroimaging

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With the implementation of molecular information to histologic findings into the WHO classification in 2016 a new era in neuro-oncology was heralded. Some of these molecular markers are diagnostic, some provide predictive and prognostic information and more exciting some markers also hold therapeutic potential. Advanced neuroimaging by magnetic resonance imaging (MRI) or positron emission tomography (PET) has the potential to visualize molecular processes in tumors longitudinally and non-invasively by displaying pathophysiological processes in tumors. Neuroimaging may not only be used to visualize pathophysiological processes but also to monitor treatment response or predict response to new therapies. Since the discovery of the IDH (isocitrate dehydrogenase) mutation in lower grade gliomas, thrilling findings and investigations have been published culminating in a positive phase III clinical study in lower grade gliomas increasing progression-free survival. Magnetic resonance spectroscopy (MRS) has been shown to have the potential to visualize the oncogenic product of an IDH mutation (namely 2-HG). During therapy with IDH inhibitors reprogramming of tumor metabolism, change in glutathione, glutamine, glutamate, lactate and also significant decreases of 2-HG have been detected by MRS. Making it a good candidate to monitor treatment response in the future. Radiomics, the extraction of a large number of features from medical images using data-characterization algorithms, also has shown to have the potential to link molecular data to imaging data. In order to gain clinical validity these exciting findings have to be validated in larger patient cohorts and imaging protocols have to be harmonized across different centers.
Disclosure: Nothing to disclose.

Sunday, June 30 2024

Advancement of neuromodulation into new areas of neurology

FW07_1 | Invasive and non-invasive sensory feedback in upper limb prostheses

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The realm of upper limb prosthetics has witnessed substantial advancements, in terms of their mechanical construction, the methods to control them and way of providing the user with sensory feedback from them. The challenge to restore sensory feedback in prosthetic hands has provided several research solutions, but virtually none has reached clinical fruition. A prosthetic hand with sensory feedback that closely imitates an intact hand and provides the user with a natural perception of touch may induce the prosthetic hand to be included in the body image and also reinforces the control of the prosthesis. The addition of sensory feedback to upper limb prostheses has been shown to improve control, increase embodiment, and reduce phantom limb pain. This talk presents a review of

non-invasive sensory feedback systems such as mechanotactile, vibrotactile, electrotactile and combinational systems which combine the modalities; multi-haptic feedback and invasive methods using both extraneural and intraneural electrodes, such as cuff electrodes and transverse intrafascicular multichannel electrodes. The presentation aims to provide a comprehensive overview of current sensory feedback techniques, their impact on the quality of life for prosthesis users, and the future direction of prosthetic sensory feedback technology. This exploration is crucial for advancing prosthetic design, offering users a closer semblance to natural limb functionality and sensation.

Disclosure: Nothing to disclose.

FW07_2 | Non-invasive stimulation of peripheral nerves using temporally interfering electrical fields

A. Williamson

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FW07_3 | Neuromodulation for chronic minimally conscious state

A. Thibaut

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EAN/EPNS: Challenges and opportunities in the management of status epilepticus across age groups

FW08_1 | A novel approach to status epilepticus in neonates

R. Cilio

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Neonatal status epilepticus differs from status epilepticus in older children and adults. Even in the context of status epilepticus, seizures in neonates are brief lasting mostly less than 2 min, even when highly recurrent. Therefore, status epilepticus it currently defined as the summed duration of seizures comprises >50% of an arbitrarily defined 1-h epoch. The recent implementation of neonatal neurocritical care including continuous video-EEG monitoring allowed for early detection of seizures in high-risk infants and accurate assessment of response to treatment. In addition, the advancements in neuroimaging, metabolic, and genetic testing have enabled the identification of a growing number of underlying causes in neonates with status epilepticus, paving the way for a targeted etiology-specific treatment, while moving away from the monolithic 'one-size-fits-all' approach. Phenobarbital is the most used ASM to treat neonatal status epilepticus. However, we should not use phenobarbital simply because it is the medication most used. Although, the most common etiologies for neonatal status epilepticus are acute symptomatic such as hypoxic-ischemic encephalopathy and stroke, for a significant minority seizures and status represent the first manifestation of epilepsy, a chronic disease. This presentation will focus on the early detection and electro-clinical characterization of neonates with status epilepticus, and etiology-specific treatment including phenobarbital for status epilepticus in the context of hypoxic-ischemic encephalopathy, sodium-channel blockers in the context of channelopathies, and levetiracetam and ketamine in neonates with congenital heart diseases.

Disclosure: Nothing to disclose.

FW08_2 | Revisiting evaluation and treatment of febrile illness-related epileptic syndrome (FIRES) and new-onset refractory status epilepticus (NORSE) in children

S. Buratti

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NORSE (new onset refractory status epilepticus) and its subset FIRES (febrile infection-related epilepsy syndrome) are rare and devastating conditions that challenge multidisciplinary care teams with diagnostic and therapeutic difficulties. Aetiologies are classified as autoimmune/inflammatory, genetic, infectious, and toxic. The diagnostic pathway is complex and in 50% of the cases, despite an extensive work up, the cause remains undetermined (cryptogenic NORSE). Clinical history, neuroimaging, continuous EEG, genetic and CSF analyses are critical to draw diagnostic hypotheses and frame the therapeutic strategies. Steroids, immunoglobulins, and immunomodulators are the mainstay of autoimmune and cryoptogenic NORSE. Novel approaches are based on timely analysis of serum and CSF cytokine levels and early cytokine-modulating therapy, mainly anakinra and tocilizumab (IL1 and IL6 receptor antagonists). International consensus recommendations based on best available evidence and expert opinion have been recently published and represent a practical framework for the clinicians. Though, lack of randomized controlled trials and scarse evidence on specific treatments represent future challenges for the scientific community. Future research developments should focus on the role of cytokines and inflammation, explore in vitro and in vivo models of NORSE, plan clinical trials, promote international biorepositories and establish studies on long-term outcomes. Despite severe sequelae and mortality (12% in children), improvement of patient management is a realistic objective to pursue. Aiming to the best outcome each patient

should be referred to a tertiary care center where structured and timely diagnostic and therapeutic pathways are implemented.
Disclosure: I have no conflicts of interest to declare.

FW08_3 | What to do when first and second-line treatment fails in adults?

C. Cornwall
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Status epilepticus (SE), the second most common neurological emergency, is a severe and potentially life-threatening complication of epilepsy and acute brain diseases with high morbidity and mortality. Refractory SE (RSE) is defined as failure to appropriate first-line treatment with benzodiazepine and failure of second-line treatment with anti-seizure medication (typically levetiracetam, valproate, or (fos-)phenytoin). Super-refractory status epilepticus (SRSE) further delineates cases where SE continues or recurs 24 h or more after the onset of anesthetic therapy, including those cases where SE recurs on the reduction or withdrawal of anesthesia. Due to increased risk of significant neuronal damage with persistent seizure activity, international guidelines emphasize early and aggressive treatment. While we have made substantial progress in understanding and treating non-refractory SE, RSE, and especially SRSE, remains a highly challenging medical condition with primarily low-evidence literature available. Diagnostic evaluation includes electroencephalography monitoring, neuroimaging, and laboratory investigations to identify possible reversible causes and guide treatment decisions. Effective management requires a multidisciplinary approach involving neurologists, and intensivists to tailor treatment strategies to individual patient needs. Continued efforts in understanding the underlying mechanisms and refining therapeutic approaches are essential to improve outcomes for patients with RSE and SRSE. Recently, there has been an increased focus on whether treatments such as ketamine, barbiturates, ketogenic diet, or hypothermia may have a beneficial effect on seizure cessation in patients with RSE and SRSE. This talk will present the available evidence on epidemiology and etiology, but also possible treatment options and prognosis in this challenging patient group.
Disclosure: C.D. Cornwall has received travel support from Jazz Pharma. There are no conflicts of interest related to this talk.

FW08_4 | End-of-life considerations in status epilepticus

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The management of super-refractory status epilepticus (SRSE) is challenging, medically and ethically. Generally speaking, patients with SRSE will either succumb to epilepsy or underlying disease and die, or they will survive with significant neurologic sequelae, or survive with good functional outcomes. However, there is a lack of robust prognostic markers that allow caregivers to predict the outcome of individual patients with a degree of certainty. Therefore, a "maximalist" approach to treatment of SRSE will necessarily often lead to patients either dying or surviving but with poor outcomes. In hindsight, treatment may appear to have been futile, exposing the patient to unnecessary burdens, and wasting scarce resources in the intensive care unit. Conversely, a "minimalist" approach may lead to patients being denied a chance to survive with meaningful recovery. A "middle of the road" approach might be ideal, but without precise prognostic markers, might just lead to just as much futility and under-treatment. Clinicians caring for SRSE patients have to navigate these challenges, knowing that some risk of unwanted outcomes is probably unavoidable. This lecture will not provide the solution to how to select which patients should be offered maximal treatment – possibly for months – and which patients ought to be allowed to die, through non-treatment decisions (NTDs) and withdrawal of life-sustaining treatment (WLST). Rather, I will try to delineate a framework for ethical considerations of end-of-life issues in SRSE, primarily using the 6-step model for ethical analysis developed by the Centre for Medical Ethics at the University of Oslo.
Disclosure: Nothing to disclose.

Anti-amyloid antibodies in Alzheimer's disease: New treatments on the horizon

FW09_1 | Current status on the development of anti-amyloid antibodies: Evidence and gaps

K. Frederiksen
Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

The amyloid cascade hypothesis has been the predominant disease model of Alzheimer´s disease and has served to provide possible drug targets for disease-modifying therapies. Research efforts have led to the development of anti-bodies targeting beta-amyloid. Therapies have demonstrated efficacy on disease progression both in terms of effects on symptoms as well as biomarkers. While evidence is mounting, there are still many unanswered questions regarding the therapies such as effects and side-effects in sub-groups, long-term effects, and understanding more detailed the mechanisms of action of drugs. These questions may be answered in future trials, but real-world evidence for example, from registries will likely also play a pivotal role.
Disclosure: Serves on an advisory board for Novo Nordisk.

FW09_2 | Clinical implementation of new disease-modifying therapies for Alzheimer's disease

L. Frölich
Zentralinstitut für Seelische Gesundheit, Geriatric Psychiatry, Mannheim, Germany

FW09_3 | Beyond amyloid – Where do we go from here?

S. Herukka
Department of Neurology, Kuopio University Hospital, Kuopio, Finland

Medical and non-medical neurostimulation in the ICU: Facts and fictions

FW10_1 | Medical and non-medical neurostimulation in coma

D. Kondziella
Copenhagen University Hospital – Rigshospitalet, Denmark

FW10_2 | Neurostimulation in refractory and super-refractory status epilepticus (SE)

L. Imbach
Swiss Epilepsy Center, Klinik Lengg, Zurich, Switzerland

Refractory status epilepticus is a neurological emergency with a high mortality rate. In particular, survivors are expected to have a poor functional clinical outcome after failure of first- and second-line treatments such as intravenous anaesthetics and combined anti-seizure medications. In this situation, neuromodulation approaches offer an alternative treatment option to resolve ongoing epileptic network dynamics. Several pilot studies and case series have shown efficacy of vagal nerve stimulation, deep brain stimulation or transcranial stimulation in super-refractory status epilepticus. This lecture provides an overview of acute neurostimulation in SE and discusses efficacy, indication, patient selection and clinical outcome. Novel approaches to optimize treatment response to neurostimulation based on personalized identification and entrainment of neural oscillations in EEG network models will also be presented.
Disclosure: Nothing to disclose.

FW10_3 | Neurostimulation in neuromuscular complications of critical illness

W. Z'Graggen
Departments of Neurology and Neurosurgery, Inselspital, University Hospital Bern, University of Bern, Bern, Switzerland

Muscle weakness is a well-known complication of critical illness. The condition was first described in 1892 by Sir William Osler as “rapid loss of flesh”. About one century later, an acquired neuromuscular dysfunction, also called “intensive care unit acquired weakness (ICUAW)” was identified as the underlying cause. This term is used for patients in whom there is clinically detected weakness without any etiology other than critical illness. Critical illness myopathy and polyneuropathy are the most common causes. ICUAW is associated with delayed recovery, prolonged hospitalization, increased mortality and morbidity. During the COVID-19 pandemic, the impact of ICUAW has become even more important and frequencies of >50% have been reported. The etiology is still unclear, but various risk factors have been identified. Beside the duration of intensive care treatment/mechanical ventilation and the severity of the acute disease, immobilization was reported as a consistent risk factor for ICUAW. This led to the hypothesis that ICUAW may be prevented by early muscle activation. The two concepts derived from this assumption are early mobilization and electrical muscle stimulation. While several smaller studies showed a positive effect of early mobilization on the incidence of ICUAW, one large, randomized trial reported a higher risk of adverse events. The effect of electric muscle stimulation on development of ICUAW was evaluated in several, mostly smaller studies using different outcome measurements. While some studies reported a beneficial effect, other trials failed to show a positive effect. Treatment duration, stimulation sites and net stimulation time are still unknown.
Disclosure: Nothing to disclose.

Cognitive reserve: Impact on intervention in neurological diseases

FW11_1 | The concepts of brain and cognitive reserve

M. Amato
University of Florence, Italy

The concepts of “brain” and “cognitive” reserve have been proposed to account for the disjunction between the degree of brain pathology and its clinical manifestations. The brain reserve model defines reserve as a physical trait: having larger brains, with more neurons and synapses, may allow brains to absorb more injury before cognitive function is affected. Brain reserve may be thought of as individual differences in the hardware of the brain. It can be conceived as a passive entity, which reflects an overt expression of impairment only after an individual's capacity falls below a critical threshold of brain damage. The cognitive reserve model posits flexibility and adaptability of cognitive/brain networks that allow the brain to actively resist the effects of age- or disease-related changes. Cognitive reserve focuses on functionality, plasticity and adaptability and may be thought of as a software that carries out the calculations in the brain, which is influenced by all aspects of life experience. Thus, the cognitive reserve model can be considered active. Given the same amount of brain reserve, some people can better cope with age- or

pathology-related brain changes than others, depending on their cognitive reserve capabilities. A plethora of studies have discussed different proxies to quantify reserve and future directions for the uniformity and reliability of these proxies are pertinent. Recently, empirical evidence pointed to the importance of studying the functional connectome as a compensatory mechanism utilized in patients with better cognitive results, which may pave the way to tailored rehabilitation strategies.

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FW11_2 | Does cognitive reserve moderate effects of therapeutic intervention? Studies in healthy and pathological aging

K. Mitterova

Applied Neuroscience Research Group, Central European Institute of Technology, Masaryk University, Brno, Czechia

Cognitive reserve is the brain's ability to compensate for the effect of accumulating senescent or pathological load to maintain cognitive functions. Understanding cognitive reserve in the context of interventions is vital for promoting cognitive health through integrating both neurodegenerative and compensatory aspects of the brain. However, these compensatory mechanisms have not received much attention in terms of their potential role as moderators with therapeutic value. Our team studied the influence of a 6-month dance intervention on cognitive and fitness aspects in seniors without dementia as moderated by different cognitive reserve proxies. The results of this work will be presented with implications of estimating the reserve using dynamic scores which better represent the actual capacity against pathological load. Recent studies have observed that cognitive reserve may manifest as altered (from optimized to hyperconnected) brain functional connectome to preserve essential cognitive functions. We will discuss how these network changes pertain to cognitive interventions and whether they can moderate the benefits of tACS stimulation on working memory in cognitively healthy seniors and elderly with mild cognitive impairment with Lewy bodies. Each of our studies utilized neuropsychological testing and fMRI before and after intervention to evaluate both behavioral and functional network changes as outcomes. Intelligence and education are known determinants of successful aging, however, the search for more dynamic markers of CR, such as (mal)adaptive network changes is pertinent for aiding the selection of the intervention candidates and evaluation of outcomes.

Disclosure: Nothing to disclose.

FW11_3 | Cognitive reserve in stroke: Enhance understanding to improve treatment

R. Umarova

Department of Neurology, University Hospital Bern, University of Bern, Bern, Switzerland

To personalize stroke treatment, we need a reliable model to predict stroke outcome and recovery trajectories for the most prevalent stroke deficits, including cognitive impairment. Lesion characteristics explain far less than half of inter-individual variability of stroke-induced symptoms. Thus, an understanding of lesion-independent factors influencing stroke outcome is urgently needed. For neurodegenerative diseases, the concept of cognitive reserve was introduced to explain the interindividual variability in manifestation of cognitive deficits in response to brain pathology. In that context, cognitive reserve (CR) is suggested to reflect the brain's ability to moderate and compensate for injury, with CR being boosted by cognitively stimulating activities across the lifespan. There is increasing evidence that the underlying concept can also be applied to stroke. In my presentation, I will report on that evidence and exemplify association between CR and both cognitive and non-cognitive stroke outcome. In addition, I will discuss future perspectives of the concept of CR in the context of stroke and particularly its potential to understand the individual recovery trajectories, improve stroke prognosis, and finally establish individualized rehabilitation approaches.

Disclosure: Nothing to disclose.

Sunday, June 30 2024

EAN/IFCN-EMEAC: Clinical neurophysiology: New developments in diagnostics and non-invasive therapy

FW14_1 | Maximising VEP validity through differentiating axonal loss and demyelination

L. Leocani

University Vita-Salute San Raffaele, Milan, Italy

Although visual evoked potentials (VEPs) are routinely used for the assessment of visual disturbances, particularly monocular within the diagnostic workup of optic neuritis, their role is being currently reduced by the use of retinal and neuroimaging techniques—for example, optical coherence tomography, magnetic resonance imaging. Nevertheless, their unique property of detecting conduction delays should not be neglected, as these are the hallmark of demyelination. Studies have shown that VEP delays may be aspecific, being encountered also in inflammatory, non-demyelinating diseases such as neuromyelitis optica spectrum disorder (NMO), retinal and macular diseases and even myopia or deliberate or unintentional poor

visual fixation of the stimulus. However, the latter conditions are not associated with severe delay, which entity should be taken into account in the differential diagnosis, together with the other clinical and neuroimaging features. Among the latter, optical coherence tomography is the ideal candidate for allowing a helpful structural and functional combination of information. Finally, VEPs allow the possibility of monitoring remyelination and recovery of conduction, which is essential in testing the efficacy of remyelination strategies.
Disclosure: Nothing to disclose.

FW14_2 | tACS for delayed progression of cognitive decline

A. Antal
Department of Neurology, University Medical Center Göttingen, Göttingen, Germany

Transcranial Alternating Current Stimulation (tACS) for delayed progression of cognitive decline Andrea Antal, Lukas Diedrich Department of Neurology, University Medical Center Göttingen, Germany Non-invasive Brain Stimulation (NiBS) techniques such as repetitive Transcranial Magnetic Stimulation (rTMS) and transcranial Electrical Stimulation (tES), including Direct Current and Alternating Current Stimulation (tDCS, tACS), allow to modulate neuronal excitability, oscillatory activity and to boost cortical functions, hereby possibly offering a therapeutic potential to slow down cognitive decline. Cognitive decline reaches medical attention for about 8%–25% of individuals aged over 65, when suffering from Mild Cognitive Impairment (MCI). Around 15% of MCI patients develop dementia within two years, supporting a medical need for early diagnosis and treatment. Recent investigations propose tACS as a potential therapeutic tool to improve network activity and cognitive functions in older individuals and those with cognitive impairments. The most frequently used stimulation frequencies are theta and gamma, including the combination of the two waveforms (i.e. theta—gamma phase—amplitude coupling). There are promising results using tACS, mainly related to the improvement of working memory or declarative memory performance, two domains that are primarily affected by cognitive decline. However, several subject-specific factors, for example, anatomical and physiological differences, age, gender, brain state before and during stimulation, and also methodological factors, such as the type of the task applied in combination with the stimulation, can confound the effects of stimulation. This talk aims to provide an overview of the commonly utilized tACS protocols, elucidating their individual merits and drawbacks.
Disclosure: Andrea Antal and Lukas Diedrich: no direct COI AA is the Vice President of the European Society of Brain Stimulation; Member-at-Large at the EMEAC – IFCN; payed consultant by NeuroConn (Ilmenau), Germany and by Electromedical Products International (Pulvinar), USA. Member of the advisory board bei PlatoScience Running projects: DFG (Viron – AN 687/9-1), EU-Horizon 2020 (PAINLESS, Nr. 101057367).

FW14_3 | Improving diagnostics by threshold tracking TMS

H. Tankisi
Aarhus University Hospital, Denmark

Paired-pulse TMS using a threshold-tracking technique measures the stimulus intensity required to obtain an MEP of or above a certain size instead of relying on the MEP amplitude as a response to a constant stimulus intensity. The first application of threshold-tracking TMS was performed for short-interval intracortical inhibition (SICI) measurements (Fisher et al., 2002). The clinical utility of threshold-tracking SICI in ALS has been shown in several studies and the method has been proposed as a potential biomarker (Vucic & Kiernan, 2013). Decreased SICI in ALS using conventional amplitude measurements was demonstrated already in 1999 (Ziemann et al., 1999). However, the advantages of threshold-tracking SICI over conventional SICI have not been investigated until recently (Tankisi et al., 2021, 2023). Beyond SICI, threshold tracking TMS has moved into short-internal intracortical facilitation, long-interval intracortical inhibition, and short and long-afferent inhibition. In this lecture, the utility of these methods in the diagnostics of various neurological disorders will be addressed. References: Fisher et al. *Exp Brain Res*. 2002;143:240.e8. Tankisi et al. *Amyotroph Lateral Scler Frontotemporal Degener*. 2023;24(1–2):139–147. Tankisi et al. *Eur J Neurol*. 2021;28(9):3030–3039. Vucic and Kiernan. *Handb Clin Neurol*. 2013;116:561–575. Ziemann et al. *Neurology*. 1997;49(5):1292–8.
Disclosure: Nothing to disclose.

Monday, July 01 2024

EAN/MDS-ES: Movement disorders in autoimmune encephalopathies

FW12_1 | General considerations on the pathophysiology of autoimmune encephalopathies

M. Titulaer
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FW12_2 | Hyperkinetic, hypokinetic and ataxic disorders in autoimmune encephalopathies

C. Colosimo
Department of Neurology, Santa Maria University Hospital, Terni, Italy

Movement disorders in autoimmune encephalopathies are a heterogeneous group of syndromes encompassing both hyperkinetic, hypokinetic, and ataxic conditions, usually characterized by acute/sub-acute onset, rapidly progressive evolution, and multifocal

localizations with several overlapping features. These movement disorders are immune-mediated, as shown by the presence of antineuronal antibodies in patients' biological samples, crucial for the diagnosis, and the potential response to immunotherapies. Clinicians should have a high index of suspicion when observing acute/subacute symptoms to achieve a prompt diagnosis and treatment. It is initially mandatory to exclude a paraneoplastic disorder. There is indeed a range of overlapping "high-risk" clinical syndromes, including but not limited to latent and overt rapidly progressive cerebellar syndrome, opsoclonus-myoclonus-ataxia syndrome, limbic encephalitis/encephalomyelitis, and stiff-person spectrum disorders. The field of movement disorders in autoimmune encephalopathies is constantly expanding with newly discovered clinical syndromes and related antibodies. Standardized diagnostic criteria and disease biomarkers are fundamental to recognize these disorders quickly, and to allow prompt treatment initiation, thus improving the long-term outcome of these conditions. Response to first and second-line immunotherapies is variable according to associated tumors and antibodies, whereas response to symptomatic treatment is usually poor. This presentation will critically reappraise the clinical features and pathophysiological mechanisms of autoimmune movement disorders, focusing on the most recent diagnostic and therapeutic strategies. The main aim is to make clinicians aware of these movement disorders and provide early diagnosing and managing these rare but potentially life-threatening conditions.

Disclosure: Nothing to disclose.

FW12_3 | Movement disorders complications of immunomodulatory therapies and checkpoint inhibitors

J. Honnorat

University Claude Bernard Lyon 1, Villeurbanne, France

Immune checkpoint inhibitors (ICI) are a class of efficient oncological treatments that enhance antitumour immunity. The use of ICI has represented a major advance in cancer treatment. By enhancing endogenous immune responses to destroy cancer cells, ICI can cause immune-related adverse events (irAEs), with possible involvement of any organ system. IrAEs are frequent, particularly those involving the skin or the endocrine system, and are usually completely reversible after temporary immunosuppression. On the opposite, neurological irAEs (n-irAEs) are relatively rare (less than 2% of all irAEs), often severe, and they carry a considerable risk of mortality and long-term disability. They can affect the peripheral nervous system (myositis, polyradiculoneuropathy, or cranial neuropathy) and, less frequently the CNS, causing encephalitis, meningitis, myelitis or abnormal movements. Although somehow reminiscent of the disorders that neurologists are familiar to deal with in their daily practice, n-irAEs are characterized by distinctive features. Several associations between the neurological phenotype and the type of ICI or the type of cancer have emerged in the last few years, and the growing administration of ICI in patients with neuroendocrine cancers has led to an increased number of reports of patients mimicking paraneoplastic neurological syndromes (PNS). Early diagnosis and initiation of immunosuppressive therapy are likely to be crucial in preventing the accumulation of neurological disability. This review aims to update current knowledge regarding the clinical presentation of n-irAEs and particularly the movement disorders. We will also discuss the essential parts of the diagnostic approach, and general recommendations for the patients' management.

Disclosure: Nothing to disclose.

EAN/ILAE: Current challenges in the management of rare and complex epilepsies, and epileptic encephalopathies

FW13_1 | Precision medicine in rare and complex epilepsies: Is it real?

A. McTague

Developmental Neurosciences, UCL Great Ormond Street Institute of Child Health, London, UK

FW13_2 | Epilepsy surgery: Towards more tailored approaches

F. Pizzo

Cerebral Rhythmology and Epilepsy Unit, La Timone, Marseille, France

FW13_3 | Palliative care in complex epilepsies: Are we ready for this?

R. Kälviäinen

University of Eastern Finland, Kuopio, Finland

Subgroup of drug-resistant complex epilepsies are progressive and management should be guided by the principles of palliative care and by relief of symptoms. End of life care (EOL) refers to patients, whose goals of care are consistent with a comfort-based approach and who are likely to die within days to weeks. Advance Care Planning (ACP) enables patients to define their preferences and expectations from therapeutic options. Advance directives (ADs) are an essential part of ACP; ADs include the presence of a living will, do-not-resuscitate order, do-not-hospitalize order, medication restriction, or feeding/hydration restriction. It is not possible to fully predict acute exacerbations, making ADs difficult to adopt and sometimes misleading. ACPs should be reviewed and discussed periodically and whenever the patient has a change in health status. Unfortunately, even the best and most updated severity-of-illness scores and risk cannot predict with certainty the fate of an individual patient. Multimodal neuro-prognostication will hopefully allow more accurate and personalized prognosis in future. Regarding status epilepticus (SE)

timely recognition and effective, early treatment with first- and second-line ASMs may prevent unnecessary hospitalizations. Rapid Epileptic Seizure Termination (REST) in outpatient setting is also useful, especially if known to be at risk for SE. Aggressive unlimited ICU treatment of refractory SE in palliative patients is not indicated and can be futile. In EOL care of complex epilepsy patients, consideration of withholding intensive care is not withholding effective treatment, but allowing patient to have a natural death in peaceful environment without prolonging their suffering unnecessarily.

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Monday, July 01 2024

EAN/EHF: Headaches with heavy burden

FW15_1 | Medication-overuse headache (MOH): Burden and management

G. Terwindt
Department of Neurology, Leiden University Medical Center, The Netherlands

Medication Overuse Headache (MOH) emerges from excessive consumption of acute headache medication, occurring in individuals enduring ≥15 headache days monthly. Despite its significant impact on quality of life, MOH often goes unnoticed. Typically, MOH patients harbour underlying migraine or tension-type headaches, commonly exhibiting frequent headaches alongside migraine symptoms like nausea, vomiting, light sensitivity, and sound sensitivity. However, manifestations can vary; overuse of analgesics may induce a diffuse, all-encompassing dull pressure in the head, while excessive triptan intake might result in daily migraine-like headaches that momentarily subside post-medication but swiftly return. Animal studies indicate that prolonged and repetitive use of analgesics and triptans can heighten susceptibility to evoked cortical spreading depression (CSD), modify pain regulation, and foster central sensitization. Individuals with episodic migraines who encounter allodynia during attacks are predisposed to migraine chronification, particularly women experiencing menstrual-related episodes. Treatment comprises a blend of preventive measures and curtailing acute medication usage, with the goal of lessening headache frequency and medication intake. Establishing a causal link between medication overuse and exacerbated headaches can be daunting; however, discontinuation often serves as indicative, though not obligatory, for diagnosing MOH, while thresholds defining medication overuse lack absolute parameters. Behavioral and educational interventions coupled with withdrawal therapy prove beneficial for MOH. A debate ensues over the superior approach: withdrawal from acute medication overuse or incorporating preventive medications targeting the underlying primary headache subtype. Interestingly, findings from preclinical models suggest that small-molecule CGRP receptor antagonists (gepants) are improbable contributors to MOH.

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FW15_2 | From chronic migraine pathophysiology to novel treatments

A. Maassen van den Brink
Erasmus University Medical Center, Rotterdam, The Netherlands

FW15_3 | Pharmacological treatment of cluster headache

P. Irimia
Department of Neurology, Clínica Universidad de Navarra, Pamplona, Spain

Cluster headache management requires a tailored treatment approach encompassing both acute and preventive strategies. Acute therapy is useful for aborting individual attacks of cluster headache and primarily involves oxygen inhalation, subcutaneous sumatriptan, or intranasal sumatriptan/zolmitriptan. The primary goal of preventive therapy is to produce a suppression of attacks and to maintain remission over the expected duration of the cluster period. Verapamil is the medication of choice for the prevention of episodic and chronic cluster headache. Glucocorticoids or occipital nerve block are often used as a bridging therapy to provide more rapid benefit during the initial titration of verapamil. Alternative agents such as lithium, topiramate, or melatonin may also be beneficial. Galcanezumab has recently emerged as an additional option for episodic cases. Noninvasive neurostimulation techniques and deep brain stimulation offer potential avenues for medically refractory cases. This presentation will comprehensively review cluster headache treatment options, ensuring an evidence-based and up-to-date approach to patient care.

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ABSTRACT

Special Sessions

Sunday, June 30 2024

What's new on EAN guidelines?

SPS02_1 | GPG Strategy 2024–2028

J. Costa
Guideline Production Group, EAN

Guideline Production Group (GPG) aims to fulfil EAN's mission to reduce the burden of neurological diseases, realizing its vision to be the home of neurology and advance high-quality patient care, as well as upholding its values. Following this and the past GPG Strategy (2021–2023), whose goals have been successfully achieved, the GPG believes that a long-term plan is needed. One of its main objectives of the new GPG Strategy for 2024–2028 is to further strengthen the internal foundations of its guideline production system, which is rooted in its robust membership. Guidelines quality highly depends on the skills, competencies, and motivation of the EAN members comprising the Guideline Taskforces. To maintain the efficient production of high-quality guidelines, GPG plans to establish infrastructures to expand the available support and resources and open opportunities to develop skills and know-how. Plans of action have been developed for this purpose and will be executed. One of the projects, which will be launched in 2024 and will be presented in this session, is an SOP for Guideline Manuscripts aiming to standardize the format of EAN guidelines and support guideline developers. Secondly, the GPG intends to establish the external presence of the EAN guidelines. The final purpose of any guideline is to improve healthcare and patient-important outcomes. The end goal is not just to publish these papers, but to use them in practice. To achieve this, the GPG plans to study the breadth of the reach of EAN guidelines and develop strategies for awareness, dissemination, and implementation.

Disclosure: Nothing to disclose.

SPS02_2 | EAN guideline on autoimmune encephalitis

M. Titulaer
Erasmus Medical Centre – University of Rotterdam Department of Neurology, The Netherlands

SPS02_3 | The role of AI in guideline production

J. Teo
Kings College Hospital; Guys & St Thomas Hospital, London, UK

Clinical guidelines traditionally have been drafted through consensus drafting of evidence-base using the hierarchy of evidence grades or levels, ranging from meta-analysis, randomized controlled trials, observational studies, real world evidence and down to case series. This talk will cover how Big Data approaches including AI techniques can be used to (1) support collecting evidence for clinical guidelines; (2) summarising evidence and potentially even (3) question-answering for guideline users. Examples include the role of language models in producing continuous systematic reviews of evidence (Refs [1, 2]) and generative language models in summarisation and question-answering. (1) https://www.thelancet.com/journals/landig/article/PIIS2589-7500(22)00032-2/fulltext (2) https://aiforhealth.app/.

Disclosure: James Teo received research grant support from NHS AI Lab, Health Data Research UK, Innovate UK, Office of Life Sciences, Dept of Science & Technology UK, NHS Genomics Networks. James Teo is co-founder and director of CogStack Ltd (commercial spin-out).

SPS02_4 | EAN CoCoCare graduation 2023

M. Leone[1]; M. Majoie[2]
[1]*Scientific Direction, IRCCS Casa Sollievo della Sofferenza, S. Giovanni Rotondo, Italy*; [2]*Department of Neurology, Academic Centre for Epileptology, Epilepsy Centre Kempenhaeghe & Maastricht University Medical Centre, Netherlands*

Clinical practice guidelines can play a crucial role in achieving more cost-efficient healthcare as they support the healthcare professional in deciding upon best efficient treatment. The Cost-Conscious Healthcare (CoCoCare) training is a training project for residents in neurology, developed in 2018 at Maastricht University, Netherlands, to equip them with competencies to make cost-conscious high-quality choices in their future work. The European Academy of Neurology (EAN) was brought into the project as part of the Consortium and collaborated to its conduction in 2019–2020. Recognizing its high value, the EAN Guideline Production Group decided to take over the programme and its first iteration was launched in early 2023, aiming to

teach 20 neurology residents and early career neurologists who wish to boost their knowledge and skills in guideline development and implementation. The course is structured as an integrated learning programme that combines e-learning as preparation of an introductory in-person kick-off meeting, and an on-the-job training. Monthly plenary webinar discussions with dedicated and experienced trainers are provided. Ninety-one participants from 21 European Countries participated in the training. Participants felt that they had learned a lot, were stimulated to apply guidelines and to reflect on their own (future) role in developing guidelines and providing cost-conscious care. The graduates of the first EAN CoCoCare programme will receive their certificates at the EAN Congress 2024 in Helsinki.
Disclosure: Nothing to disclose.

EAN/ESC: Heart & brain interactions: Cognition and gender

SPS03_1 | The role of heart disease for cognitive impairment – The cardiologist' perspective

W. Doehner
Charite Universitätsmedizin Berlin, Germany

SPS03_2 | Cognitive impairment and heart disease – The neurologist' perspective

G. Tsivgoulis
Second Department of Neurology, National and Kapostrian University of Athens, Greece

Introduction: Cognitive impairment and heart disease pose increasing challenges in an aging population, significantly impacting patient well-being. Their intricate connection has been extensively studied, revealing mutual influences on progression.
Methods: This lecture delves into the neurologist's perspective on the dynamic interplay between cognitive impairment and heart disease, aiming to illuminate underlying factors.
Results: Vascular disease plays a pivotal role in influencing both heart disease and cognitive impairment. Hypertension, atherosclerosis, and diabetes affect cerebral perfusion, leading to cerebral small-vessel disease and cognitive decline. Additionally, heart failure and valvular disease exacerbate cerebral hypoperfusion, while coronary artery disease correlates with carotid artery disease and intracranial atherosclerosis. Apart from small-vessel disease, heart disease, particularly conditions such as atrial fibrillation, can increase the risk of stroke, which, in turn, can cause cognitive impairment, depending on the severity and location of the brain injury. Furthermore, chronic inflammation, prevalent in both heart disease and neurodegenerative disorders, may further contribute to cognitive decline. Finally, lifestyle factors are of outmost importance in the relationship between heart disease and cognitive impairment. Adopting a heart-healthy lifestyle, including regular exercise, a balanced diet, and smoking cessation, can benefit both cardiovascular health and cognitive function. Effective screening strategies tailored to detect cognitive impairment in cardiac patients, while considering sex-specific disparities, are essential.
Conclusion: Addressing the intricate relationship between heart disease and cognitive impairment necessitates a collaborative, multidisciplinary approach between cardiologists and neurologists, aiming to optimize patient outcomes and enhance quality of life.
Disclosure: Nothing to disclose.

SPS03_3 | Sex differences in heart-brain interaction – The cardiologist' perspective

C. Gebhard
University Hospital Inselspital Bern, Switzerland

SPS03_4 | Sex differences in brain-heart interaction – The neurologist' perspective

M. Endres
Klinik für Neurologie, Charité-Universitätsmedizin Berlin, Germany

Sex and gender play an important role in cardiovascular disease and stroke. This review lecture will summarize important aspects of sex and gender in the pathophysiology and clinical course of these diseases from a neurological perspective. Diseases of both the heart and the brain share the same risk factors such as hypertension, diabetes, smoking and dyslipidemia and are also affected by inflammation, atherosclerosis and neuroendocrine changes, where sex and gender play an important role. A special focus of the lecture will be direct heart-brain interactions, in particular the so-called stroke-heart syndrome and also neurological causes of Takotsubo syndrome. For example, it has recently been shown that post-stroke myocardial injury occurs more frequently in women and also leads to greater disability.
Disclosure: ME reports grants from Bayer and fees paid to the Charité from Amgen, AstraZeneca, Bayer Healthcare, Boehringer Ingelheim, BMS, Daiichi Sankyo, Sanofi, Pfizer, all outside the submitted work.

Clinical Grand Round: Diagnosing specific etiology in neurological disorders

SPS04_1 | Back pain and tendon areflexia in a young female

S. Laakso[1,2]
[1]*Neurocenter, Helsinki University Hospital, Helsinki, Finland;*
[2]*Translational Immunology Research Program, University of Helsinki, Helsinki, Finland*

This is a case of a woman in her twenties who first presented with severe back pain and paresthesia of the legs that was relieved by extension of the spine in a wheel pose. The patient will be examined, and the findings evaluated during the Grand Round session.

Disclosure: Lecture fees Argenx, Biogen, Janssen, Merck, Novartis, Roche, Sanofi; congress expenses Merck, Novartis; advisory fee Argenx, Novartis, Roche, Sanofi, UCB Pharma; investigator for the clinical study Clarion (Merck) and subinvestigator for the clinical study Fenhance (Roche).

SPS04_2 | Adolescent onset complex movement disorders (dystonia, dyskinesia and myoclonus) and migraine

R. Ortiz[1,2]

[1]*Department of Neurology and Rehabilitation, Tampere University Hospital, Tampere, Finland*; [2]*University of Tampere, Tampere, Finland*

A 26-year-old female has experienced slowly progressive walking difficulties for 8 years, along with lower limb weakness, spasticity, hyperreflexia, loss of vibration sense, and paresthesia. Additionally, she exhibits mild head tremor. Clinical examination and further studies revealed this rare cause.

Disclosure: Funding for expert's opinion and/or speaker honoraria (Finnish Movement Disorders Association, Orion, Abbvie-Allergan), travel expenses (Ipsen, Orion) and advisory board membership (movement disorder division of the Finnish Neurological Society).

SPS04_3 | Dizziness and loss of balance in a young male

M. Jokela

Neurocenter, Turku University Hospital and Neuromuscular Research Center, Tampere University Hospital

A previously healthy young male was evaluated because of dizziness, wide-based gait and loss of balance. In this session, the patient will undergo a neurological examination and results of diagnostic evaluations will be presented.

Disclosure: Nothing to disclose.

Monday, July 01 2024

Pregnancy in women with neurological diseases

SPS05_1 | Multiple sclerosis

A. Chan

Neurology Department, Inselspital Bern, Bern, Switzerland

Multiple sclerosis (MS) has a strong female gender preponderance and predominantly affects persons with MS (pwMS) at younger age. Thus, family planning and pregnancy are core aspects in patient management, with increasing complexity due to the growing number of disease-modifying immunotherapies (DMTs). Many DMTs have scarce or no safety data in pregnancy and breastfeeding and are thus labeled as contraindicated during these periods. In addition, often very long wash out intervals between DMT cessation and conception are stipulated. In view of relevant biological determinants (e.g. terminal half-life, penetration through placenta, bioavailability) this is in many instances an overly conservative approach. This is especially true in situations where non-treatment poses a considerable risk for the pwMS with pregnancy wish. Thus, in selected situations and if clinically necessary, shorter wash out intervals or even the continuation of immunotherapy can be considered for some substances. Currently, there are heterogeneous recommendations and guidelines active across different regions, also reflecting separate approval/reimbursement situations. Individualized approaches with careful consideration of the benefit-risk profile and interprofessional cooperation between the treating neurologist, obstetrician-gynecologist and pharmacist/pharmacologist ideally with involvement of experienced centers are necessary.

Disclosure: No disclosure.

SPS05_2 | Neuromuscular diseases

C. Sommer

Department of Neurology, University Hospital of Würzburg, Germany

Pregnancy in women with neuromuscular diseases presents unique challenges due to the impact of these conditions on function, mobility, overall health, and restrictions in treatment options. Whereas some neuromuscular diseases affect mostly men, others are more prevalent in women, including those of childbearing age. Examples are spinal muscular atrophy, myasthenia gravis, and Charcot-Marie-Tooth disease. Women with neuromuscular diseases may face higher risks during pregnancy, including respiratory complications and increased fatigue. Pregnancy can exacerbate existing muscle weakness in myasthenia gravis, in particular in the first trimester or in the puerperium. Cardiorespiratory function may be further impaired in pregnancy in mitochondrial diseases. Many drugs are contraindicated in pregnancy, and treatment needs to be adapted. Depending on the severity of the neuromuscular disease and associated complications, women may require specialized care during labor and delivery; for example, in spinal muscular atrophy, delivery is mostly by cesarian section. A multidisciplinary approach is needed in most cases to optimize maternal and fetal health while minimizing risks associated with the underlying neuromuscular condition.

Disclosure: CS has been a consultant for Algiax, Bayer, Grifols, Nevro and Takeda. She has given educational talks for CSL Behring, GSK, Grifols, Kedrion, Pfizer, and TEVA.

SPS05_3 | Cerebrovascular diseases

D. Leys
University of Lille, France

Background: As approximately 10% of strokes occur before the age of 45 years, it is important to inform women who have had a stroke about risks associated with a future pregnancy.
Objective: To determine what are the risks of recurrent stroke, other vascular events, and complication of pregnancy in case of pregnancy occurring after an ischaemic stroke or a cerebral venous thrombosis.
Method: Literature review.
Results: In women who have history of ischaemic stroke: (i) the risks of recurrent stroke and of new vascular events are increased compared to women who never had a stroke, but not increased compared to non-pregnant periods; (ii) the risks of serious complications of pregnancy (miscarriages, stillbirth, premature delivery, eclampsia) is increased. Women who have history of cerebral venous thrombosis have an increased risk of recurrence, but this risk seems lower if they receive anticoagulant therapy. In women who need anticoagulation during pregnancy, low molecular weight heparin is the treatment of choice. Vitamin K antagonists can safely be given after 13 weeks of pregnancy and should be stopped 1 month before delivery. Oral direct anticoagulants are not recommended.
Conclusion: After an ischaemic stroke the risk of recurrent ischaemic event (cerebral or of other location) is not increased by the pregnancy, but the risk is mainly that of obstetrical complications. In women with history of cerebral venous thrombosis, the risk of recurrence is higher but limited with appropriate anticoagulation.
Disclosure: Nothing to disclose.

SPS05_4 | Epilepsy

K. Vonck, V. De Herdt
Ghent University Hospital, 4Brain, Belgium

Epilepsy is one of the most common chronic neurological disorders affecting women of childbearing age. Treating and counseling women with epilepsy (WWE) at childbearing age is a specific challenge, especially with many new ASMs becoming available. Information prior to conception and pregnancy is of paramount importance as both the epilepsy and the treatment may affect the fetus. Neurologists should be involved as early as possible to discuss anticonception and pregnancy planning in WWE, risk of seizures during pregnancy, risk of fetal complications due to ASM intake, delivery and breastfeeding. During pregnancy there is a risk of a higher seizure frequency related to hormone changes, water and sodium retention, stress, and decreasing blood levels of ASMs. In WWE there is a higher percentage of congenital malformation and risk of cognitive and behavioral disturbances in offspring associated with certain ASM intake. Drug level monitoring throughout pregnancy and following delivery is advised. Due to its well-established advantages breastfeeding should be considered but all drugs transfer into breastmilk to some extent by simple diffusion. Infants should be observed for signs of sedation. Pregnancy in WWE can be managed on an individual basis and is therefore safe and should not be discouraged.
Disclosure: Advisory board and/or speaker's bureau and/or consultancy for Synergia Medical, Livanova, Pharvaris, Angelini Pharma, Precisis, Al Mann Foundation

EAN/EPA: Non-invasive therapeutic neuromodulation in Parkinson's Disease and neuropsychiatric disorders

SPS06_1 | Non-invasive neurophysiological tools in humans

A. Suppa
Sapienza University of Rome, Italy

SPS06_2 | Therapeutic neuromodulation in Parkinson's disease

A. Macerollo
The Walton Centre NHS Foundation Trust for Neurology and Neurosurgery, Liverpool, UK

Therapeutic neuromodulation represents an umbrella term including different non-invasive brain stimulation techniques such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS). rTMS is a treatment that uses pulsing magnetic fields to activate or suppress the brain centres associated with a number of medical and psychiatric disorders. tDCS passes current through the scalp, skull, and meninges in order to stimulate the brain. A small electric current (1–2 mA) is delivered to the scalp by a battery-driven device connected to two saline-soaked surface electrodes. Both techniques as showed potential benefit for Parkinson's disease (PD), particularly in patients with pharmacorefractory motor symptoms or who are not candidates for surgical interventions such as deep brain stimulation (DBS). The main limitations in PD are low spatial resolution and superficial targeting. In the last few years a different therapeutic neuromodulation technique labelled transcranial-focused ultrasound stimulation (TUS) has attracted the attention of several neurologists and neuroscientists. Since the first medical application of ultrasounds in 1950s, the use of this procedure has evolved and is currently investigated as a new therapeutic role. Alongside with rTMS and tDCS, it has been demonstrated to be safe and promising in initial studies on patients with Parkinson's disease. The main benefit compared to the other two neuromodulations intervention is the possibility to reach superficial as well as deep cerebral targets with high spatial resolution. If rTMS can have a target of TMS of a few centimeters squares, TUS can reach targets of millimeters. It is possible to reach the basal ganglia with TUS but not with rTMS or tDCS.
Disclosure: Nothing to disclose.

SPS06_3 | Deep brain stimulation with transcranial focused ultrasound: Application to movement disorders and psychiatric disorders

J. Aubry
Physics for Medicine Paris, Paris, France

Since the late 1920s, less than 10 years after Paul Langevin filed the first patent on the development of an ultrasound transducer, intense research has focused on the medical applications of high-intensity focused ultrasound, particularly for cerebral applications. Unfortunately, for a long time, the skull constituted an impenetrable barrier to ultrasound. In the late 1990s, the use of multi-element arrays and the development of new aberration correction techniques laid the theoretical and technological foundations for transcranial ultrasound focusing. After introducing the most recent transcranial focusing techniques, we will show that world-first clinical results provide evidence that ultrasound neurostimulation is a revolutionary tool enabling, for the first time, to achieve deep brain stimulation in a non-invasive way. Clinical results will be presented on essential tremor, addiction and depression.

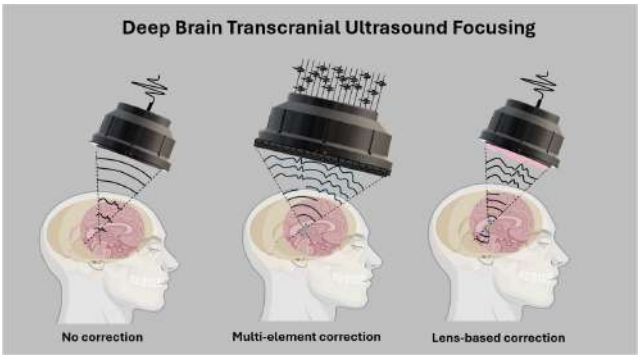

FIGURE 1 Defocusing effect of the skull bone and latest techniques for precise ultrasound transcranial focusing.

Disclosure: Jean-Francois Aubry holds five patents on transcranial ultrasound.

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ABSTRACT

Oral Presentations

Saturday, June 29 2024

Ageing and dementia 1

OPR-001 | **Distressing dreams, cognitive decline, and risk of dementia: A prospective study of three population-based cohorts**

A. Otaiku
UK Dementia Research Institute, Imperial College London, London, UK

Background and aims: Distressing dreams are associated with faster cognitive decline and increased dementia risk in people with Parkinson's disease (PD). Whether distressing dreams are associated with cognitive decline and dementia in people without PD is unknown. This study investigated the association between self-reported distressing dream frequency and the risk of cognitive decline and incident dementia in community-dwelling men and women in the general population.

Methods: Risk of cognitive decline was evaluated in 605 middle-aged adults from the Midlife in the United States (MIDUS) study who were followed-up over 13 years. Cognitive decline was defined as having an annual rate of decline in global cognitive function ≥1 standard deviation faster than the mean decline rate. Risk of incident all-cause dementia was evaluated in 2600 older adults from the Osteoporotic Fractures in Men Study (MrOS) and the Study of Osteoporotic Fractures (SOF), who were followed-up over 7 years. Distressing dream frequency was assessed in all cohorts at baseline using item 5 h of the Pittsburgh Sleep Quality Index. The association between self-reported distressing dream frequency and later cognitive outcomes was evaluated using multivariable logistic regression.

Results: Compared with middle-aged adults who reported having no distressing dreams at baseline, those who reported having weekly distressing dreams had a 4-fold risk of experiencing cognitive decline (adjusted odds ratio [aOR] = 3.99; 95% CI: 1.07, 14.85). Amongst older adults, the difference in dementia risk was 2.2-fold (aOR = 2.21; 95% CI: 1.35, 3.62).

Conclusion: Distressing dreams predict cognitive decline and all-cause dementia in middle-aged and older adults in the general population.

Disclosure: Nothing to disclose.

OPR-002 | **Exploring family history in Alzheimer's disease: Evidence for X-chromosome linked and recessively inherited risk factors**

C. Bernardes[1]; R. Guerreiro[2]; J. Brás[2]; J. Durães[1]; I. Baldeiras[3]; M. Lima[1]; M. Almeida[3]; I. Santana[1]; M. Tábuas-Pereira[1]
[1]*Neurology Department, Coimbra University Hospital Centre, Coimbra, Portugal;* [2]*Department of Neurodegenerative Science, Van Andel Institute, Grand Rapids, MI, USA;* [3]*Center for Neuroscience and Cell Biology, Coimbra, Portugal*

Background and aims: Alzheimer's Disease (AD) heritability is estimated to be around 70–80%. Yet, much of it is yet to be explained. Studying transmission patterns in different populations may help to understand factors contributing to the development of AD. In this study, we aimed to analyse family history patterns in a large cohort of Portuguese AD patients.

Methods: We collected family history from patients with AD and cognitively healthy controls over 75. We compared the proportion of subjects with AD depending on their family history (to assess X-linked and Y-linked associated inheritance patterns) and on the parents' birthplace (as a proxy of remote consanguinity). Linear regressions to study the association of these variables with different endophenotypes were performed.

Results: We included 3073 participants, 2183 cognitively healthy controls and 890 patients with AD. Men with a mother with dementia develop AD more frequently than women with a mother with dementia. In female patients with a CSF-supported diagnosis of AD, paternal history of dementia is associated with lower CSF total Tau, but increased CSF phosphorylated Tau. People whose parents are from the same town have higher risk of dementia. In multivariate analysis, this proxy is associated with a lower age of onset and higher CSF phosphorylated Tau, but higher CSF amyloid-beta42.

Conclusion: Our study gives evidence, at a population level, of X-linked risk factors for AD. We also add evidence to remote consanguinity as a risk factor for AD.

Disclosure: Nothing to disclose.

OPR-003 | Regulation of conditioned fear memory extinction by the orexin system in the medial prefrontal cortex

P. Yi[1]; M. Lin[2]; F. Chang[3]
[1]*Department of Sport Management/Aletheia University, Taiwan, China;* [2]*Graduate Institute of Brain and Mind Sciences/National Taiwan University, Taiwan, China;* [3]*Graduate Institute of Veterinary Medicine/National Taiwan University, Taiwan, China*

Background and aims: Post-traumatic stress disorder (PTSD) disrupts discernment of trauma-related fear memories, causing emotional distress and sleep disruptions. The orexin system, originating from the lateral hypothalamus (LH), is implicated in fear memory recall post-extinction. Lesions in the medial prefrontal cortex (mPFC), a LH downstream projection, hinder fear memory extinction. We proposed that the LH-mPFC pathway crucially contributes to conditioned fear memory extinction and modulates rapid eye movement (REM) sleep, impacting memory processing.
Methods: Using chemogenetic technique, we selectively manipulated the LH-mPFC pathway by activating or inhibiting it during extinction learning, and behavior tasks were assessed. Concurrently, electrocorticography (EEG) measured sleep–wake states under these manipulations.
Results: Extinction acquisition heightened activity in both the mPFC and LH. Activating the LH-to-mPFC pathway maintained elevated freezing levels during fear memory extinction, while silencing initially lowered freezing levels, decreasing rapidly. This manipulation not only affected freezing expression but also influenced the formation of the extinction engram, impacting fear memory retrieval and anxiety tasks. These findings underscore the pivotal role of the LH-to-mPFC pathway in extinction acquisition. Pathway augmentation induced insomnia-like features, particularly during the light period.
Conclusion: Our results suggest that the LH-to-mPFC orexinergic projection regulates conditioned fear memory extinction and may disrupt REM sleep, providing insights into the intricate interplay between fear regulation, memory processing, and sleep disturbances in PTSD.
Disclosure: Nothing to disclose.

OPR-004 | Significance of plasma p-tau217 in predicting long-term dementia risk: Insights from machine learning approaches

Z. Xiao[1]; X. Zhou[1]; Q. Zhao[1]; Y. Cao[2]; D. Ding[1]
[1]*Institute of Neurology, Huashan Hospital, Fudan University, Shanghai, China;* [2]*Clinical Epidemiology and Biostatistics, Department of Medical Sciences, Faculty of Medicine and Health, Örebro University, Örebro, Sweden*

Background and aims: The role of plasma biomarkers for predicting incident dementia in the general population is still undetermined.
Methods: A total of 1857 baseline non-demented older adults with follow-ups within 10 years were included from a community-based cohort. Consensus diagnoses of dementia and Alzheimer's disease (AD) were based on clinical criteria. The Recursive Feature Elimination algorithm was used to select the important features from 90 baseline candidate predictors for developing dementia and AD prediction models. Area Under the Receiver Operating Characteristic Curve (AUC) was used to evaluate models' performance. Models were validated in the testing sets and subsets.

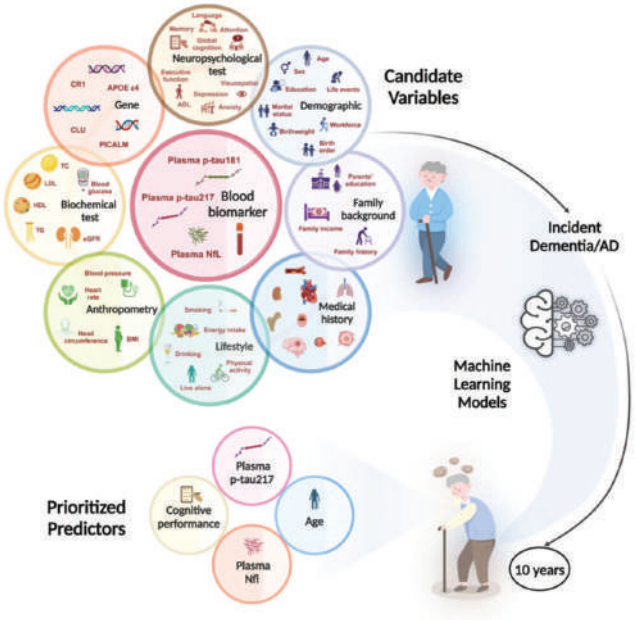

FIGURE 1 Illustration of the candidate variables and research process.

Results: During the follow-up of 12,716 person-years, 207 participants developed dementia (including 145 AD). The constructed Logistic Regression, Naive Bayes, Bagged Trees, and Random Forest models showed moderate-to-high AUCs predicting future dementia (AUCs = 0.709–0.808) in the testing sets. Age, neuropsychological tests, and plasma p-tau217 were the prioritized variables in all models. The models also showed robustness in diverse subgroups.

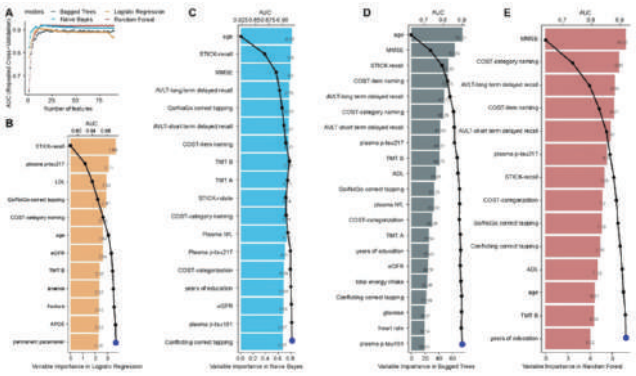

FIGURE 2 The selected models and variable importance for predicting dementia.

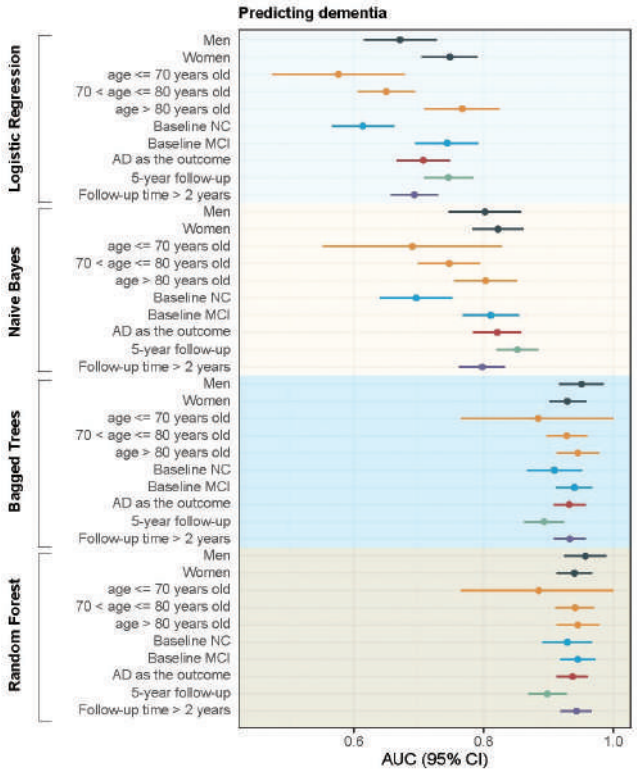

FIGURE 3 Subgroup analyses of the models for predicting dementia.

Conclusion: Plasma p-tau217, combined with age and cognitive performance, showed important values in predicting incident dementia among community older adults. In the resource-limited settings, using these variables may be convenient and cost-effective to identify participants with high risk of dementia in the general population.
Disclosure: Nothing to disclose.

OPR-005 | Autonomic dysfunction in REM sleep behavior disorder: Heart rate variability analysis to explore neurodegeneration

M. Figorilli[1]; P. Sattar[3]; E. Casaglia[1]; M. Mascia[1]; E. Facchini[2]; G. Baldazzi[3]; N. Mandas[4]; D. Pani[3]; P. Mattioli[6]; L. Giorgetti[5]; D. Arnaldi[6]; M. Puligheddu[1]
[1]*Department of Medical Sciences and Public Health, Sleep Disorder Research Center, University of Cagliari, Cagliari, Italy;* [2]*MeDSP Lab, Department of Electrical and Electronic Engineering, University of Cagliari, Cagliari, Italy;* [3]*MeDSP Lab, Department of Electrical and Electronic Engineering, University of Cagliari, Cagliari, Italy; Department of Medical Sciences and Public Health, Sleep Disorder Research Center, University of Cagliari, Cagliari, Italy;* [4]*MeDSP Lab, Department of Electrical and Electronic Engineering, University of Cagliari, Cagliari, Italy; The Hadron Academy, Istituto Universitario di Studi Superiori IUSS, Pavia, Italy;* [5]*Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DI-NOGMI),Clinical Neurology, University of Genoa, Genoa, Italy;* [6]*Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DI-NOGMI), Clinical Neurology, University of Genoa, Genoa, Italy; Neurophysiopathology Unit, IRCCS Ospedale Policlinico San Martino, Genoa, Italy*

Background and aims: Autonomic dysfunction is common along the alpha-synucleinopathy continuum from prodromal stage (isolated REM sleep behavior disorder, iRBD) to overt Parkinson's disease (PD). This study aims to investigate autonomic dysregulation in iRBD, RBD-PD and PD patients by examining sleep-related Heart Rate Variability (HRV) parameters.
Methods: 40 iRBD (67 ± 8 y.o., 73% males), 16 PD (67 ± 10 y.o., 50% males), 30 PD-RBD (71 ± 8 y.o., 66% males) and 24 controls (CG, 59 ± 10 y.o., 46% males) subjects were enrolled from two Italian sleep centers. A 5-min artifact-free ECG signal from N2, N3, and REM phases was investigated for time-domain HRV analysis. Intergroup significant differences have been assessed by nonparametric statistical analysis, for each sleep phase separately.
Results: When comparing iRBD and CG subjects, lower HRV parameters were observed in N2 ($p < 0.025$ for all) and REM ($p < 0.04$ for STDNN and R20) phases. iRBD showed lower HRV also when compared to PD-RBD in N2 ($p < 0.006$, for STDNN, SDSD, RMSSD), and PD in N2 ($p < 0.025$, for STDNN, SDSD, RMSSD, pR50) and in N3 ($p < 0.05$, for STDNN, SDSD, RMSSD). Conversely, the PD group showed significant reduction when compared to the CG ($p < 0.03$), as well as a significant increase when compared to the PD-RBD group ($p < 0.05$, R20 and pR20 in REM).
Conclusion: These findings suggest that the disrupted autonomic regulation is evident in the early alpha-synucleinopathy stage during N2 and REM sleep, even more than in overt PD. Longitudinal studies are warranted to determine whether autonomic dysfunction in iRBD could serve as a prognostic biomarker, aiding in the prediction of alpha-synucleinopathy subtypes development.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 1

OPR-006 | NLRP3-inflammasome inhibition reduces stroke induced inflammation and delays infarct growth before recanalization

M. Bellut
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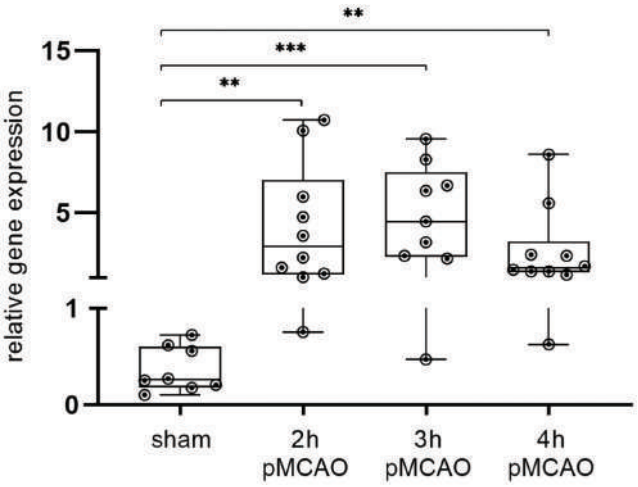
Background and aims: The NLRP3-inflammasome is a multiprotein complex regulating the activation of the innate immune system. NLRP3-dysregulation has been implicated in various inflammatory and autoimmune diseases. In experimental ischemic stroke, NLRP3-inhibition mitigated ischemia/reperfusion-injury and secondary infarct growth after recanalization. In the present study, we examined

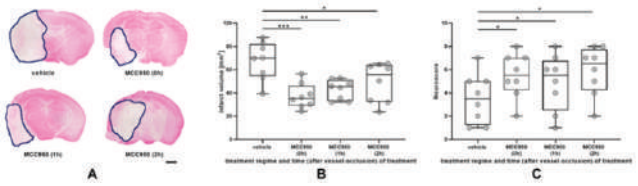
whether NLRP3-inhibition might alleviate stroke progression already under large vessel occlusion (LVO) before recanalization.

Methods: We occluded the middle cerebral artery in C57Bl/6-mice for up to 4 hours and examined the NLRP3-mRNA expression under LVO. In a subsequent experiment, C57Bl/6-mice were prophylactically or therapeutically (after 1 h and 2 h of vessel occlusion) treated with the NLRP3-inflammasome inhibitor MCC950. We then assessed stroke volumes, the NeuroScore, IL1b-levels (immunoblot) and blood–brain-barrier (BBB) integrity (albumin extravasation).

Results: We detected a 5–10-fold upregulation of NLRP3-mRNA expression already under LVO ($n = 10$/group). Its inhibition reduced stroke sizes significantly [vehicle/prophylactic/MCC950(1 h)/MCC950(2 h)-treatment: 67.4 ± 16.4 mL/37.2 ± 10.2 mL/42.9 ± 8.4 mL/49.1 mL ± 12.1 mL] ($n = 9$/group). Consequently, the IL1b-release decreased cortically by 20% ($n = 9$/group) while the integrity of the BBB and the NeuroScore ($n = 9$/group) improved significantly. We observed these improvements in both the prophylactic and therapeutic settings.



NLRP3 gene expression levels increase during pMCAO.



NLRP3 inhibition reduces infarct volume after prophylactic (MCC950 0 h) and delayed treatment, 1 h (MCC950 1 h) and 2 h (MCC950 2 h) post stroke onset.

Conclusion: As main finding we show that blocking of NLRP3 mitigates cerebral inflammation and infarct growth already under LVO and partly preserves the ischaemic penumbra, "buying time" before recanalization. This may have a major clinical impact in the future since infarct progression under LVO is a major caveat for an unfavourable clinical outcome despite successful recanalization.

Disclosure: Nothing to disclose.

OPR-007 | Antiplatelets in emergent carotid stenting after intravenous thrombolysis: A multicenter retrospective matched analysis

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Background and aims: Mechanical thrombectomy (MT) with emergent carotid stenting (eCAS) is beneficial in patients with tandem occlusion (TO). Our aim was to address safety and efficacy of different intra-procedural antiplatelet regimens in patients undergoing eCAS after intravenous thrombolysis (IVT) and define predictors of parenchymal hemorrhage (PH).

Methods: The databases of 17 European stroke centers were screened for consecutive patients with TO who received MT with eCAS. Intra-procedural antiplatelet therapy was categorized in: (1) low intensity regimen, (2) high intensity regimen, and (3) high intensity regimen followed by i.v. Glycoprotein IIb/IIIa inhibitors (GPI) infusion. Propensity score matching (PSM) was used to estimate differences in outcome between treatment groups. Outcome measure included the occurrence of PH type 2 and type 1 and the 90-day mRS score 0–2.

Results: 621 patients were collected, 48.5% received IVT. After PSM there was no significant difference between IVT and non-IVT patients under different antiplatelet regimens concerning rates of PH type 2 and type 1. Subgroup analysis showed increased rate of PH type 2 in IVT patients receiving high intensity regimen plus GPI maintenance, but without difference in clinical outcome. In multivariate analysis, presence of atrial fibrillation (OR 4.089, 95% CI 1.759–9.508), high intensity antiplatelet regimen with GPI maintenance (OR 2.364, 95% CI 1.086–5.147) and stent thrombosis (OR 2.631, 95% CI 1.160–5.970) were predictors of PH type 2.

Table 1: Effect of IVT on outcome measures after PSM of patients from the entire cohort

	IVT (n=222)	Non-IVT (n=222)	p value *
Parenchymal hemorrhage type 2, number/total (%)	15/222 (6.76%)	18/222 (8.11%)	0.718
Parenchymal hemorrhage type 1, number/total (%)	53/222 (23.87%)	51/222 (22.97%)	0.911
Extracranial bleeding, number/total (%)	12/222 (5.41%)	5/222 (2.25%)	0.136
Stent thrombosis, number/total (%)	20/222 (9.01%)	25/222 (11.26%)	0.530
mTICI score 2b-3, number/total (%)	187/217 (86.18%)	194/219 (88.58%)	0.474
mRS score 0-2, number/total (%)	131/201 (65.17%)	104/188 (55.31%)	**0.049**
90-day mortality, number/total (%)	22/201 (10.95%)	25/188 (13.30%)	0.535

IVT = intravenous thrombolysis; PSM = propensity score matching; mTICI = modified Treatment In Cerebral Infarction; mRS = modified Rankin Scale; * statistical significance was considered at $p < 0.05$.

Table 2: Outcome measures after PSM of IVT and non-IVT patients under different intra-procedural antiplatelet regimens.

	Low APT regimen			High APT regimen			High APT regimen plus GPI maintenance		
	IVT (n = 94)	non-IVT (n = 94)	p value*	IVT (n = 28)	non-IVT (n = 28)	p value*	IVT (n = 63)	non-IVT (n = 63)	p value*
Parenchymal hemorrhage type 2, number/total (%)	2/94 (2.1%)	8/94 (8.5%)	0.100	2/28 (7.7%)	3/26 (11.5%)	1.000	**10/63 (15.9%)**	**2/63 (3.2%)**	**0.016**
Parenchymal hemorrhage type 1, number/total (%)	24/94 (25.5%)	26/94 (27.7%)	0.869	3/26 (11.5%)	7/26 (26.9%)	0.291	13/63 (20.6%)	17/63 (27.0%)	0.531
Extracranial bleeding, number/total (%)	4/94 (4.3%)	1/94 (1.1%)	0.368	2/26 (7.7%)	0/26 (0.0%)	0.490	5/63 (8.0%)	2/63 (3.2%)	0.440
Stent thrombosis, number/total (%)	8/94 (8.5%)	11/94 (11.7%)	0.630	4/26 (15.4%)	2/26 (7.7%)	0.668	10/63 (15.9%)	7/63 (11.1%)	0.603
mTICI score 2b-3, number/total (%)	77/91 (84.6%)	82/92 (89.1%)	0.390	25/26 (96.1%)	24/26 (92.3%)	1.000	49/62 (79.0%)	56/62 (90.3%)	0.133
90-day mRS score 0-2, number/total (%)	51/79 (64.6%)	37/68 (54.4%)	0.240	19/26 (73.1%)	11/22 (50.0%)	0.138	30/62 (48.4%)	34/62 (54.8%)	0.590
90-day mortality, number/total (%)	10/79 (12.7%)	12/68 (17.6%)	0.488	3/26 (11.5%)	1/22 (3.9%)	0.614	8/62 (12.9%)	8/62 (12.9%)	1.000

PSM = propensity score matching; IVT = intravenous thrombolysis; APT = antiplatelet; mTICI = modified Treatment In Cerebral Infarction; mRS = modified Rankin Scale; * Statistical significance was considered at $p < 0.05$.

Table 3. Multivariate logistic regression analysis for predictors of PH type 2

	OR	95% CI	p value*
Hypertension	1.588	0.787 - 3.203	0.196
Atrial fibrillation	**4.089**	**1.759 - 9.508**	**0.001**
Diabetes	1.300	0.570 - 2.016	0.533
Antiplatelet regimen for eCAS **			
High intensity	1.938	0.773 - 4.862	0.283
High intensity + GPI maintenance	**2.364**	**1.086 - 5.147**	**0.030**
Antiplatelet regimen after eCAS ***			
SAPT	0.428	0.091 - 2.016	0.283
DAPT	**0.217**	**0.061 - 0.770**	**0.018**
Stent thrombosis	**2.631**	**1.160 - 5.970**	**0.021**

PH = parenchymal hemorrhage; OR = odds ratio; CI = confidence interval; eCAS = emergent carotid stenting; GPI = Glycoprotein IIb/IIIa inhibitors; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; * Statistical significance was considered at $p < 0.05$; ** = Coefficients are relative to low intensity regimen; *** = Coefficients are relative to no antiplatelet therapy.

Conclusion: Different intra-procedural antiplatelet regimens for eCAS are safe after IVT. Increased risk of PH type 2 is associated with use of intra-procedural GPI maintenance in IVT patients and presence of atrial fibrillation.

Disclosure: Nothing to disclose.

OPR-008 | Stroke recurrence and overall mortality in CPAP treated post-stroke obstructive sleep apnea patients

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Background and aims: Obstructive sleep apnea (OSA) is strongly associated with stroke development and is identified in up to 70% of stroke patients. It is unclear whether treatment with continuous positive airway pressure (CPAP) reduces re-stroke risk or mortality among post-stroke patients. Previous studies examining the impact of CPAP on mortality in post-stroke patients have either had limited follow-up periods or involved small sample sizes.

Methods: We conducted a retrospective cohort study using data from the Danish National Patient Registry covering the period from 2003 to 2016, involving 1821 patients diagnosed with sleep-disordered breathing (SDB) and a prior ischemic stroke or transient ischemic attack (TIA). Patients were categorized into three groups: CPAP adherent, CPAP non-adherent and no CPAP treatment. By utilizing Cox hazard regression, we assessed the risk of recurrent stroke or TIA and overall mortality among these groups over a 5-year follow-up period.

Results: CPAP treatment improved survival rate in patients categorized as adherent compared to patients with no CPAP treatment (hazard ratio: 0.62; 95% CI: 0.50–0.76; $p < 0.001$). This effect persisted after adjusting for age, sex, and pre-existing comorbidities within 3 years (the Quan updated Charlson Comorbidity Index). There was no observed reduction in the risk of recurrent stroke/TIA between the CPAP groups.

Conclusion: In this large, registry-based study, we found that CPAP-adherence reduced the overall mortality in post-stroke/TIA patients with SDB. CPAP treatment did not seem to affect the risk of re-stroke/TIA during the 5 years of follow-up.

Disclosure: Nothing to disclose.

OPR-009 | Argatroban for ischemic stroke with early neurological deterioration: A meta-analysis of randomized controlled trials

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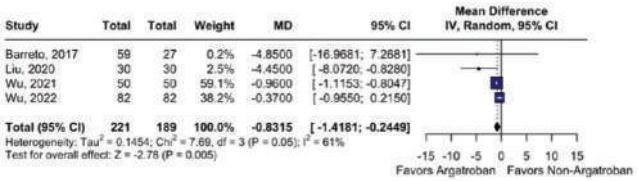
Background and aims: The presence of early neurological deterioration in acute ischemic stroke (AIS) underscores the urgent and intricate nature of managing this medical condition. Currently, argatroban is under investigation as a potential combination treatment, but there still a lack of evidence for its efficacy. Consequently, it becomes imperative to ascertain whether this compound contributes to improvement in neurological function following AIS.

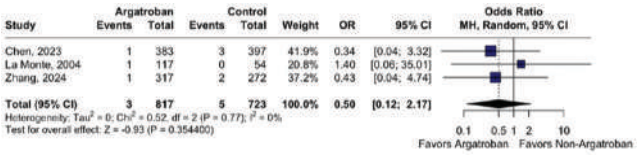
Methods: We systematically searched databases (PubMed, Embase, Web of Science, and Cochrane) until January 10, 2024. Odds ratio (OR) and mean differences (MDs) with 95% confidence intervals (CIs) were calculated using a random-effects model. Heterogeneity was assessed using I^2 statistics. The statistical analysis was performed using R software, version 4.3.1.

Results: A total of 9 studies and 2043 patients were included. As compared to the control group, Argatroban treated patients exhibited significantly improved NIHSS score at 7- and 90-days post stroke (MD −0.8315, 95% CI −1.418 to −0.2449, $p = 0.005$; MD −0.3903, 95% CI −1.9313 to 1.1506, $p = 0.62$) respectively. Argatroban treatment reduced the occurrence of parenchymal hematoma (PH). There

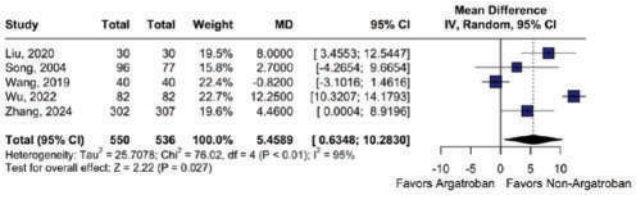
were no significant changes in the Modified Rankin Score (mRS) and symptomatic intracranial hemorrhage (sICH) occurrence in patients treated with Argatroban when compared to placebo group. Finally, patients on the placebo group had a significantly improved modified Barthel Index (mBI).



A forest plot of the change in the National Institutes of Health Stroke Scale (NIHSS) outcome of 7 days.



A forest plot of the change in the Parenchymal Hematoma (PH) outcome.



A forest plot of the modified Barthel Index (mBI) outcome.

Conclusion: Among these patients, treatment with argatroban plus drug improve NIHSS scores, most prominently at 7 days. These results demonstrate a benefit of Argatroban on reducing neurological deficits on AIS patients subject to thrombolytic therapy without increasing the risk of sICH.

Disclosure: The authors declare that they have no disclosure.

OPR-010 | Increased apnea-hypopnea index and elevated hypoxic burden are associated with atrial fibrillation in ischemic stroke

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Background and aims: Sleep apnea (SA) increases the risk of cardiovascular disorders (CVD). SA is highly prevalent in stroke and is associated with an increased prevalence of atrial fibrillation (AF). Which markers of SA, the apnea-hypopnea index (AHI) or the hypoxic burden (HB), better predict AF in stroke, remains unknown.

Methods: This cross-sectional analysis utilized data from the Bernese Sleep & Stroke Cohort, an integral component of the Swiss Stroke Registry. During acute hospitalization, patients underwent respiratory polygraphy, leading to dichotomization into AHI+/ AHI- groups using a 20/h threshold. Further classification into HB+/HB- groups occurred with the 75% percentile as the threshold. Multivariate logistic regression assessed the associations between distinct combinations of HB and AHI (HB+/AHI+, AHI+/HB-, and HB+/AHI-) in comparison to HB-/AHI- on prevalent AF, adjusting for various confounders.

Results: In the analysis of 1010 patients (mean age 66y, 62% males), AF was diagnosed in 197 (20%) patients. HB+ was present in 254 (25%) patients, and AHI+ was present in 360 (36%) patients. The HB+/AHI+, AHI+/HB−, HB+/AHI−, and HB−/AHI− groups constituted 20%, 16%, 5%, and 59% of the total, respectively. Compared to the HB−/AHI− group, the HB+/AHI+ group was independently associated with prevalent AF (adjusted OR: 1.68; 95% CI: 1.10–2.55). No significant difference was observed in AHI+/HB− and HB+/AHI- groups.

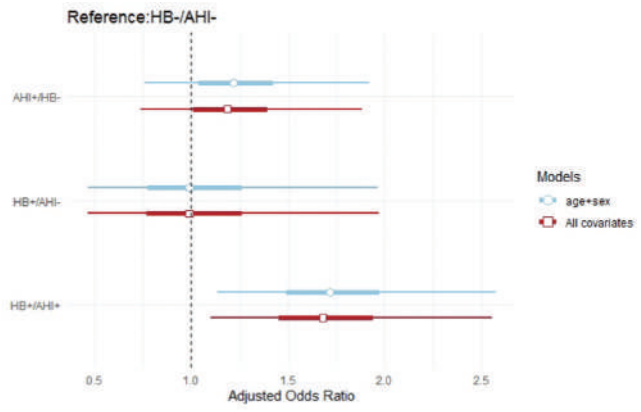

FIGURE 1 Adjusted Odds Ratios for prevalent AF across distinct combinations of HB and AHI (HB+/AHI+, HB+/AHI−, and AHI+/HB−), in comparison to the baseline group HB−/AHI−

	HB-/AHI- (N=597)	AHI+/HB- (n=159)	HB+/AHI- (n=53)	AHI+/HB+ (n=201)	Total (n=1010)	P value
Demographics						
Age (mean, sd)	63.200 (15.079)	69.930 (12.628)	73.417 (10.312)	69.656 (12.155)	66.116 (14.369)	< 0.001
Sex (Male)	319 (53.4%)	119 (74.8%)	32 (60.4%)	156 (77.6%)	626 (62.0%)	< 0.001
BMI	25.202 (3.991)	27.481 (4.441)	26.642 (4.542)	28.979 (23.897)	26.388 (11.363)	< 0.001
Smoking	157 (26.3%)	37 (23.3%)	11 (20.8%)	58 (28.9%)	263 (26.0%)	0.522
Sleep features						
AHI	7.122 (4.968)	31.387 (11.283)	12.870 (5.112)	45.77 (18.195)	18.934 (18.810)	< 0.001
ODI	8.024 (5.464)	27.124 (11.716)	16.242 (10.768)	41.673 (19.057)	18.159 (17.345)	< 0.001
AHI≥30/h	0 (0.0%)	63 (39.6%)	0 (0.0%)	157 (78.1%)	220 (21.8%)	< 0.001
CAI	0.635 (1.307)	5.317 (8.387)	0.749 (1.206)	10.797 (13.580)	3.403 (8.067)	< 0.001
CAI≥5/h	11 (1.8%)	56 (35.2%)	0 (0.0%)	101 (50.2%)	168 (16.7%)	< 0.001
CSA	4 (0.7%)	13 (8.2%)	0 (0.0%)	28 (13.9%)	45 (4.5%)	< 0.001
Stroke/TIA features						
NIHSS at admission	2.559 (3.913)	3.339 (3.884)	2.421 (2.825)	4.075 (4.739)	2.973 (4.074)	< 0.001
CE	98 (17.3%)	31 (20.1%)	9 (17.3%)	59 (29.9%)	98 (17.3%)	0.02
Supratentorial	454 (81.2%)	135 (88.8%)	39 (78.0%)	174 (89.2%)	802 (83.9%)	0.011
Infratentorial	129 (23.1%)	20 (13.2%)	12 (24.0%)	23 (11.8%)	184 (19.3%)	< 0.001
Event type						
Ischemic Stroke	538 (90.1%)	146 (91.8%)	49 (92.5%)	186 (92.5%)	919 (91.0%)	0.702
TIA	59 (9.9%)	13 (8.2%)	4 (7.5%)	15 (7.5%)	91 (9.0%)	
Cerebro-cardiovascular Risk factors						
Hypretension	339 (56.8%)	117 (73.6%)	46 (86.8%)	170 (84.6%)	672 (66.5%)	< 0.001
Diabetes	83 (13.9%)	25 (15.7%)	11 (20.8%)	54 (26.9%)	173 (17.1%)	< 0.001
Dyslipidemia	396 (66.3%)	124 (78.0%)	39 (73.6%)	158 (78.6%)	717 (71.0%)	0.001
Atrial fibrillation	88 (14.7%)	38 (23.9%)	12 (22.6%)	59 (29.4%)	197 (19.5%)	< 0.001

TABLE 1 Baseline characteristics between HB−/AHI−, AHI+/HB−, HB+/AHI−, AHI+/HB+ groups.

Conclusion: In stroke, an elevated HB with an increased AHI, rather than either SA measures in isolation, is associated with a higher prevalent of AF. These findings underscore the potential of both markers in enhancing risk stratification for CVD.

Disclosure: Swiss National Science Foundation grant #320030_149752.

Headache & pain 1

OPR-011 | Compensated hypogonadism identified in males with cluster headache: A prospective case-controlled study

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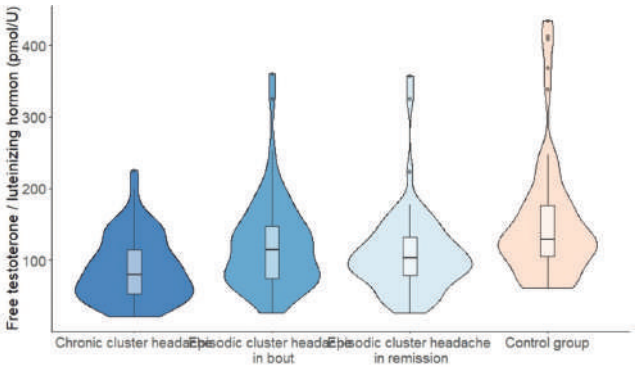
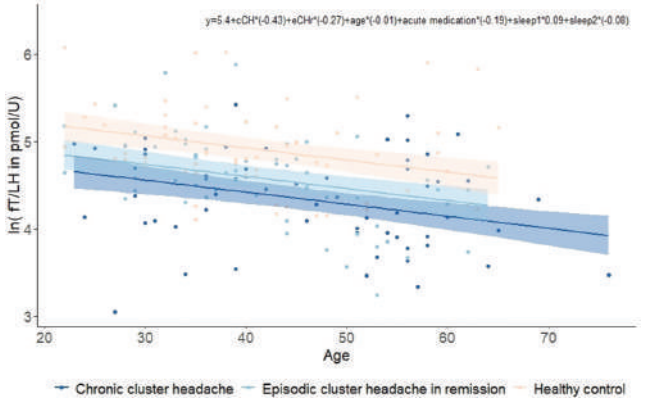
Background and aims: Androgens have been hypothesized to be involved in the pathophysiology of cluster headache due to the male predominance, but whether androgens are altered in patients with cluster headache remains unclear.

Methods: We performed a prospective, case-controlled study in adult males with cluster headache. Sera were measured for hormones including testosterone, luteinizing hormone (LH), and sex hormone-binding globulin in 60 participants with episodic cluster headache (during a bout and in remission), 60 participants with chronic cluster headache, and 60 age- and sex-matched healthy controls. Free testosterone (fT) was calculated according to the Vermeulen equation. Shared genetic risk variants were assessed between cluster headache and testosterone concentrations.

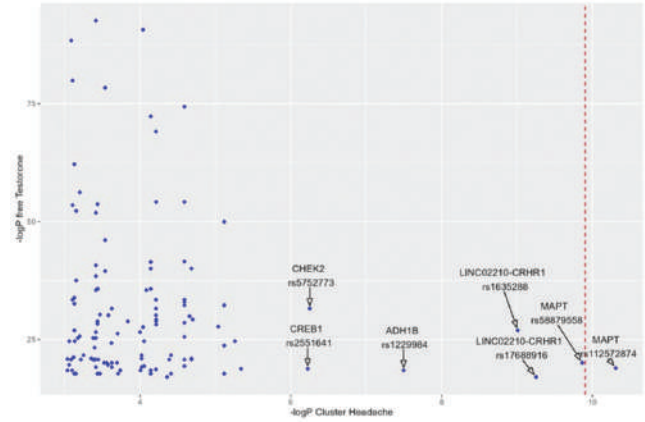
Results: The mean fT/LH ratio was reduced by 35% (95% CI: 21%–47%, $p<0.0001$) in patients with chronic cluster headache and by 24% (95% CI: 9%–37%, $p=0.004$) in patients with episodic cluster headache compared to controls after adjusting for age, sleep duration, and use of acute medication. Androgen concentrations did not differ between bouts and remissions. Furthermore, a shared genetic risk allele, rs112572874 (located in the intron of the microtubule associated protein tau (MAPT)), between fT and cluster headache was identified.



Violin plot of free testosterone/luteinizing hormone (fT/LH) -ratio in serum in participants with different types of cluster headache and in healthy, sex- and age- matched controls.



Linear regression of the free testosterone/luteinizing hormone (fT/LH) -ratio in serum as a function of age.



Shared genetic risk variants of cluster headache and serum free testosterone concentration.

Conclusion: Our results demonstrate that the male endocrine system is altered in patients with cluster headache to a state of compensated hypogonadism, and this is not an epiphenomenon associated with sleep or the use of acute medication. Together with the identified shared genetic risk allele, this may suggest a pathophysiological link between cluster headache and fT.

Disclosure: Nothing to disclose.

OPR-012 | Cluster tics in cluster headache: A cross-sectional and controlled study

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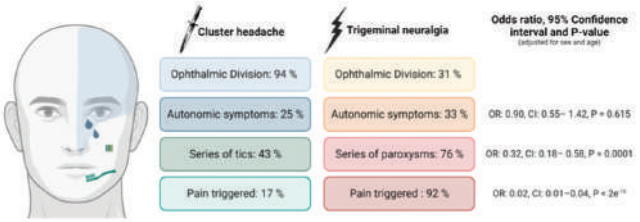
Department of Neurology, Danish Headache Center, University of Copenhagen, Rigshospitalet-Glostrup, Glostrup, Denmark

Background and aims: This explorative study aimed to investigate the lifetime prevalence of cluster tics in patients with cluster headache, characterize cluster tics, including identifying possible associations to different clinical characteristics, and further investigate specific traits associated with cluster tics compared to trigeminal neuralgia.

Methods: A total of 424 patients with cluster headache were included in this controlled cross-sectional cohort study based on a semi-structured interview. The comparator cohort consisted of 576 patients diagnosed with trigeminal neuralgia, who had previously participated in a standardized, purpose-built, semi-structured interview.

Results: Cluster tics were reported in 200 out of 424 (47%) of patients with cluster headache. The odds of experiencing cluster tics were higher for males compared to females (OR: 1.93, 95% CI: 1.27–2.96, $p=0.002$), and for patients with chronic cluster headache compared to patients with episodic cluster headache (OR: 1.74, 95% CI: 1.15–2.62, $p=0.008$). We found that cluster tics presented as orbital pain in 70% of patients, and that, in comparison to trigeminal neuralgia paroxysms, the odds of a paroxysm being a cluster tic was low if the attack was triggerable (OR: 0.02, 95% CI: 0.01–0.04, $p<2e\text{-}16$).



Odds ratios (OR) for having been diagnosed with trigeminal neuralgia (TN) prior to interview when presenting with specific attack traits, adjusted for age and sex.

Conclusion: The lifetime prevalence of cluster tics in patients with cluster headache was 47%. The cluster tics were associated with the chronic cluster headache, and in contrast to the paroxysms in TN, cluster tics were associated to male sex, often had an orbital location of pain and were non-serial and non-triggerable.

Disclosure: Nothing to disclose.

OPR-013 | Vascular compression in trigeminal neuralgia discloses trigeminal root somatotopic organization

G. De Stefano[1]; D. Litewczuk[1]; E. Ripiccini[2]; S. Maarbjerg[3]; G. Di Pietro[1]; P. Falco[1]; C. Leone[1]; E. Galosi[1]; A. Truini[1]; G. Di Stefano[1]
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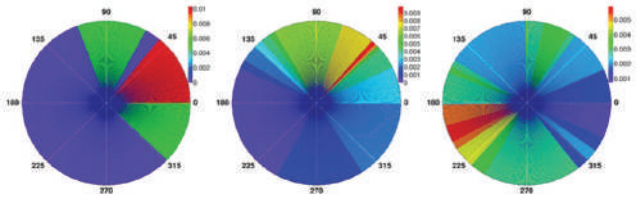
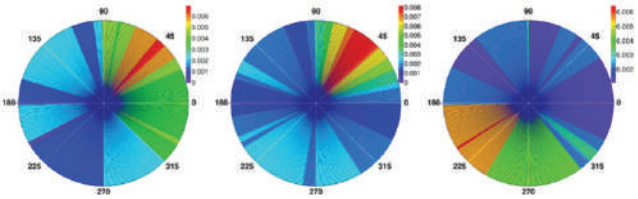
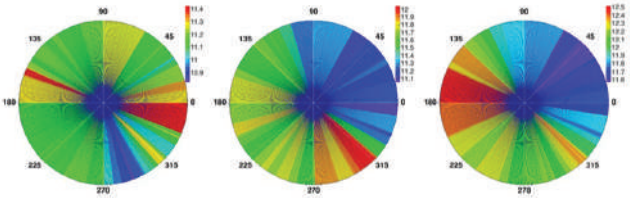
Background and aims: In Trigeminal Neuralgia pain is localized in the distribution of one or more branches of the trigeminal nerve. A hallmark of TN is the presence of discrete skin areas able to trigger pain attacks when touched. In classical TN, trigeminal reflexes are normal but it is possible to recognize a vascular compression with morphological changes of trigeminal nerve root.
Methods: We enrolled 53 patients with clinically defined TN, normal trigeminal reflexes testing, and evidence of neurovascular compression at 3-Tesla MRI. From MRI images we measured the polar coordinates of the impacting vessel on the trigeminal root circumference and then correlate it with pain distribution, trigger zones and latencies of the early components of the trigeminal reflexes.
Results: Pain in V1, V2 and V3 is associated, respectively, with vascular compression in the medial, superior and lateral aspect of the nerve ($p < 0.05$). Cutaneous trigger zones are associated with corresponding region of the circumference ($p < 0.05$). Increased latency of the R1 component of the blink reflex is associated with medial compression, while increased latency of the SP1 component of the masseter inhibitory reflex is associated with inferomedial compression when the reflex is evoked from the infraorbital nerve, and with lateral compression when it is evoked from the mental nerve ($p < 0.05$).



Relative frequency of location of neurovascular compression along the root circumference as derived by MRI data of TN patients with pain limited to one trigeminal division, V1 (left), V2 (middle) or V3 (right).



Relative frequency of location of neurovascular compression along the root circumference as derived by MRI data of TN patients reporting as trigger zones the forehead (left), the cheek (middle) or the jaw (right).



Mean latency of the early component of the trigeminal reflexes in patients with MRI evidence of neurovascular compression along a given zone of the trigeminal root. Reflexes were evoked from V1 (left), V2 (middle) and V3 (right).

Conclusion: Our study showing that pain distribution, trigger zones and increased latencies of the early components of the trigeminal reflexes are correlated with specific sites of neurovascular compression along trigeminal root circumference discloses its somatotopic organization.
Disclosure: Nothing to disclose.

OPR-014 | Endogenous pain control mechanisms during the migraine cycle and in chronic migraine with/without medication overuse

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Background and aims: The offset analgesia (OA) phenomenon refers to the disproportionately large decrease in the perceived pain following a slight decrease in intensity of a noxious warm stimulus. This is considered as expression of activation of the endogenous pain-modulation system, whose dysfunction is could be involved in the pathophysiology of episodic migraine (EM) and chronic migraine (CM) with or without medication overuse (MO).
Methods: We enrolled 67 subjects with EM (in different phases of the migraine cycle), 30 patients with CM with/without MO, and 30 healthy controls. All subjects underwent an experimental paradigm consisting of 3 stimulus offset trials (OT) and 3 constant temperature trials (CT) at the level of the supraorbital region. Visual analogue scale (VAS) values were recorded during the OT and CT.
Results: Interictal EM patients and CM patients with MO did not show the OA phenomenon. A paradoxical pronociceptive facilitation during the offset trial was observed in the CM group without MO and in the preictal and ictal EM subjects. The OA phenomenon was restored in in the postictal phase. Only in patients with CM with MO we observed lack of adaptation to pain during the CT. The magnitude

of VAS changes during the offset trials negatively correlated with scores at 12-item Allodynia Symptom Checklist, migraine disability assessment (MIDAS), and depression section of the Hospital Anxiety and Depression Scale (HADS).

Conclusion: A dysfunction in the endogenous pain-modulation system may play a role in the recurrence of migraine attacks and in the process of migraine transformation from episodic to chronic pattern.

Disclosure: none.

OPR-015 | Cortical inflammation in migraine measured with quantitative magnetic resonance imaging: A REFORM study

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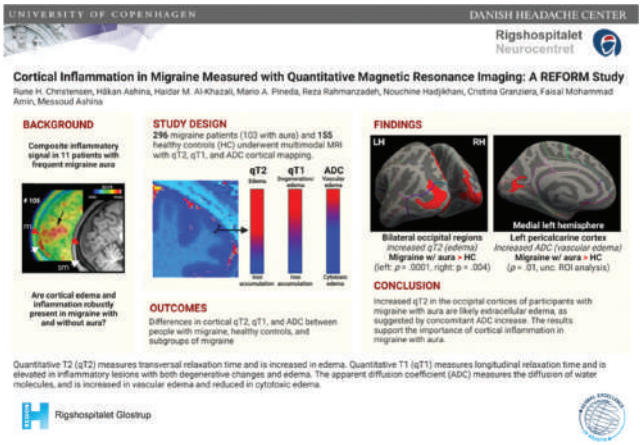
Background and aims: We aimed to investigate cortical inflammation using a novel quantitative, multimodal magnetic resonance imaging (MRI) technique in adult participants with migraine compared to age- and gender-matched healthy controls.

Methods: Participants underwent a single MRI session. Cortical quantitative T2 (qT2), quantitative T1 (qT1), and ADC values, considered surrogate markers of neuroinflammation, were measured in the cortical ribbon and compared between participants with migraine (with and without aura) and healthy controls. A general linear model was used with a vertex-wise threshold of $p<0.05$ and a cluster-wise threshold of $p<0.05$, adjusted for age and gender.

Results: A total of 296 participants with migraine (103 with aura and 180 with chronic migraine) and 155 age and gender matched healthy controls were included in the analysis. Participants with migraine had increased qT2 in the left occipital cortex compared to healthy controls ($p<0.0001$). In participants with migraine with aura, the increased qT2 was more widespread and located bilaterally in the occipital cortices compared to healthy controls (left, $p<0.0001$; right, $p=0.004$). Exploratory analysis revealed higher ADC values within the qT2 clusters in participants with migraine with aura than in controls ($p=0.01$). No significant differences were observed in qT1 values between the two groups.

Conclusion: Cortical inflammation is more prevalent in migraine with aura than in migraine without aura. The increased qT2 values in the occipital cortices of participants with migraine with aura are likely extracellular edema, as suggested by the concomitant ADC increase. These results support the importance of cortical inflammation in migraine pathogenesis, particularly in migraine with aura.

Visual abstract.



Disclosure: The study was funded by the Lundbeck Foundation Professor Grant (R310-2018–3711). Funding sources had no influence on study design, patient inclusion, or data interpretation. H.A. reports personal fees from Teva, outside of the submitted work. C.G. is supported by: The University Hospital Basel (USB), as the employer of Cristina Granziera has received the following fees, which were used exclusively for research support: (i) advisory board and consultancy fees from Actelion, Novartis, Sanofi-Genzyme, Jannsen, and F. Hoffmann-La Roche; (ii) speaker fees from Biogen, F. Hoffmann-La Roche, Novartis, Jannsen, and Genzyme-Sanofi; (iii) research support by F. Hoffmann-La Roche. F.M.A. has received personal fees from Pfizer, Teva, Lundbeck, Novartis, Eli Lilly, outside of the submitted work. M.A. is a consultant, speaker, or scientific advisor for AbbVie, Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva and a primary investigator for ongoing AbbVie/Allergan, Amgen, Eli Lilly, Lundbeck, Novartis, and Teva trials. Messoud Ashina has no ownership interest and does not own stocks of any pharmaceutical company. Messoud Ashina serves as associate editor of Cephalalgia, associate editor of the Journal of Headache and Pain, and associate editor of Brain. R.C., H.M.A., M.O-P., R.R., and N.H. report no relevant conflicts of interest.

Motor neurone diseases 1

OPR-016 | Peripherin: A novel early diagnostic and prognostic biomarker in Amyotrophic Lateral Sclerosis

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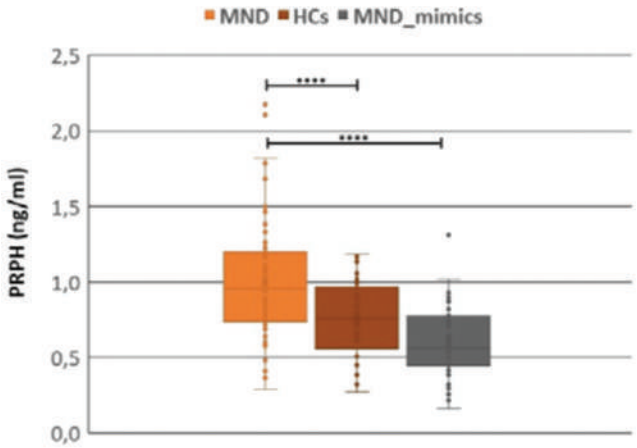
Background and aims: motor neuron diseases (MND) are complex and heterogeneous neurodegenerative diseases. Biomarkers could help in early diagnosis, in defining patients' prognosis, and stratification. The most studied and promising biomarkers are neurofilaments (Nfs). A particular type of Nfs is peripherin, mainly expressed in neurons of the peripheral nervous system. There are no studies in literature led in humans evaluating peripherin in plasma.
Methods: sandwich-ELISA was used to quantify plasma peripherin from 120 ALS MND (including 12 ALS/FTD and 10 PLS), 9 HSP, 46 MND-mimics (including myelopathy, radiculopathy, axonal neuropathies, Hirayama disease, IBM, benign fasciculation syndrome, functional syndrome, myasthenia, post-polio syndrome) and 38 healthy-controls (HCs). Plasma was collected at the time of diagnosis or some months earlier. 46 ALS were evaluated longitudinally. ALSFRSr, MRC, spirometry, genetic tests, disease progression rate (PR), blood examinations, neuropsychological tests were performed. We analysed data using Kruskal–Wallis, ANCOVA and Cox regression analysis.
Results: peripherin plasma levels is different between groups ($p < 0.0001$); Bonferroni's correction shows higher levels of peripherin in MND compared to MND-mimics and HCs. Comparing ALS with PLS and HSP peripherin resulted to be higher ($p < 0.001$). Differences are confirmed co-variating for age and sex. ROC curve shows a good capability of peripherin to discriminate MND from MND mimics (AUC = 0.79).



Peripherin levels in MND, MND-mimics and healthy controls.

Conclusion: peripherin plasma levels result to be increased in MND (in particular in classic ALS) compared to MND mimics since the early phases of the disease. Further multicentre studies, testing together other fluid biomarkers, are needed to better explain role of peripherin in diagnosis and prognosis in MND.
Disclosure: Nothing to disclose.

OPR-017 | Rate of change in upper and lower motor neuron burden is associated with survival and in amyotrophic lateral sclerosis

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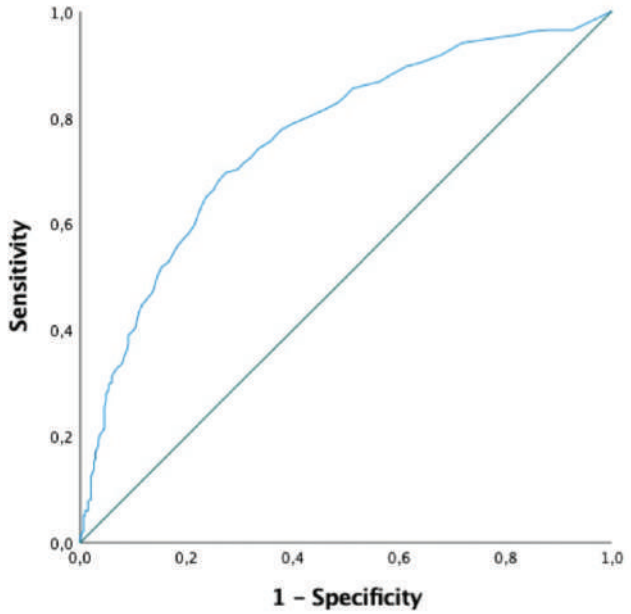
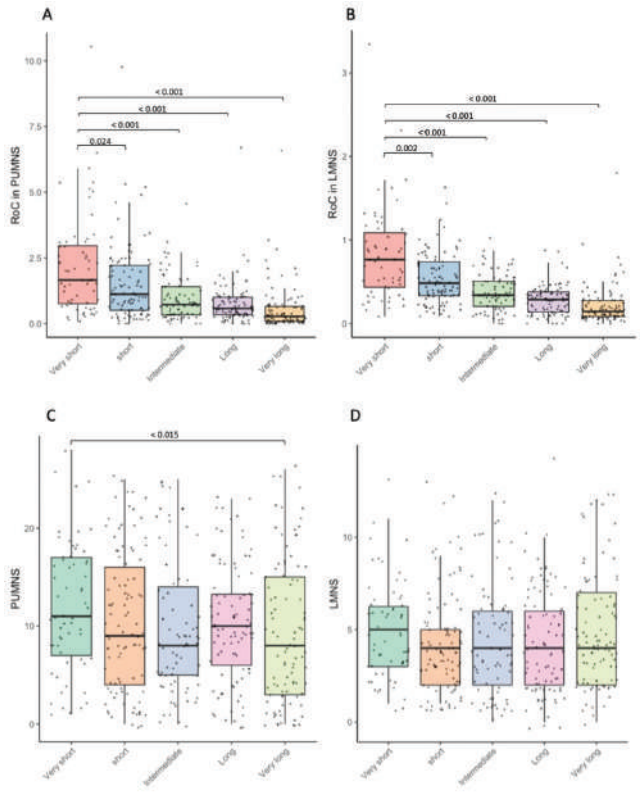
Background and aims: The role of upper (UMN) and lower motor neuron (LMN) involvement in amyotrophic lateral sclerosis (ALS) has been extensively studied in relation to clinical phenotype and survival. Conversely, it is not known whether the rate of change in UMN (ΔUMN) and LMN (ΔLMN) signs provides useful information on ALS evolution.
Methods: A retrospective inpatient cohort of 1000 ALS patients was evaluated. Burden of UMN and LMN signs was assessed using the Penn Upper Motor Neuron Score and Lower Motor Neuron Score, respectively. The time interval between symptom onset and first evaluation was used to quantify ΔUMN and ΔLMN values. Survival, time from symptom onset to percutaneous endoscopic gastrostomy (PEG), and to non-invasive ventilation (NIV) were used as outcome measures. For a subset of patients, we compute the ENCALS survival model.
Results: ΔUMN and ΔLMN values are negatively associated with survival (ΔUMN: HR = 1.30; ΔLMN: HR = 4.22) time to PEG (ΔUMN: HR = 1.34; ΔLMN: HR = 4.46) and time to NIV (ΔUMN: HR = 1.23; ΔLMN: HR = 5.0). A cut-off value of 0.195 for ΔLMN was identified to predict patients with estimated short vs. prolonged survival. ENCALS groups characterized by shorter survival were significantly associated with higher ΔUMN and ΔLMN scores when compared to those with longer survival.

	Exp(B)	95,0% inferior CI	95,0% superior CI	p value
Age at onset	1,039	1,028	1,05	<,001
Site of onset	1,136	0,871	1,482	0,348
ΔFS	1,43	1,221	1,675	<,001
C9orf72 hexanucleotide expansion	0,374	0,247	0,567	<,001
RoC in PUMNS	1,016	0,936	1,102	0,707
RoC in LMNS	2,537	1,791	3,594	<,001

Multivariate Cox regression investigating the effect of RoC in LMNS and PUMNS after adjusting for variables that are known to be associated with survival in ALS.



ROC curve illustrating the reliability of variable RoC in LMNS in predicting patients with short (survival <36 months) vs. prolonged (survival >36 months) survival.



Distribution of RoC in PUMNS (A), RoC in LMNS (B), PUMNS (C) and LMNS (D) among different ENCALS survival groups.

Conclusion: ΔUMN and ΔLMN might represent reliable clinical indexes to estimate disease evolution and survival in ALS patients. Indeed, these two measures provide distinct clinical information in addition to that derived from the total burden of UMN and LMN signs at first evaluation.

Disclosure: Alessio Maranzano, Francesco Gentile, A. Doretti, Eleonora Colombo, Aoife Wall, Mauro Treddenti, Valerio Patisso, Alberto De Lorenzo, Claudia Gendarini, Claudia Maria Cinnante, Claudia Morelli, Stefano Messina, Federico Verde report no disclosure. Vincenzo Silani received compensation for consulting services and/or speaking activities from AveXis, Cytokinetics, Italfarmaco, LiquidWeb, Srl and Novartis Pharma AG. He receives or he has received research support from the Italian Ministry of Health, AriSla, and E-Rare Joint Translational Call. He is on. the Editorial Board of Amyotrophic Lateral Sclerosis and Frontotemproal Degeneration, European Neurology, American Journal of Neurodegenerative Disease and Frontiers in Neurology. Nicola Ticozzi received compensation for consulting services from Amylyx Pharmaceutical and Zambon Biotech SA. He received research funding from the Italian Ministry of Health and AriSLA. He is associate editor of Frontiers in Aging Neuroscience.

OPR-018 | Circulating endocannabinoid signatures of disease activity in amyotrophic lateral sclerosis

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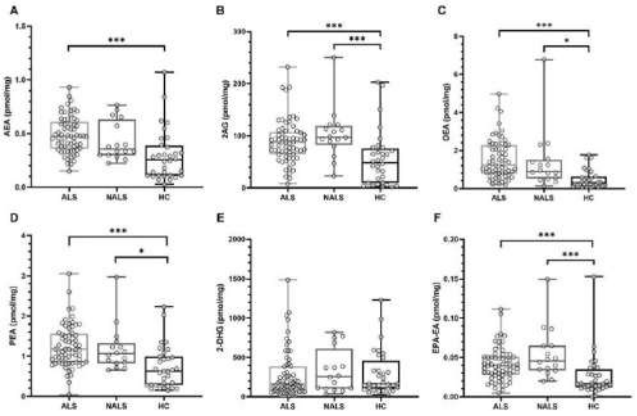
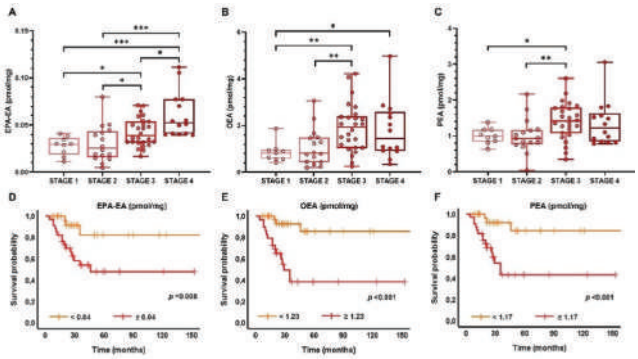
[2]*Endocannabinoid Research Group, Institute of Biomolecular Chemistry (ICB), National Research Council (CNR), Pozzuoli, Italy*

Background and aims: Evidence from the preclinical model of amyotrophic lateral sclerosis (ALS) has consistently demonstrated altered levels of circulating endocannabinoids (eCBs) that may contribute to disease activity and course. Results from human studies are sparse and inconclusive. Main aim of this study was to determine the association between eCB levels and disease activity in patients with ALS.
Methods: Serum concentrations of the eCBs 2-arachidonoylglycerol (2-AG) and N-arachidonoylethanolamine (AEA), and related lipids palmitoylethanolamine (PEA), oleoylethanolamine (OEA), eicosapentaenoyl-ethanolamide (EPA-EA), 2-docosahexaenoyl-glycerol (2-DHG) and docosahexaenoyl-ethanolamide (DHA-EA) were measured in samples from 65 ALS patients, 32 healthy controls (HC) and 16 neurological disease controls (NALS). Moreover, 46 ALS patients underwent a longitudinal study. Disease activity and progression were correlated with eCBs levels.
Results: Circulating eCBs were higher in ALS than in HC ($p < 0.001$), but not compared to NALS. Across clinical stages, ALS patients showed increased levels of PEA, OEA, and EPA-EA ($p < 0.02$), which were confirmed by the longitudinal study ($p < 0.03$). Serum PEA and OEA levels were independent predictors of survival and OEA was higher in patients complaining of appetite loss. Cluster analysis revealed two distinct profiles of circulating eCBs associated with two

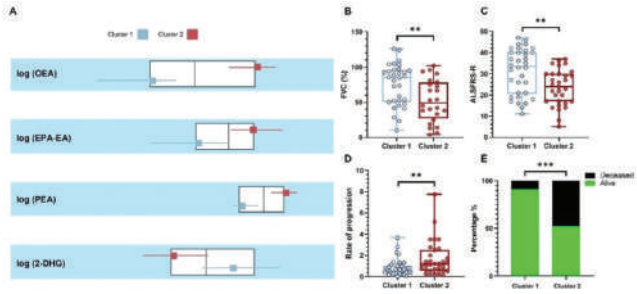
patterns of disease activity (severe vs. mild). Patients belonging to the "severe" cluster showed significantly higher levels of OEA and lower levels of 2-DHG compared to NALS and HC.



Comparison of circulating eCBs levels among the three groups: ALS, NALS and HC.



Circulating eCBs levels across ALS clinical stages and their association with survival.



Cluster analysis of circulating eCBs and clinical correlates of cluster membership.

Conclusion: Specific circulating eCBs profiles are indicative of different disease activities. This study paves the way for an individually-designed rather than a "one-fit-all" targeting the eCB system for therapeutic purposes.

Disclosure: Nothing to disclose.

OPR-019 | Skin innervation across ALS clinical stages: New biomarkers of disease progression and survival

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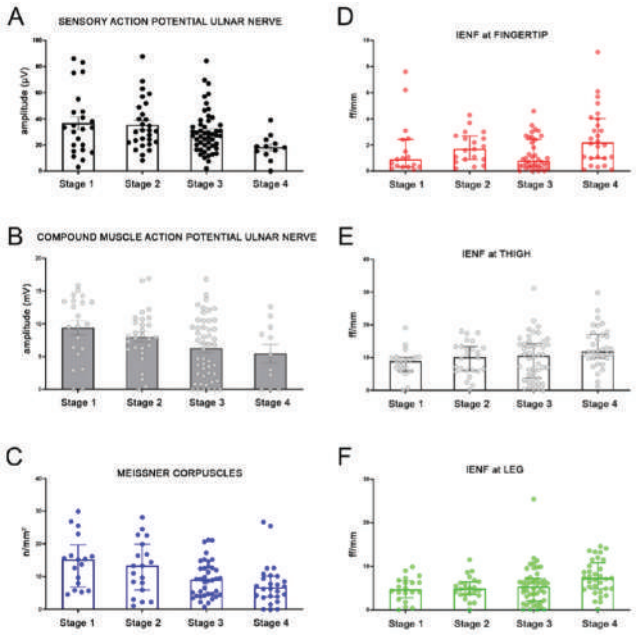
[1]*Department of Neurosciences, Reproductive Sciences and Odontostomatology, University of Naples Federico II, Naples, Italy;* [2]*Istituti Clinici Scientifici Maugeri IRCCS, Skin biopsy lab, Neurological Rehabilitation Unit of Telese Terme Institute, Telese Terme, Italy*

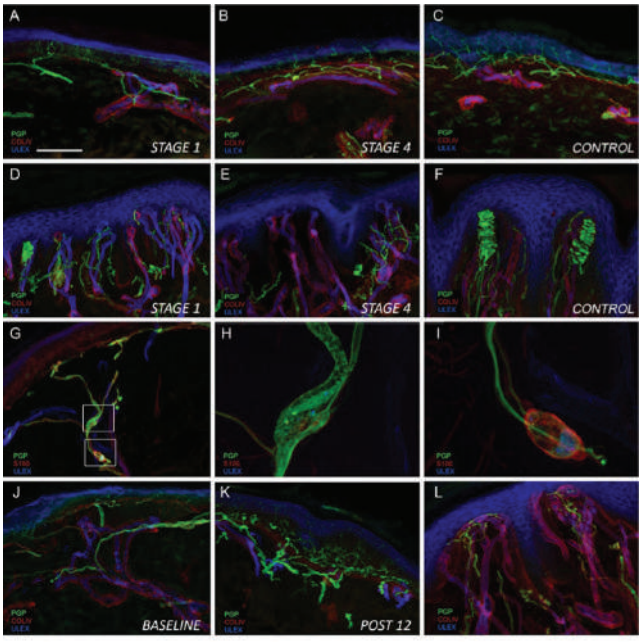
Background and aims: Aims of this study were to assess sensory involvement by applying a morpho-functional approach on a large population of ALS patients stratified according to King's stages and to correlate these findings with the severity and prognosis of the disease.

Methods: We recruited 149 ALS patients and 41 healthy controls (HC). Patients underwent clinical questionnaires, nerve conductions studies (NCS) and 3 mm-punch skin biopsy from leg, thigh and fingertip. We assessed intraepidermal nerve fibers (IENF) and Meissner corpuscles (MC) density by applying indirect immunofluorescence technique. Moreover, a subset of 65 ALS patients underwent a longitudinal study with repeated skin biopsies. Serum Neurofilament light chain (NfL) levels were measured in 40 patients.

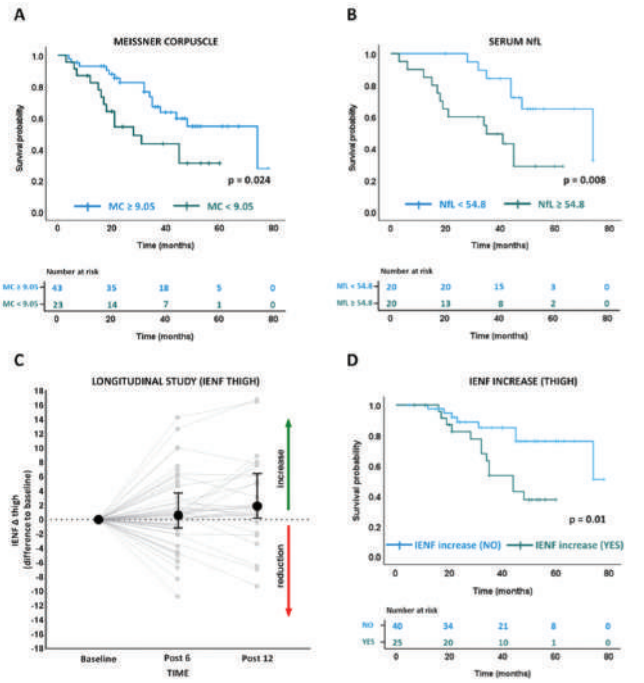
Results: Sensory symptoms and sensory NCS abnormalities were present in 32.2% and 24% of patients, respectively, and increased across clinical stages. Skin biopsy showed a significant loss of IENF and MC in ALS compared with HC (all $p<0.001$). Across the clinical stages, we found a progressive reduction in MC ($p=0.004$) and an increase in IENF (all $p<0.027$). Interestingly, the MC density inversely correlated with NfL level ($r=-0.424$, $p=0.012$), and survival analysis revealed that low MC density, higher NfL levels, and increasing IENF over time were associated with a poorer prognosis (all $p<0.024$).



Morpho-functional assessment of peripheral nerve fibers across ALS clinical stages Bar dot plots showing (A) a significant reduction from King's stage 1 to stage 4 in the sensory nerve action potential (SNAP) recorded from the fifth finger ($p = 0.034$)



Cutaneous innervation across King's ALS clinical staging and in the longitudinal study. Confocal images of punch biopsies from hairy and glabrous skin in ALS patients (A, B, D, E, G, H, J, K, L) versus controls (C and F). Green, nerve fibres; blue, epide.



Kaplan–Meier survival curves based on morphological and NfL data, and skin biopsy longitudinal study Kaplan–Meier curves of survival probability among ALS patients stratified by median value of (A) Meissner corpuscles (MC) density (*n*/mm2), (B) serum neuro.

Conclusion: In patients with ALS, peripheral sensory involvement worsens in parallel with motor disability. Furthermore, the correlation between skin innervation and disease activity may suggest the use of skin innervation as a putative prognostic biomarker.
Disclosure: Nothing to disclose.

Peripheral nerve disorders

OPR-020 | Heterogeneous real-life strategies in therapeutic approach of chronic inflammatory demyelinating polyradiculoneuropathy

A. De Lorenzo[1]; P. Doneddu[2]; F. Manganelli[3]; D. Cocito[4]; R. Fazio[5]; A. Mazzeo[6]; A. Schenone[7]; C. Briani[8]; V. Di Stefano[9]; M. Filosto[10]; G. Marfia[11]; G. Cosentino[12]; A. Clerici[13]; G. Antonini[14]; L. Benedetti[15]; G. Piscosquito[16]; M. Carpo[17]; G. Lauria Pinter[18]; G. Siciliano[19]; G. Cavaletti[20]; M. Lucchetta[21]; T. Rosso[22]; M. Luigetti[23]; M. Inghilleri[24]; E. Nobile-Orazio[25]
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Background and aims: Despite the existence of therapeutic recommendations in the 2010 EFNS/PNS and 2021 EAN/PNS guidelines for managing Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP), the sequence of therapy to be used remains unsettled.

Methods: A comparative analysis was conducted, examining therapeutic strategies and responses in 524 CIDP patients from tertiary referral centers included in a large national database.

Results: Intravenous immunoglobulins (IVIg) emerged as the most commonly used first-line therapy (53%), followed by steroids (33%) and plasmapheresis (3%). A consistent proportion of patients (8%) received combined first-line therapy with IVIg and steroids or (3%) monotherapy with immune suppressants. In acute-onset CIDP, IVIg and plasmapheresis were often used. There were also differences in relation to the early or late age at onset and to CIDP variants. Immune suppressants were often used as maintenance monotherapy (10%). There was a substantial variability among different centers in the choice of first- and second-line therapy, number of therapies performed, use of immunosuppressants and subcutaneous immunoglobulin (SCIg). A consistent proportion of patients responded to IVIg (86%) or steroid (85%) when used as second line therapy and only 7% of the patients failed to respond to two first-line therapies. There was no distinctive features between responder and not responder patients beside a more frequent ataxia at onset and greater disability at enrollment.

Conclusion: The absence of specific indications from guidelines may explain the notable heterogeneity in the therapeutic choice in CIDP patients. Therapeutic response significantly decreases after two failed attempts, but the identification of non-responders remains challenging.

Disclosure: Nothing to disclose.

OPR-021 | Serum neurofilament light chain as a biomarker in Guillain-Barré syndrome: Origin and prognostic value

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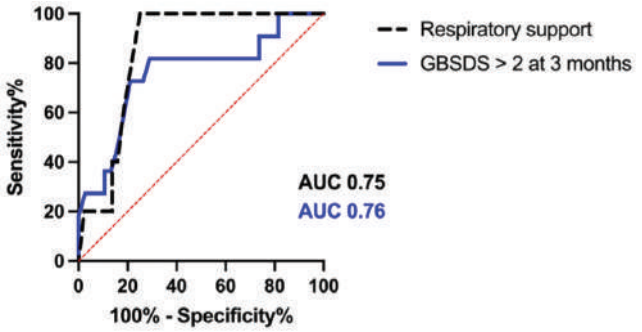
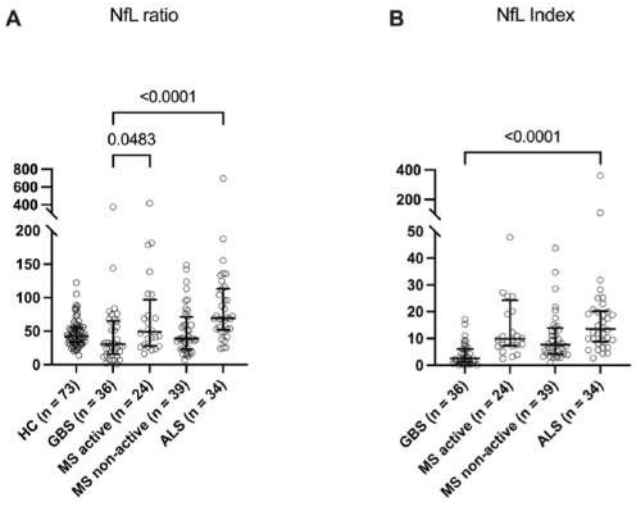
Background and aims: Our objective was to determine the origin serum neurofilament light chain (sNfL) and the utility of the sNfL Z-score, NfL ratio and NfL index as prognostic biomarkers in Guillain-Barré syndrome (GBS).

Methods: We included 96 patients with GBS between 1989 and 2014 in Western Sweden. Outcome measures were GBS disability scale (GBSDS) at 3 and 12 months and the need of respiratory support. Receiver operator characteristics curves were calculated for sNfL Z-score for the risk of respiratory support and GBSDS >2 at 3 months. NfL ratio and NfL index were compared with healthy controls (HC), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS).

Results: The sNfL Z-score was higher for respiratory support (median 3.7, IQR 3.2–4.0 vs. median 2.7, IQR 1.6–3.5), GBSDS >2 at 3 months (median 3.5, IQR 3.2–4.0, vs. median 2.6, IQR 1.7–3.4) and 12 months (median 3.6, IQR 3.5–3.8, vs. median 2.6, IQR 1.8–3.5). No association was seen between NfL ratio or index and outcome. The area under the curve for the sNfL Z-score was 0.75 (95% CI 0.61–0.89) for respiratory support and 0.76 (95% CI 0.58–0.93) for GBSDS >2 at 3 months. The NfL ratio and index were lower in GBS than HC, MS, and ALS.



ROC curves for sNfL Z-score. AUC for GBSDS >2 at 3 months was 0.76 (95% CI 0.59–0.93, $p = 0.009$). AUC for respiratory support 0.75 (95% CI 0.61–0.89, $p = 0.004$). ROC = receiver operator characteristics; AUC = area under curve.



(A) NfL ratio in healthy controls (HC), Guillain-Barré syndrome (GBS), multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS). (B) NfL index in GBS, MS and ALS presented as median, interquartile range and individual values. The columns represent.

Conclusion: The sNfL Z-score at onset is a promising predictive biomarker for prognosis in GBS. Our results suggest that peripheral nerves are a significant contributor to sNfL in GBS.

Disclosure: The study was supported by grants from the Swedish State Support for Clinical Research (ALFGBG-722081), NEURO Sweden, NEURO Gothenburg, the Edit Jacobson Foundation, the Rune and Ulla Amlövs Foundation for Neurological Research, the MS Research Foundation of the Swedish MS Society, the Gothenburg Society of Medicine, and grants from Berit Linnea and Ragnar Bakken Foundation. Henrik Zetterberg has served at scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, Alzinova, ALZPath, Annexon, Apellis, Artery Therapeutics, AZTherapies, CogRx, Denali, Eisai, Nervgen, Novo Nordisk, Optoceutics, Passage Bio, Pinteon Therapeutics, Prothena, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures in symposia sponsored by Cellectricon, Fujirebio, Alzecure, Biogen, and Roche, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program (outside submitted work) Jan Lycke has received travel support and/or lecture honoraria and has served on scientific advisory boards for Amgen, Almirall, Biogen, Bristol Myers Squibb, Celgene, Genesis Pharma, Janssen, Merck, Novartis, Roche, Sanofi and Sandoz; and has received unconditional research grants from Biogen and Novartis, and financial research support from Sanofi.

OPR-022 | Activin-IIB-receptor inhibition prevents muscle atrophy and hastens motor recovery in experimental autoimmune neuritis

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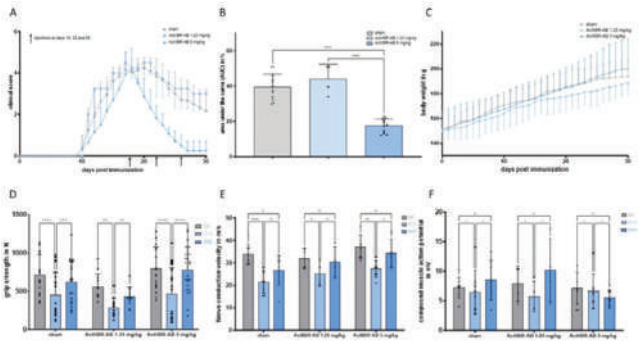
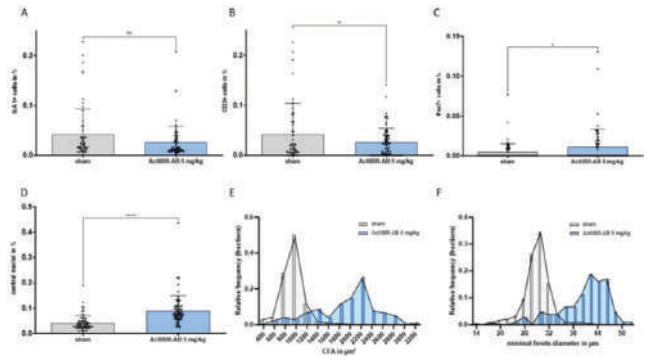
Background and aims: Muscle atrophy due to neuronal denervation is a significant determinant of the functional outcome in immune-mediated neuropathies after cessation of autoinflammation. Activin-IIB receptors (ActIIBR) are critically involved, and the blockade of these receptors has recently been explored in primarily degenerative muscular diseases. We examined the potential of ActIIBR blockade on motor recovery in the experimental autoimmune neuritis (EAN) animal model.

Methods: EAN was induced using myelin P253-78 protein in female Lewis rats. With the beginning of the recovery phase at day 18 post immunization, rats were treated with either sham, 1.25 mg/kg body weight, or 5 mg/kg body weight of a synthesized ActIIBR antibody subcutaneously every fourth day. Functional motor outcome was assessed using a neuritis score, grip strength, and balance beam paired with cinematic tracing until day 30. Nerve conduction studies, histological analyses of the sciatic nerve and the tibialis anterior muscle, real-time PCR, and muscle proteomics were performed.

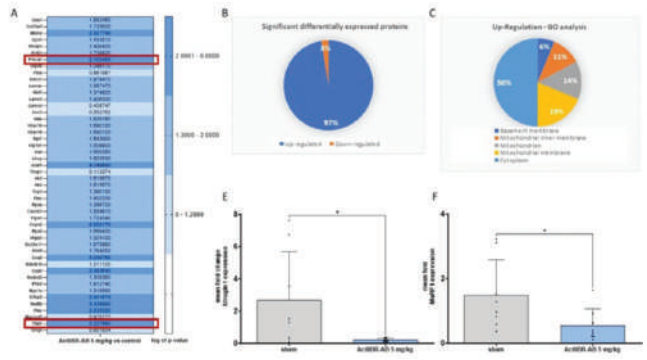
Results: Treatment with 5 mg/kg ActIIBR-antibody ameliorated EAN severity at day 30 (p-value: <0.0001). The grip strength nearly returned to baseline. No group differences were seen for nerve conduction studies and cellular inflammation in the sciatic nerve. Histologically, an increased cross-sectional area and ferret's diameter were observed. Muscle proteomics indicated alteration of the pAKT pathway, leading to a reduced expression of Atrogin1- and MuRF1 (p-values: 0.014 and 0.038).



Treatment with 5 mg/kg of the ActIIBR antibody enhances functional recovery after EAN.



ActIIBR inhibition prevents muscle atrophy and induces muscle hypertrophy without affecting cellular inflammation of the sciatic nerve.



Proteomics and real-time PCR analysis of the tibialis anterior muscles revealing reduced muscle degradation by downregulation of Atrogin-1 and MuRF-1 via ActIIBR-inhibition.

Conclusion: Blockade of the ActIIBR prevents muscle atrophy via Atrogin-1 and MuRF-1 downregulation, thereby hastening motor recovery in EAN. Further studies are warranted to investigate the role of ActIIBR blockade in autoimmune neuropathy.

Disclosure: FK was supported by the Cologne Clinician Scientist Program (CCSP), Project No. 413543196. I. Gerlach, I. Klein, M. Koch, G. R. Fink, G. Gatto, H.C. Lehmann and M. Schroeter reported no disclosures related to this study.

OPR-023 | Intracutaneous amyloid deposition predicts ulterior nerve conduction studies deterioration in ATTRv carriers

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Background and aims: Hereditary transthyretin amyloidosis (ATTRv) is an autosomal dominant systemic disease, leading to harmful tissue protein deposition, mainly in the heart and nerves, with an overall poor prognosis. While new disease-modifying treatments are being developed, it appears crucial to find markers of disease onset and progression for optimal timing in treatment initiation. Nerve conduction studies offer an objective, reproducible and non-invasive although late mean of following large nerve disease.

Methods: We studied 107 ATTRv carriers with normal nerve conduction studies (NCS) and sought to find elements predictive of ulterior NCS decline, defined as a 20% decrease of the average of the bilateral sural and fibular sensory nerve action potential (SNAPs).

Results: During a median follow-up of 5 years, 15/107 (14%) carriers presented a NCS deterioration. On univariate analysis, intracutaneous amyloid deposition (ICAD) (HR = 10.8, 95% CI(3.1 to 34.5), $p < 0.0001$) and difference of age with age of disease onset in proband (HR = 1.1, 95% CI(1.0 to 1.1), $p = 0.002$) were significantly associated with ulterior NCS decline. After multivariate analysis, skin amyloid deposition remained significantly and strongly associated with further worsening (HR = 10.3, 95% CI (2.4 to 45.5), $p = 0.0014$). EOVal30Met genotype, presence at baseline of cardiac denervation, skin denervation, an interventricular septum thickness superior to 12 mm, abnormal short-term heart rate variability, abnormal SUDOSCAN or neurological physical examination were not significantly associated with electric deterioration on univariate testing.

Conclusion: ATTRv carriers with intracutaneous amyloid deposition at initial evaluation were more likely to present NCS deterioration during follow-up compared to those without. Search of ICAD should be recommended during follow-up of asymptomatic carriers.

Disclosure: Nothing to disclose.

OPR-024 | Neuropathy in anti-MAG+/− IgM gammopathy: Population analysis and evaluation of old and innovative severity measures

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Background and aims: IgM Monoclonal Gammopathy (IgM-MG) often coexists with peripheral polyneuropathy. Distal demyelinating polyneuropathy (DADS) with anti-MAG antibodies is the best-known variant. Lack of appropriate endpoints poses challenges in assessing treatment efficacy. We provide a thorough clinical and paraclinical characterization of 38 anti-MAG+/– subjects with IgM-MG and evaluate various traditional and innovative measures of disease severity.

Methods: Participants underwent detailed collection of haematological, neurological, and therapeutic history, anti-MAG reactivity testing, and extensive electrodiagnostic assessment including Terminal Latency Index (TLI) determination. A broad clinical evaluation comprised multiple scales (mRS, ONLS, Berg Balance Scale, INCAT-SS, IRODS), functional tests (9-holes peg test, grip strength determination, 10-metres and 2-minutes walking test), and the EuroQoL questionnaire. A balance assessment was performed through posturography (i.e. the tracking of a standing subject's centre-of-gravity movement).

Results: 24 subjects exhibited anti-MAG reactivity, with 21 displaying electrodiagnostic signs of demyelination. Of the 14 seronegative individuals, one showed electrodiagnostic signs consistent with DADS. TLI reduction was found in at least some nerve in many demyelinating cases, but it was frequently unassessable due to nerve inexcitability or entrapment. Attached charts illustrate the performance of each assessment as a measure of disease severity.

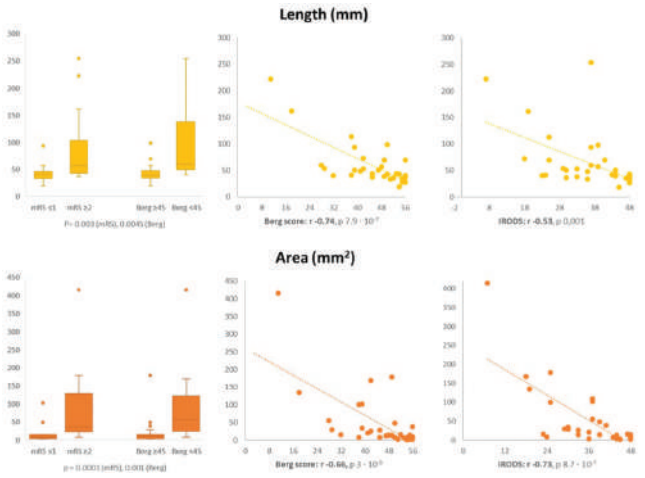
	mRS 1 n = 20 mean age 71.6 y	mRS = 2 n = 10 mean age 76.4 y	mRS = 3 n = 7 mean age 77.7 y	p	Berg >45 n = 21 mean age 69.5 y	Berg ≤45 n = 16 mean age 79.75 y	p
IRODS	44.1	31.2	22.7	$4 \cdot 10^{-6}$	42.8	26.8	$1.2 \cdot 10^{-5}$
Berg	51.9	37.4	33.3	$1.5 \cdot 10^{-5}$	52.2	31.4	//
INCAT-SS	5.3	5.6	9.4	0.18	5.2	8.25	0.43
ONLS	1.9	3.5	4.6	$1.4 \cdot 10^{-3}$	1.95	4.3	$1.4 \cdot 10^{-4}$
Grip (kPa)	68.4	52.5	41.9	$3.2 \cdot 10^{-5}$	68.9	45.3	$7.4 \cdot 10^{-4}$
9HPT (s)	30.6	36.6	81	$2 \cdot 10^{-3}$	31.5	55.9	$4.8 \cdot 10^{-3}$
10MWT (s)	4	8	7.6	$2.1 \cdot 10^{-5}$	4.2	7.7	$8.2 \cdot 10^{-5}$
2MWT (m)	168.6	111.9	96.4	$5.2 \cdot 10^{-5}$	167.4	101.8	$1.3 \cdot 10^{-3}$
H100 (0-100)	74.2	52.7	59.3	0.05	71.1	56.7	0.082
Leght, OE (mm)	44.1	76.1	99.9	0.011	43.9	77.6	$4.5 \cdot 10^{-3}$
Area, OE (mm^2)	15.6	55.4	125	$4.9 \cdot 10^{-4}$	21	81.8	$1.4 \cdot 10^{-3}$
Lenght, CE (mm)	80.6	237.9	240	$7.1 \cdot 10^{-6}$	81.8	250.8	0.018
Area, CE (mm^2)	58.1	171.2	332.6	$9.3 \cdot 10^{-3}$	65.9	231.3	0.053
Lenght RI	1.76	3.9	3.24	$7.1 \cdot 10^{-3}$	1.82	3.96	0.049
Area RI	5.67	4.96	6.61	0.35	6.03	5.11	0.93

IRODS: Inflammatory Rash-Built Overall Disability Scale. Berg: total Berg Balance Scale score. INCAT-SS: Inflammatory Neuropathy Cause and Treatment Sensory Sumscore. ONLS: Overall Neuropathy Limitations Scale. Grip: grip strength as measured with a Martin vigorimeter. 9HPT: 9-holes peg test completion time in seconds. 10MWT: ten-meters walking test. 2MWT: two-minutes walking test. H100: answer to the sixth question of the EuroQoL questionnaire (i.e. perceived health rated from 1 to 100). Length: total distance of the centre of gravity during a 10-seconds posturography. Area: a measure of the sway amplitude of the centre of gravity during posturography. OE: open eyes. CE: closed eyes. RI: Romberg Index (CE/OE). A Berg score of 45 or lower is predictive of a high risk of falls (Shumway-Cook et al., Physical Therapy, 1997).

Comparison of disease measures in subject stratified by mRS class (left) and by a Berg balance score value (right). A Berg score of 45 or lower is predictive of a high risk of falls (Shumway-Cook et al., Physical Therapy, 1997).

	IRODS		Berg balance scale	
	r	p	r	p
IRODS	1	//	0,825	$3.4 \cdot 10^{-10}$
BERG	0.825	$3.4 \cdot 10^{-10}$	1	//
INCAT	-0.53	$6.5 \cdot 10^{-4}$	-0,41	0.012
ONLS	-0.86	$4.3 \cdot 10^{-12}$	-0,76	$4.1 \cdot 10^{-8}$
Grip (kPa)	0.585	$1.15 \cdot 10^{-4}$	0,54	$5.5 \cdot 10^{-4}$
9HPT (s)	-0.66	$1.2 \cdot 10^{-5}$	-0,59	$2.3 \cdot 10^{-4}$
10MWT (s)	-0.76	$6.2 \cdot 10^{-8}$	-0,755	$1.05 \cdot 10^{-7}$
2MWT (m)	0.77	$5.7 \cdot 10^{-8}$	0,72	$1.05 \cdot 10^{-6}$
H100	0.31	0.056	0,14	0.39
Leght, OE (mm)	-0.53	$1.35 \cdot 10^{-3}$	-0,74	$7.9 \cdot 10^{-7}$
Area, OE (mm2)	-0.73	$8.7 \cdot 10^{-7}$	-0,66	$3 \cdot 10^{-5}$
Lenght, CE (mm)	-0.28	0.12	-0,54	$1.8 \cdot 10^{-3}$
Area, CE (mm2)	-0.52	$2.9 \cdot 10^{-3}$	-0,37	0.042
Lenght RI	-0.17	0.33	-0,5	$4.3 \cdot 10^{-3}$
Area RI	-0.1	0.58	0.09	0.65

Pearson correlation coefficient for each disease measure and IRODS (left) and Berg (right) scores.



Performance of the posturography measures “length” (above) and “area” (below) as disability indexes. Data for the “open eyes” test are shown.

Conclusion: The correlation between anti-MAG antibodies and “DADS” neuropathy is robust but not universal. TLI can help the diagnosis, but not every nerve will have an index <0.25 and its utility is limited by inexcitability or false positives due to median nerve entrapment at the wrist. Posturography emerges as a potential objective, quantitative outcome for future trials.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

OPR-025 | Prediction of the global functional outcome of intensive inpatient rehabilitation after stroke using machine learning

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Background and aims: Prognostic data-driven solutions could support the outcome prediction and, eventually, the optimisation of the rehabilitation pathway. We aimed at the development, cross-validation, and external validation of machine learning-based prognostic models for the prediction of the global functional outcome of patients undergoing intensive inpatient rehabilitation after stroke.
Methods: Patients addressing an evidence-based intensive inpatient rehabilitation pathway within 30 days from stroke from two multicentric prospective studies were enrolled. Data related to standardized comprehensive multidimensional assessment were collected and fed within the model for feature selection (figure 1). The outcome of interest was the modified Barthel Index(mBI) at discharge. Different algorithms were optimised, nested cross-validated, externally tested, and interpretability techniques were applied for the analysis of the contributions of predictors.

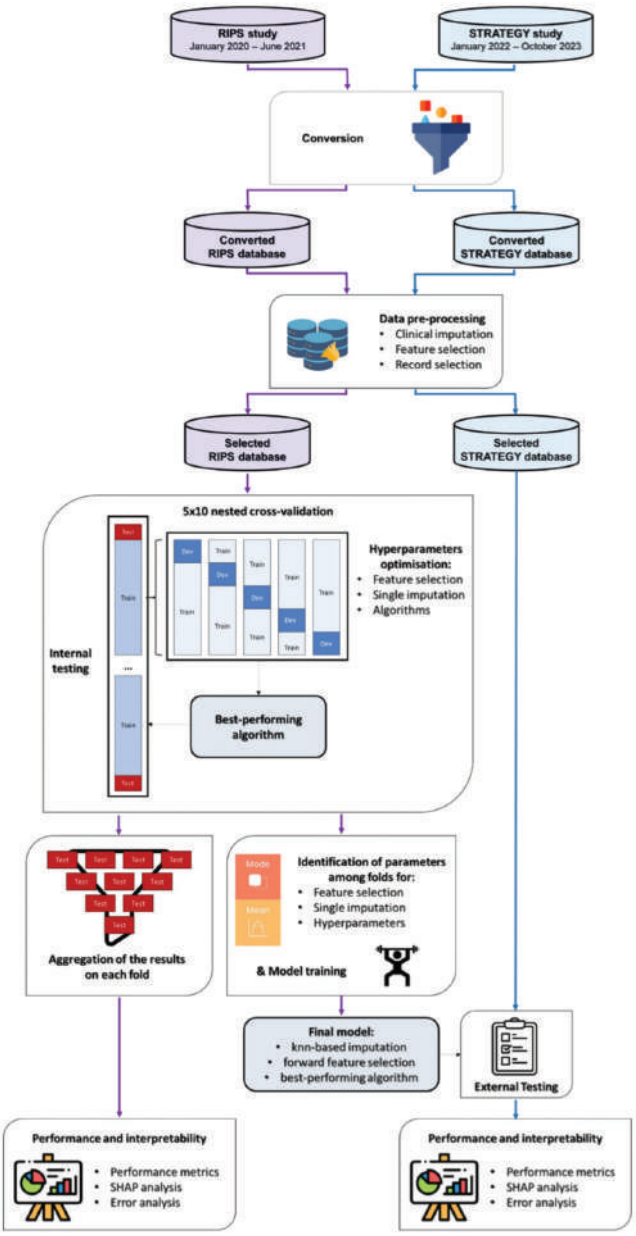

FIGURE 1 Analysis pipeline.

Results: Total numbers of 220 and 180 patients were considered for training and test sets, respectively (figure 2). Respectively a 50.9% and 56.7% of women, 79.5% and 78.9% of ischaemic, and a median [IQR] age of 80.0 [15.0] and 78.0 [17.0] were registered on the two datasets. The Support Vector Machine obtained the best validation performances and a median absolute error of 11.5 [15.0] and 9.2 [13.0] on the internal and external testing, respectively. The baseline variables providing with the main contributions to the predictions resulted in mBI, motor upper-limb score, age, and cognitive score (figure 3).

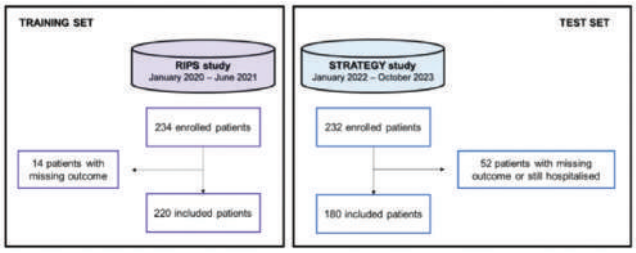

FIGURE 2 Flow chart of the study.

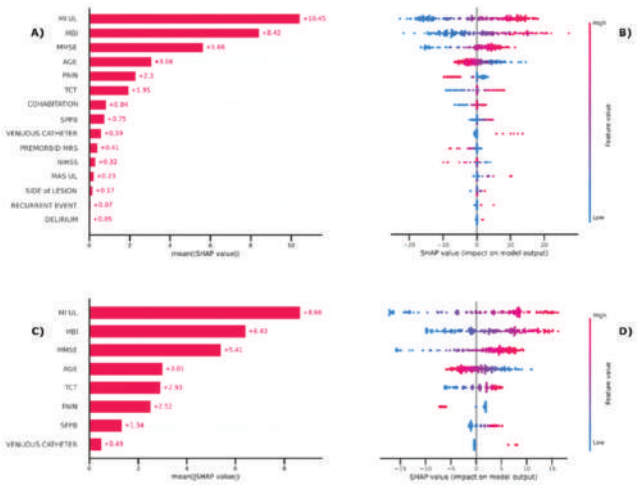

FIGURE 3 Contributions of the predictors to the outcome prediction aggregated among each fold. In panels A-C, bar plots of the global contributions are presented, whilst in panels B-D, beeswarm plots with patient-wise contributions are presented. The res.

Conclusion: Our results indicate the suitability of this solution for supporting clinicians in formulating a functional prognosis at the admission to intensive inpatient post-stroke rehabilitation and in promptly identifying features potentially predicting an unfavourable outcome.
Disclosure: Nothing to disclose.

OPR-026 | **In-hospital death matters: A machine learning approach to anterior circulation mechanical thrombectomy**

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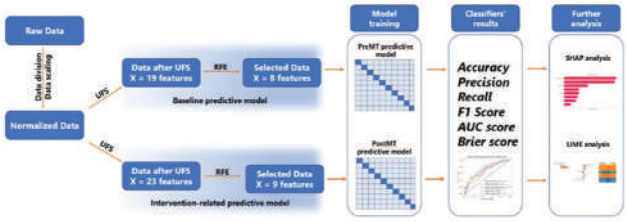
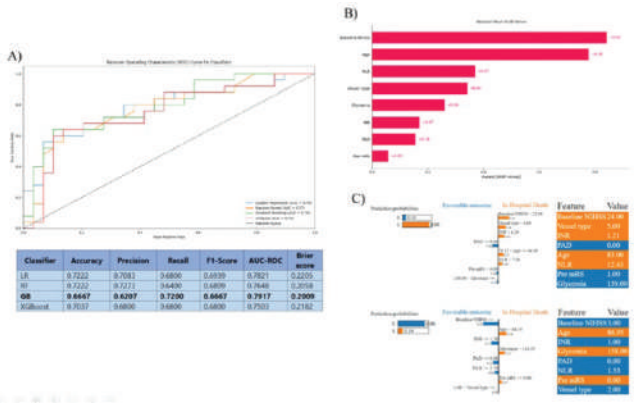
Background and aims: Although the popularity of mechanical thrombectomy (MT) has grown significantly in the past decade, there is still a literature gap concerning post-procedural in-hospital mortality, the main contributing factors, and the possibility of predicting it. The aim was to employ interpretable machine learning (ML), which could potentially aid in understanding existing ambiguities.
Methods: This retrospective study included 602 anterior circulation ischemic stroke patients who underwent MT. Patients were divided into two groups: (I) died ($n=133$), in which the fatal outcome occurred during the in-hospital stay, and (II) survived ($n=469$). Python 3.10.9 was used for the machine learning model build-up, and based on the input features, two models were constructed: (I) the preMT model, which consisted of baseline features, and (II) the postMT model, which included baseline and MT-related features. The ML models' training, internal evaluation, and performance testing followed feature selection. Interpretation frameworks explained the decision-making process.

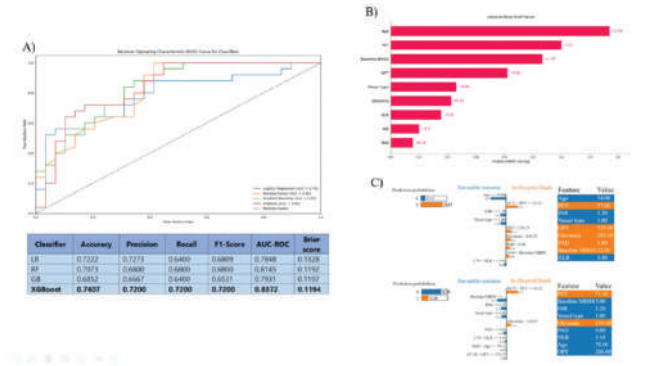


Summarized steps of the analysis. After a two-step process of feature selection, with univariate feature selection (UFS) as the first step, and Recursive Feature Elimination (RFE) as the second, models were trained, evaluated, and tested.

Results: For the preMT model (AUC = 0.792), selected features were age, baseline NIHSS value, neutrophil-to-lymphocyte ratio (NLR), INR, vessel type, peripheral arterial disease (PAD), baseline glycemia, and premorbid modified Rankin scale (pre mRS), while in the postMT model (AUC = 0.837), added features included puncture to procedure end time (PET), and onset to puncture time (OPT).



(A) Evaluation metrics of the preMT model and the receiver operating characteristic curves (ROCs) of 4 classifiers; (B) The SHAP (Shapley Additive Explanations) analysis graph; (C) Local Interpretable Model-Agnostic Explanations (LIME) plot.



(A) Evaluation metrics of the postMT model and the receiver operating characteristic curves (ROCs) of 4 classifiers; (B) The SHAP (Shapley Additive Explanations) analysis graph; C) Local Interpretable Model-Agnostic Explanations (LIME) plot.

Conclusion: To the best of our knowledge, this study represents a pioneer research that utilized interpretable models for predicting in-hospital death following anterior circulation MT. The constructed models need further extensive evaluation before they can be practically applied.

Disclosure: Nothing to disclose.

OPR-027 | Ethnic differences in access to care and treatment in patients with suspected acute stroke: A retrospective cohort study

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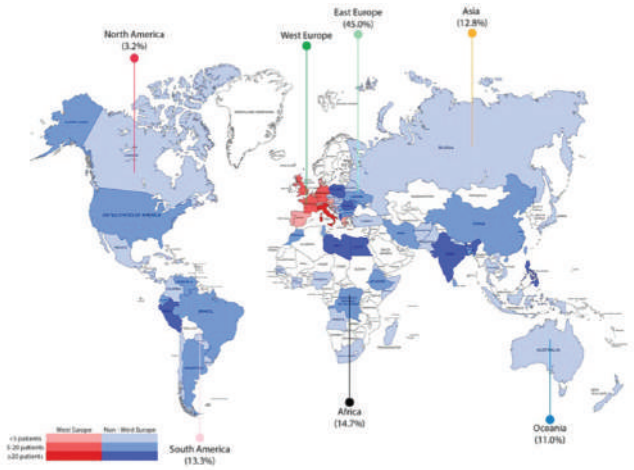
Background and aims: Data concerning unequal healthcare access of acute stroke patients based on ethnicity or race are inconclusive in Europeans. The primary objective was to evaluate the effect of geographic origin/race on access to acute stroke care and treatments. Secondly, we evaluated the effect of geographic origin/race on stroke risk factors, outcomes, and admission for stroke mimics.



A graphic representation of the geographical origin of the included population. The percentages refer to the number of patients from various continents compared to the total number of non-Western Europeans.

Methods: In this retrospective, cohort study, we enrolled adult patients admitted to the emergency department of a comprehensive stroke center for suspected stroke. Based on geographic origin, patients were divided into two groups: Western Europeans (WE) and non-Western Europeans (nWE). For each nWE subjects, we included four sex- and age-propensity score matched patients in the WE group. We then divided patients in three further subgroups (White/Black/Asian) based on race. Univariate comparisons were performed using Mann–Whitney, Kruskal-Wallis, and χ^2-tests, as appropriate. Logistic regression was used to perform the adjusted analyses.

Results: 618 patients were enrolled in the nWE group and 2444 in the WE group. Belonging to the nWE group is an independent predictor of lower likelihood of receiving intravenous thrombolysis ($p=0.005$). Considering Black/Asian/White subgroups, ED accesses for stroke mimics were less frequent among racial minority groups ($p=0.038$). Furthermore, Black and Asian individuals had a higher incidence of brain hemorrhages than Whites ($p=0.003$). No differences in stroke outcomes were found.

	OR (95% CI)	p-value
Non-Western EUs	0.531 (0.341–0.828)	**0.005**
Speech disorders	1.791 (1.264–2.536)	**0.001**
Motor impairment	1.903 (1.280–2.830)	**0.001**
Sensory impairment	0.747 (0.398–1.402)	0.363
Headache	0.597 (0.296–1.204)	0.150
Altered consciousness	0.935 (0.574–1.524)	0.788
Dizziness	0.231 (0.069–0.768)	**0.017**
NIHSS at admission	1,078 (1.056–1.101)	**<0.001**
Heart Failure	0.734 (0.432–1.248)	0.253
Previous stroke/TIA	2.055 (1.424–2.965)	**<0.001**
Solid cancer	0.273 (0.093–0.803)	**0.018**
Charlson Comorbidity Index	0.933 (0.850–1.024)	0.143

Abbreviations: OR, Odd Ratio; CI, Confidence Interval; EUs, Europeans; NIHSS, National Institute of Health Stroke Scale; TIA, Transient Ischemic Attack.

TABLE 1 Results of the multivariate logistic regression for the prediction of thrombolytic treatment.

Conclusion: Racial and ethnic disparities in healthcare are a challenging issue even in universal healthcare systems, likely due to differences in socioeconomic status, and they and should be addressed promptly through education campaigns of healthcare personnel.

Disclosure: Nothing to disclose.

OPR-028 | Polysomnographic parameters as predictors of outcome in patients with ischemic stroke: A preliminary report

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Background and aims: Limited literature exists on sleep architecture in ischemic stroke (IS). This study aims to assess whether macrostructure and microstructure sleep parameters can predict outcomes in patients with IS.

Methods: Seventy-seven with IS admitted to the Stroke Unit were prospectively collected. Patients underwent 24 hour polysomnography within seven days from the stroke. Macro and micro (Cycling Alternating Pattern - CAP) sleep architecture and respiratory parameters were analyzed. Three-month modified Ranking Scale(mRS) was used as the outcome measure. Sleep parameters were analyzed between groups with excellent (mRS = 0–1) and poor outcome (mRS = 2–6) using univariate and multivariate approaches, correcting for potential confounders (sex, age, NIHSS, pre-stroke mRS).

Results: The study group showed a median age of 73 years (IQR = 20), and an admission NIHSS = 12 (IQR = 11). Forty-three patients had excellent outcome (55.8%). Median total sleep time (TST) was 374 minutes (IQR = 104). Patients with excellent outcome showed higher REM sleep [13.0% (IQR = 8.6) vs. 6.9% (IQR = 7.5); $p = 0.002$)], higher N1 stage of NREM sleep [13.3% (IQR = 10.5) vs. 8.2% (IQR = 5.7; $p = 0.001$)], higher number or sleep cycles [3 (IQR = 2) vs. 1 (IQR = 3); $p = 0.030$)], shorter daytime sleep [10 (IQR = 75) vs. 75 minutes (IQR = 126); $p = 0.005$)], and higher CAP rate [43.7% (IQR = 25.0) vs. 24.9% (IQR = 30.8); $p = 0.001$)]. None of the analyzed respiratory parameters were associated with outcome. Multivariate analysis confirmed that higher CAPrate($p = 0.030$) and less daytime sleep($p = 0.017$) were associated to excellent outcome.

Conclusion: Macro and, mostly, microstructure parameters of sleep in ischemic stroke seem to be correlated with outcome, in particular higher CAP rate is associated with better outcome. Further investigations are needed to reinforce these findings.

Disclosure: Nothing to disclose.

Neuroimaging in neuroinflammation

OPR-029 | Amyloid PET as biomarker of white matter damage in recently diagnosed multiple sclerosis and its clinical relationship

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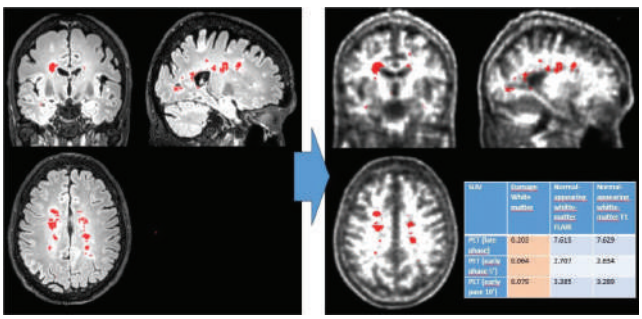
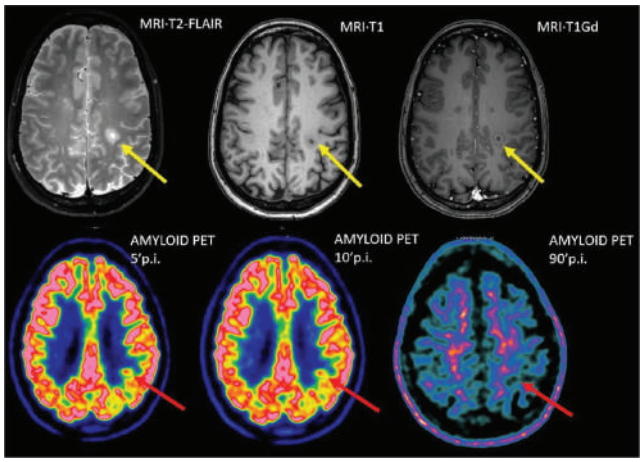
Background and aims: White matter (WM) demyelination in multiple sclerosis (MS) can be measured in vivo using amyloid positron emission tomography (PET). Our aim was to evaluate amyloid uptake in damaged (DWM) and normal-appearing WM (NAWM) of MS patients and the relation to their clinical status.

Methods: This prospective longitudinal study enrolled patients with recent MS onset between March to May 2023. Participants underwent a neurological examination, disability (EDSS), neuropsychological (SDMT) and quality of life (EQ-5D) assessment, brain MRI and 18F-florbetaben PET in early (0–10′) and late phase (90′) post-i.v., MRI and PET images were co-registered and results are presented as standardized uptake values (SUV), using cerebellum (SUVRc) and NAWM (SUVRwm) as the reference region.

Results: Ten patients were included (35.10 ± 11.32 years; 70% female). We found, both in early- and late-phase, a lower mean SUVR in DWM compared to NAWM ($p < 0.01$) in all patients. SUVRwm correlated with EQ-5D index (r:0.652, $p = 0.041$). A trend toward lower SUVRwm was observed in the highly active onset group compared to non- highly active group (0.62 ± 0.43 vs.. 3.62 ± 3.20, $p > 0.05$). Considering only highly active onset patients, SUVRwm correlated with EDSS score (rho = −0.896, $p = 0.0031$). The lesions analysis showed a correlation between SUVmean in DWM with EDSS and SDMT scores (rho: −0.534, $p = 0.004$ and rho: 0.670, $p = 0.006$, respectively); and SUVRc with SDMT (rho: 0.585, $p = 0.022$).



Standardized uptake values (SUV) analysis by co-registered MRI and amyloid PET images.



Active lesion analysis by MRI and amyloid PET images.

Conclusion: Preliminary results of this work in progress suggest that amyloid PET could be a promising tool to monitor myelin changes in MS and may have a predictive role in disease activity and progression.
Disclosure: This work has received funding from the call for "NEURO-RECA grants for scientific research in neurology in 2021" with file number NEURORECA-0007-2022.

OPR-030 | Validation of an automated deep learning algorithm for the identification of confluent Multiple Sclerosis lesions

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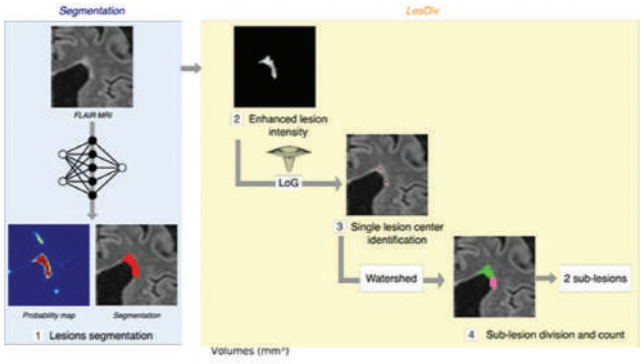
Background and aims: Lesion count is a crucial biomarker in Multiple Sclerosis diagnosis and follow-up. Deep Learning (DL) models are a powerful aid for this task, providing an automated segmentation of lesions. These models tend to underestimate the true number of lesions, and segment confluent lesions as a single connected component. To improve the accuracy of the lesion counting, a novel post-processing algorithm named LesDiv that can recognize individual lesions component in confluent lesions has been validated, automatically identifying single lesion center using the input FLAIR and lesion probability map produced by the DL segmentation model.
Methods: 60 MS patients with 440 clusters of lesions were included. Two neurologists, with expertise in Multiple Sclerosis MRi analysis, independently performed ground truth sub-lesion counts and delineations. To compare the algorithm with alternative methods, an alternative pipeline that uses the Hessian filter instead of the LoG (described by Dworkin et al.), named Hessian Division, was implemented.



Flowchart of our proposed LesDiv algorithm.

Results: The analysis showed excellent reliability between the two human experts in terms of sublesion counting and delineation: Mean Absolute Error (MAE) = 0.45, Pearson Coefficient (R^2) = 0.88, Dice = 0.526. LesDiv showed good reliability with the analysis performed by the two human experts: MAE = 0.75, R^2 = 0.75, Dice = 0.52, compared with Expert 1 analysis. Hessian Method showed a lower reliability with the two experts: MAE = 0.99, R^2 = 0.67, Dice = 0.48 compared with Expert 1 analysis.

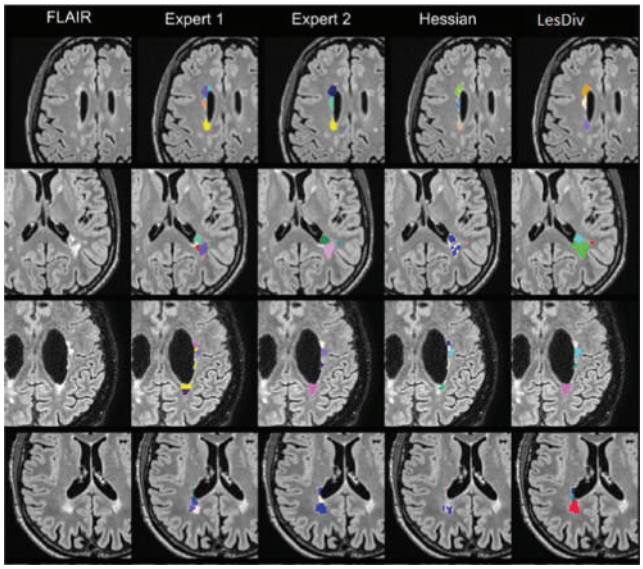


Illustration of expert counts and automated counts.

Reference count	Evaluated count	MAE (↓)	R2 (↓)	Dice (↑)
Expert 1	**Expert 2**	**0.4738**	**0.8760**	**0.5261 ± 0.3528**
LesDiv	Expert 1	0.7931	0.7515	0.5203 ± 0.4135
LesDiv	Expert 2	0.8109	0.7410	0.4827 ± 0.4000
LesDiv	Consensus	0.7134	0.7937	-
Hessian	Expert 1	0.9975	0.6763	0.4783 ± 0.3912
Hessian	Expert 2	1.0657	0.6796	0.4841 ± 0.3753
Hessian	Consensus	0.8971	0.7393	-

Comparison of experts and automated counts. MAE = Mean Average Error. R2 = Pearson correlation coefficient.

Conclusion: Lesion segmentation in MS is a complex and time-consuming analysis. LesDiv is an automated deep learning algorithm, that showed significant correlation with human analysis in the identification of single lesions from confluent MS lesions.
Disclosure: Nothing to disclose.

OPR-031 | Cellular soma and neurite density abnormalities in multiple sclerosis paramagnetic rim and core-sign lesions

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Background and aims: In multiple sclerosis (MS), susceptibility-weighted imaging (SWI) may reveal white matter lesions (WML) with a paramagnetic rim ("paramagnetic rim lesions" [PRLs]) or diffuse hypointensity ("core-sign lesions"), reflecting different stages of WML evolution. Using soma and neurite density imaging (SANDI) model on diffusion-weighted magnetic resonance imaging (MRI), we characterized the microstructural abnormalities of MS PRLs and core-sign lesions and their clinical relevance.
Methods: Forty MS patients and 20 healthy controls (HC) underwent a 3 T brain MRI. Using SANDI, the fractions of neurite (fneurite) and soma (fsoma) and size of soma (rsoma) were quantified in PRLs (including their core and rim separately), and core-sign lesions identified on SWI.
Results: Among 1811 WMLs, 122 (6.7%) core-sign lesions and 97 (5.4%) PRLs were identified. Compared to HC and MS normal-appearing white matter, all MS WML showed significantly lower fneurite and fsoma and higher rsoma (FDR-$p < 0.001$). Compared to isointense WML, core-sign lesions showed a significantly higher fneurite, and lower fsoma and rsoma (FDR-$p <= 0.001$). Compared to isointense WML and core-sign lesions, PRLs showed a significantly lower fneurite, higher fsoma, and higher rsoma (FDR-$p \le 0.005$). The PRL-core showed significantly lower fneurite, and higher rsoma than PRL-rim (FDR-$p < 0.001$). Lower PRL fneurite ($\beta <= -0.006$, FDR-$p \le 0.015$) and higher rsoma ($\beta >= 0.032$, FDR-$p <= 0.024$) were significantly associated with a longer disease duration and more severe disability.
Conclusion: In PRLs, the significant and clinically-relevant neurite loss and increased soma fraction and size possibly reflect increased astrogliosis and activated microglia. Core-sign lesions exhibit milder axonal loss, microglia density and astrogliosis, supporting their less destructive nature.
Disclosure: P Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He has received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). E Pagani, A Meani, M Rubin, M Palombo have nothing to disclose. M Margoni reports grants and personal fees from Sanofi Genzyme, Merck Serono, Novartis and Almiral. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. M. Filippi received compensation for consulting or speaking activities from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

OPR-032 | Discriminating MS from MOGAD using deep learning attention maps

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Background and aims: Relapsing remitting multiple sclerosis (RRMS) and myelin-oligodendrocyte antibody-associated disease (MOGAD) are distinct diseases, but their differentiation can be challenging in clinical practice due to overlapping clinical and MRI features. The application of deep learning (DL)-models to MRI is a promising approach to provide a structurally based classification of diseases, while the study of DL-derived attention maps may indicate the most relevant anatomical regions for DL-stratification. We aimed to build a MRI-based DL-model to differentiate RRMS from MOGAD and to assess group differences using probability attention maps (PAM).

Methods: In this cross-sectional study, we analysed 345 FLAIR brain MRIs from RRMS (*n*.201, 117F, mean [SD] age: 39 years [±11], median EDSS: 2 [0–8], mean [SD] disease duration: 93 months [±94]) and MOGAD (*n*.144, 81F, mean [SD] age: 41y [±13], median EDSS: 2 [0–8.5], mean [SD] disease duration: 71 months [±96]), retrospectively collected from 17 centres. Patients were divided into three independent groups (training, validation, external test sets). The study design is illustrated in Figure 1.

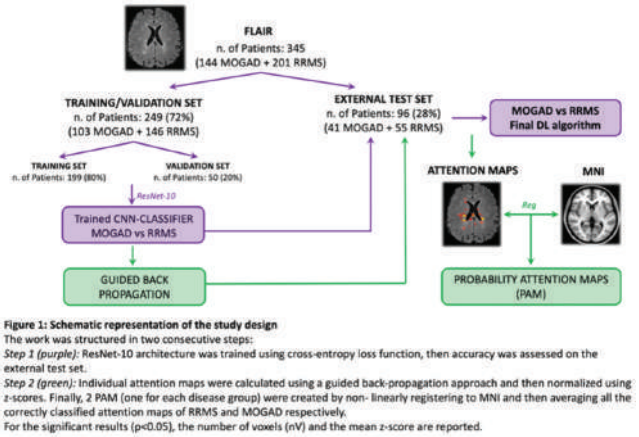

Figure 1: Schematic representation of the study design
The work was structured in two consecutive steps:
Step 1 (purple): ResNet-10 architecture was trained using cross-entropy loss function, then accuracy was assessed on the external test set.
Step 2 (green): Individual attention maps were calculated using a guided back-propagation approach and then normalized using z-scores. Finally, 2 PAM (one for each disease group) were created by non- linearly registering to MNI and then averaging all the correctly classified attention maps of RRMS and MOGAD respectively.
For the significant results ($p<0.05$), the number of voxels (nV) and the mean z-score are reported.

FIGURE 1 Schematic representation of the study design.

Results: A DL discriminatory model between the two diseases was built (accuracy/specificity/ sensitivity: 84%/85%/84%) and successfully validated in the external test set without retraining (accuracy/specificity/sensitivity: 72%/68%/76%). PAM revealed the relevant role of insula (nV: 271, *z*-score: 3.10), hippocampus (nV: 839, *z*-score: 3.44), periventricular areas (nV: 669, *z*-score: 3.47) for RRMS, while the selective role of the cingulate cortex (nV: 2360, *z*-score: 2.71) for the identification of MOGAD (Figure 2).

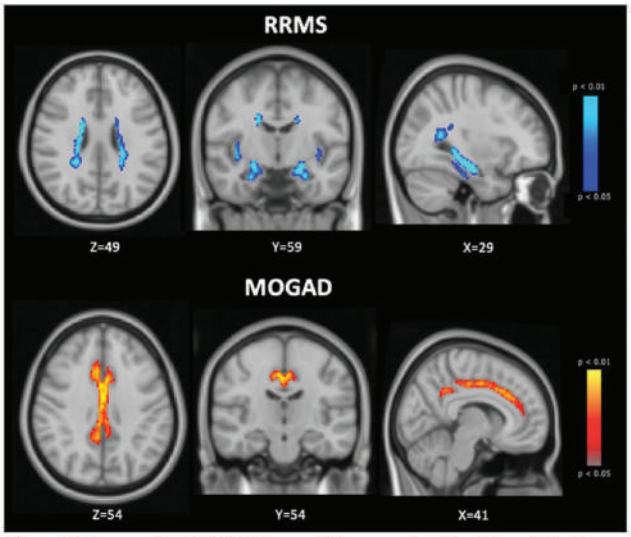

Figure 2: Topographical distributions of the areas significantly contributing to the differentiation between patients with RRMS and with MOGAD
Significant voxels are shown in a colour scale from light blue to dark blue for RRMA and from yellow to red for MOGAD, from the most to the less significant, respectively.

FIGURE 2 Topographical distributions of the areas significantly contributing to the differentiation between patients with RRMS and with MOGAD.

Conclusion: We developed a DL-model to accurately differentiate RRMS from MOGAD on FLAIR MRI. PAM provided additional clues on how damage is distributed in the two diseases.

Disclosure: The present research was conducted thanks to the 2019 ECTRIMS-MAGNIMS fellowship (awarded to R.C.). The Authors have nothing to disclose in relation to this work.

Sunday, June 30 2024

Child neurology/developmental neurology

OPR-033 | Rehabilitation of attention with a tablet-based app in pediatric Multiple Sclerosis: A randomized, multicenter study

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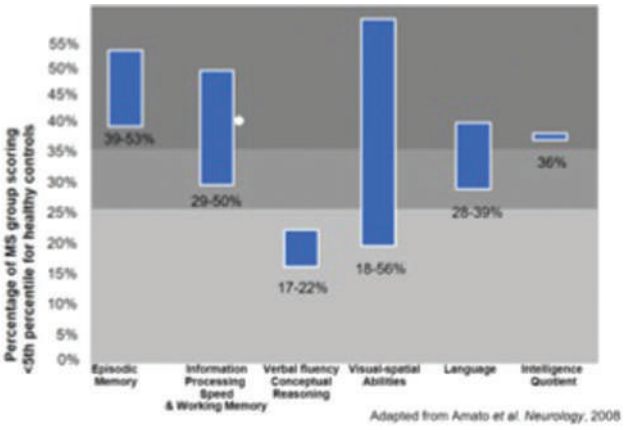
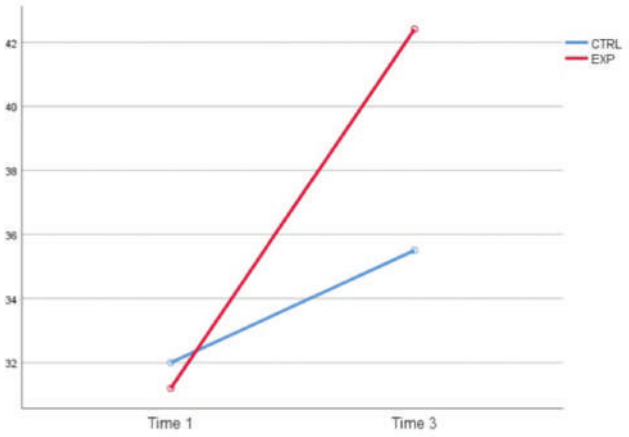
Background and aims: Cognitive impairment affects approximately 30% of pediatric onset Multiple Sclerosis (POMS) patients with a negative impact on everyday life1. The aim of this study was to evaluate the feasibility and effectiveness of a home-based, computer-assisted training of attention in patients with POMS.



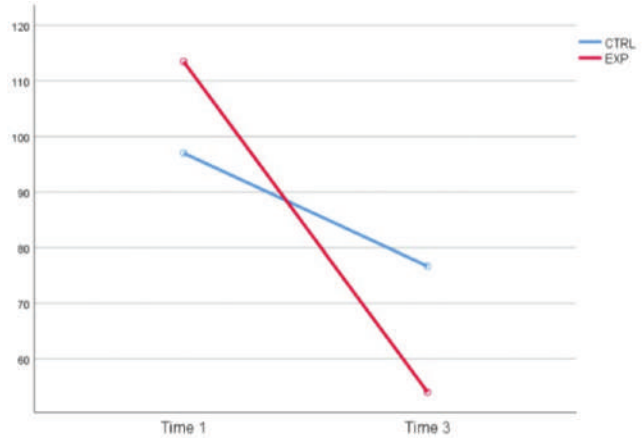
Some studies have highlighted a particular involvement of language in patients with POMS, which is commonly spared in adults. Additionally, a lower intelligence quotient (IQ) has been observed in patients with an earlier onset of the disease.

Methods: Inclusion criteria were diagnosis of MS, age 9–18 years, impairment on at least one attention test. Subjects were randomized to specific training (ST) or non-specific training (n-ST), delivered through a customized module based on attention exercises in COGNI-TRAcK2. The main feature of the ST is the implementation of working load algorithms and procedures for intensiveness regulation. The effectiveness of the ST on attention was primarily assessed on the Symbol Digit Modalities Test (SDMT)3 using an analysis of variance for repeated measures. Secondary objectives included effectiveness on other cognitive tests and everyday-life activities. The evaluations were performed at baseline, end of training, 3-month follow-up.

Results: 22 relapsing–remitting patients were included: data of 8 subjects in n-ST and 4 subjects in ST were available. As for the primary outcome, SDMT score improved in the ST group (from 31.2 at baseline to 42.4 after 3 months, $p=0.043$). This effect was evident also in Trial Making Test B ($p=0.047$). There was no benefit in other neuropsychological measures.



As for the primary outcome, mean score on the SDMT improved in the ST group (from 31.2 + 9.8 at baseline to 42.4 + 18 at the end of training, $p=0.524$) and remained stable in the n-ST group (from 32 + 7.3 at baseline to 35.5 + 9.7 at the end of training, $p=0.284$).



The positive effect of ST was also evident in Trail Making Test B, which improved in each group of patients: in ST group from 113.5 + 16.3 at baseline to 54 + 8.5 at the end of treatment ($p = 0.047$) and in n-ST group from 97 + 39 at baseline to 76.7 + 41.4 at the.

Conclusion: These preliminary findings point to a potential benefit of a home-based, computer-assisted training of attention in patients with POMS. Early rehabilitation in POMS can mitigate the negative impact of cognitive impairment in patient's lifestyle and school activities.

Disclosure: C. Masciulli nothing to disclose; E. Portaccio received fees from Biogen, Merck Serono, Sanofi, Teva and Novartis; R. G. Viterbo received speaker honoraria from Biogen Idec and Teva; M. Zaffaroni received honoraria from Almirall, Biogen Idec, Genzyme, Merck Serono, Novartis and Teva; M. Pardini received research support from Novartis and Nutricia and honoraria from Merk and Novartis, G. Mancardi received honoraria from Bayer Schering, Biogen Idec, Sanofi-Aventis, and Merck Serono Pharmaceuticals, R. Guerrini received honoraria from Biocodex, UCB, Eisai Inc, ValueBox, and Viropharma, M. Rocca received honoraria from Bayer, Biogen, Bristol Myers Squibb, Celgene, Genzyme, Merck Serono, Novartis, Roche, and Teva, M. Filippi received fees from Almiral, Alexion, Bayer, Biogen, Celgene, Eli Lilly, Genzyme, Merck-Serono, Novartis, Roche, Sanofi, Takeda, and Teva Pharmaceutical Industries; M. Trojano received honoraria from Biogen, Sanofi, Merck, Roche, and Novartis; M.P. Amato received honoraria from Biogen Idec, Merck Serono, Bayer Schering Pharma, and Sanofi Aventis.

OPR-034 | Ambulatory 24-h continuous polysomnography as diagnostic tool for narcolepsy type 1 in adult and pediatric patients

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Background and aims: Narcolepsy type 1 (NT1) is diagnosed on average 10 years after the onset. We evaluated the contribution of 24-hour continuous polysomnography (PSG) as an alternative tool for the diagnosis of NT1 in adults and children.

Methods: Consecutive patients evaluated at the Bologna Narcolepsy Center from 2013 to 2022 for suspected hypersomnia were included. The 807 participants underwent 48-hour ambulatory PSG monitoring preceding the multiple sleep latency test (MSLT). The accuracy of night1 and day2 PSG was tested for the diagnosis of NT1 ($n = 322$), employing the 2023 international criteria as the standard reference for the ROC curve analysis.

Results: The detection of daytime-sleep-onset REM period (SOREMP) ≥1, with an area under the curve (AUC) of 0.84 (95% CI, 0.82–0.87), 84.4% sensitivity and 84.5% specificity, resulted superior to nighttime-PSG measures, including nighttime-SOREMP ($p < 0.001$) and comparable to 24-hour-SOREMP count. In the entire cohort, the combination of daytime-SOREMP ≥1 with cataplexy provided 78.9% sensitivity and 98.4% specificity, with AUC 0.89 (95% CI 0.86–0.91) superior to the combination of nighttime-SOREMP with cataplexy (AUC 0.78, 95% CI 0.76–0.81, $p < 0.001$) and not inferior to MSLT criteria for narcolepsy (AUC 0.90, 95% CI 0.88–0.92). These results were confirmed separately in adult and pediatric patients, except that, in pediatric patients (130/243 with NT1), nighttime-SOREMP (AUC 0.86, 95% CI 0.82–0.90) was not inferior to daytime-SOREMP ≥1.

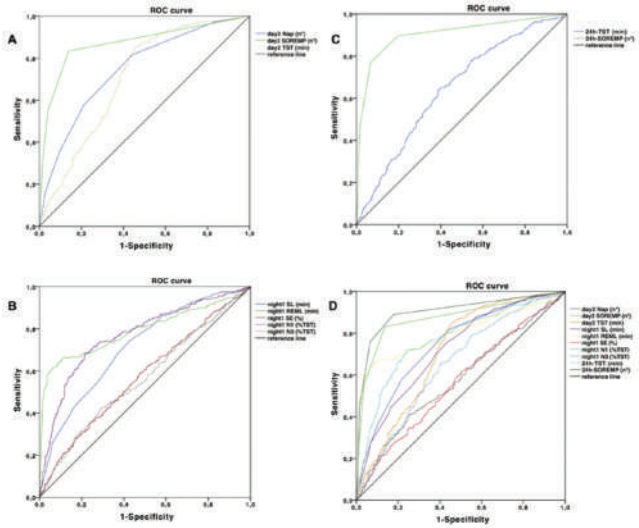

FIGURE 1 Receiver operating characteristic (ROC) curve analysis for diagnosis of narcolepsy type 1 of the polysomnographic variables from daytime (A), nighttime (B), daytime and nighttime combined (C), and all the variables together (D).

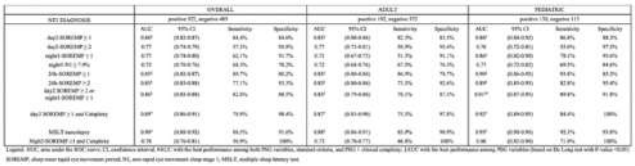

TABLE 1 Receiver operating characteristic (ROC) curve analysis for the diagnosis of narcolepsy type 1, in different age groups.

Conclusion: Continuous daytime-PSG is accurate for identifying NT1 in all age groups and appears superior to nighttime-PSG and not inferior to 24-hour monitoring. Daytime-PSG, applicable outside sleep laboratory settings, can anticipate the diagnosis of NT1 in both adults and children.

Disclosure: Nothing to disclose.

OPR-035 | Survival differences between genders in PDHA1-related pyruvate dehydrogenase deficiency

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Background and aims: Pyruvate dehydrogenase complex deficiency (PDHD) is the prototypic inborn error of mitochondrial metabolism, leading to neurodevelopmental disorder with lactic acidosis, CNS structural abnormalities. Disease causing variants in the X-linked PDHA1 are the most common genetic cause of PDHD, consequently, mainly males should be affected. In the literature, both genders are reported. We here assess the gender differences in survival in PDHA1- related PDHD.

Methods: Affected individuals with PDHA1- related PDHD were recruited via literature review ($n = 512$) and international collaboration ($n = 418$). All variants were (re)classified according to NM_000284.3 reference transcript, interpreted via American College of Medical Genetics (ACMG) criteria. (Likely) benign variants were excluded. Survival probability was assessed using Kaplan–Meier estimator.

Results: In total, 930 cases with known gender and genotype were included (females 51.6%, $n = 480$), harbouring a total of 324 different PDHA1 disease causing variants. The overall median survival was 12.5 years (95% Confidence interval (95% CI) 8–20 years; $n = 317$). Males had significantly ($p < 0.001$) lower survival probability than females, median survival in males and females were 3.6 years (95% CI 2.5–9.42; $n = 146$) and 22 years (95% CI 16.0–30.0; $n = 159$), respectively. Males with neonatal or infantile presentation had significantly lower survival probability than females with neonatal ($p < 0.001$; $n = 136$) or infantile ($p < 0.001$; $n = 83$) presentation.

Conclusion: Interestingly, we found equal number of cases between both genders, males had significantly lower survival probability. In females, X-inactivation could lead to milder phenotypes with better survival even with the same genotype as in males. Some males with severe phenotype could result in spontaneous pregnancy termination explaining similar frequency.

Disclosure: This abstract is part of a larger study analysing the genotypical and phenotypical landscape of PDHA1-related PDHD. This study was made possible through large collaboration with more than 150 different specialists worldwide.

OPR-036 | Abstract withdrawn

OPR-037 | Clinical and instrumental gait phenotyping in subjects with GLUT-1 deficiency syndrome

M. Corrado[1]; R. De Icco[1]; V. Grillo[1]; V. De Giorgis[1]; V. Vacchini[2]; C. Varesio[2]; M. Celario[2]; D. Trabassi[3]; S. Castiglia[3]; M. Serrao[3]; C. Tassorelli[3]

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Background and aims: Gait disturbances and movement disorders are frequent in patients with GLUT-1 deficiency syndrome (GLUT1-DS), a rare disease also characterized by seizures and cognitive dysfunction. This study aimed to assess the ability of a set of instrumental gait indexes to identify gait disorders in GLUT1-DS, and to detect potential correlations with the clinical phenotype and biochemical parameters.

Methods: We recorded a 30-meter gait of 16 subjects with GLUT1-DS and of 16 matched healthy subjects (HS). We performed gait analysis with an inertial sensor. Based on trunk acceleration we calculated: spatio-temporal gait parameters, pelvic kinematics, harmonic ratios (HR), recurrence quantification analysis (RQA), stride length coefficient of variation (CV), the longest short-term Lyapunov's exponent (sLLE), and the log dimensionless jerk score (LDLJ). Along with the instrumental gait recording, we performed a comprehensive clinical and biochemical phenotyping.

Results: GLUT 1-DS (mean age 19.1 ± 13.7 years) showed lower values of HR and single support (SS) phase (Figure 1; $p < 0.05$), indicating impaired gait smoothness. Moreover, they showed higher values of CV and sLLE (Figure 2; $p < 0.01$), suggestive of higher dynamic instability and variability of gait. The CV negatively correlated with ketonemia ($r = -0.61$, $p < 0.05$). Nine subjects (52%) had clinically evident gait disorders, mainly characterized by choreo-ataxic gait.

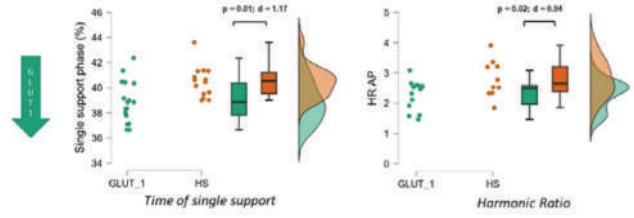

FIGURE 1 Differences in time of single support (SS) and harmonic ratio (HR) between HS (orange) and GLUT1-DS (green).

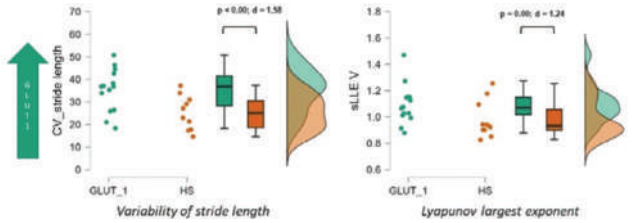

FIGURE 2 Differences in coefficient of variation (CV, i.e. variability of stride length) and the longest short-term Lyapunov's exponent (sLLE) between HS (orange) and GLUT1-DS (green).

Conclusion: GLUT1-DS exhibited multiple alterations in the trunk acceleration-derived gait indexes, which were suggestive of impaired gait stability and smoothness. Interestingly, increased gait variability correlated with low ketonemia, possibly suggesting this feature as a marker of poor therapeutic adherence.

Disclosure: Nothing to disclose.

MS and related disorders 1

OPR-038 | Long-term outcomes of Phase-1 study of neural stem cell transplantation in progressive multiple sclerosis

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Background and aims: Human fetal neural progenitor/stem cells (hfNPCs) transplant feasibility and safety in progressive multiple sclerosis (PMS) has been demonstrated in STEMS, a phase I clinical trial (NCT03269071). Higher dose of hfNPCs was associated with significantly lower rates of brain and gray matter (GM) atrophy after 2 years. We present long-term (LT) follow-up (FU) of STEMS trial.

Methods: Patients underwent clinical (comprehensive of Expanded Disability Status Scale [EDSS] and Symbol Digit Modalities Test [SDMT]) and brain MRI evaluation at minimum 4.5 year FU. New T2-hyperintense and Gd-enhancing lesions were counted. T2-lesion volume (T2LV), percentage brain (PBVC), GM (PGMVC) and white matter (PWMVC) volume changes were estimated.

Results: FU was available for 11/12 patients (median duration 5.6 years). At LT, EDSS and SDMT were significantly worsened compared to 2 year FU ($p <= 0.08$). Five (45%) patients showed new T2-hyperintense lesions, whereas T2LV was unchanged ($p = 0.07$); no patient showed Gd-enhancing lesions. Brain, GM and WM volumes were decreased at LT compared to 2-year FU. Interestingly, atrophy rates at LT were lower compared to the first 2-year changes (significant for PGMVC: 2-years vs. baseline = −0.76%; LT vs. 2-years = −0.47%, $p = 0.04$). No significant correlation was found between number of injected hfNPCs and variation of EDSS, SDMT or MRI measures.

Conclusion: Although no clear dose–response effect has been found in hampering disability, cognition or brain atrophy progression, lower rates of GM atrophy were found at LT FU, which could imply that hfNPCs maintain their neuroprotective effect over time.

Disclosure: M Azzimonti, I Gattuso, E Pagani, A Genchi, L Storelli, P Vezzulli, E Brambilla, A Falini, and G Martino have nothing to disclose. L Moiola compensation for speaking activities and/or consulting services from Merck, Biogen, Novartis, Roche, Sanofi, and TEVA. V Martinelli compensation for speaking and/or consultancies and support for participation in congresses from Biogen, Merck-Serono, Novartis, Genzyme and TEVA Pharmaceutical Industries. MA Rocca consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health (IMH), Italian Ministry of University and Research, and FISM. M. Filippi compensation for consulting or speaking activities from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM.

OPR-039 | Parental smoking exposure and risk for multiple sclerosis among adults: The EnvIMS study

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Background and aims: Active smoking is a known risk factor for Multiple sclerosis (MS) development and poor prognosis. However, the impact of past exposure to parental smoking (ParS), including maternal smoking during pregnancy (MSDP) is not well defined. We aimed to investigate how these types of early age exposures affect MS risk among adults.

Methods: Using the data collected by the EnvIMS study, a large multinational case–control population-based study, we investigated the association between MS and smoking habit, MSDP and maternal/paternal smoking (MaS, PaS) in Canadian, Italian, and Norwegian populations. Data were collected with EnvIMS-Q, designed to investigate environmental exposures during early life stages. Adjusted odds ratios (aOR) for index age and participants' smoking status are presented with 95% confidence intervals (95% CI).

Results: We included 1565 Canadian, 2040 Italian, and 2674 Norwegian subjects. An association between MS and MSDP and MaS was observed among Norwegians: aOR 1.38 (1.12, 1.71) and 1.39 (1.17, 1.65), respectively. A tendency for PaS to be associated with MS was found among Canadians: aOR 1.21 (0.97, 1.51). No significant association to ParS (any) was detected in the Italian population.

Conclusion: Selective exposure to ParS at early age may differentially increase MS risk in the general population and independently from the subject's past/current smoking habit. The developmental origin of health and disease ('DOHaD') theory may help interpret these findings. The absence of an association between MS and past exposure to ParS in other populations may reflect its smaller effect on MS risk compared to other factors.

Disclosure: The authors declare no conflict of interest. The EnvIMS study was supported by Fondazione Italiana Sclerosi Multipla, FISM, grants n. 2007/R/14, and n. 2008/R/19; Financially supported by the European Union – Next Generation EU – NRRP M6C2 – Investment 2.1 Enhancement and strengthening of biomedical research in the NHS - PNRR-MAD-2022-12,376,868.

OPR-040 | Retinal layer thinning differentiates disease-modifying treatment effects in relapsing MS when using a rebaseline

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Background and aims: We aimed to investigate whether retinal layer thinning measured by optical coherence tomography (OCT) can differentiate effects of disease-modifying treatment (DMT) in relapsing MS (RMS) using a rebaseling concept.

Methods: From an ongoing prospective observational study, we included RMS patients, who 1) had an OCT scan 6–12 months after DMT start (rebaseline), 2) ≥1 follow-up OCT ≥12 months after rebaseline, and 3) adhered to the DMT during follow-up. Differences between DMT substances in thinning of peripapillary retinal nerve fiber layer (pRNFL) and macular-ganglion-cell-plus-inner-plexiform layer (GCIPL) were analyzed using mixed-effects linear regression adjusting for age, sex, disease duration and relapses during follow-up.

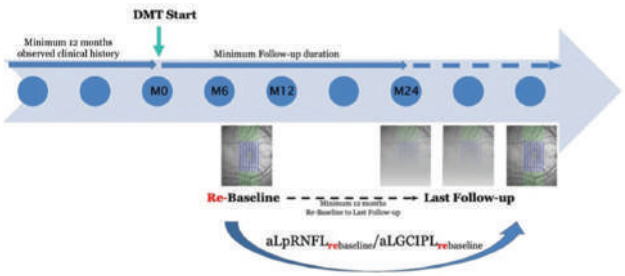

FIGURE 1 Study design.

Results: Of 291 RMS patients (mean age 30.8 years [SD 7.9], 72.9% female, median disease duration 9 months [6–94], median rebaseline-to-last-follow-up-interval 37 months [12–87]). Mean annualized percent loss rates (%/year) of retinal layer thinning in reference to dimethyl-fumarate ($n = 84$, GCIPL 0.28, pRNFL 0.53) were similar under teriflunomide ($n = 18$, GCIPL 0.34, pRNFL 0.59, not significant [ns]), glatiramer acetate ($n = 24$, GCIPL 0.32, pRNFL 0.56, ns) and interferon beta ($n = 13$, GCIPL 0.33, pRNFL 0.60, ns), appeared slightly lower under sphingosine-phosphate-1-receptor modulators ($n = 27$, GCIPL 0.19 [$p = 0.093$], pRNFL 0.42 [$p = 0.097$]) and cladribine ($n = 23$, GCIPL 0.20 [$p = 0.095$], pRNFL 0.42 [$p = 0.099$]), and were significantly lower under natalizumab ($n = 47$, GCIPL 0.09, pRNFL

0.24; $p < 0.001$ respectively) and anti-CD20 monoclonal antibodies ($n = 55$, GCIPL 0.10, pRNFL 0.23; $p < 0.001$ respectively).

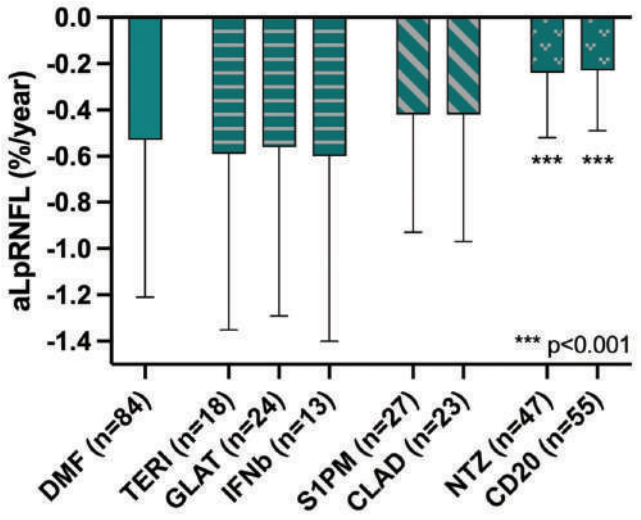

FIGURE 2 Annualized pRNFL loss differentiates disease-modifying treatment effects in RMS.

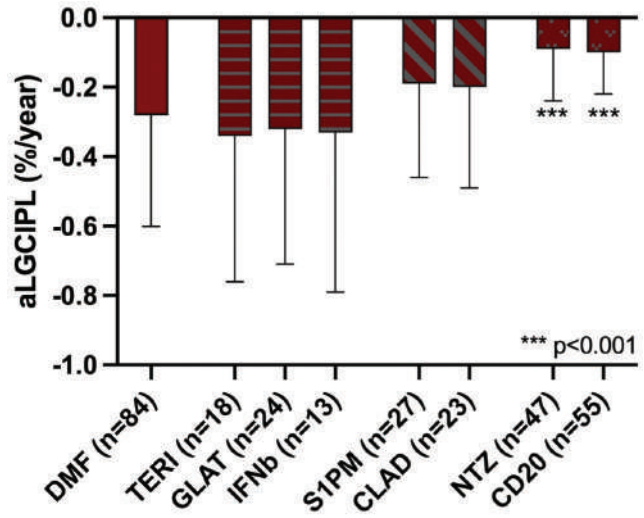

Figure 23 Annualized GCIPL loss differentiates disease-modifying treatment effects in RMS.

Conclusion: Applying a rebaseling concept, retinal layer thinning differentiates DMT effects in RMS and, thus, may be a useful biomarker to mediate DMT efficacy on neuroaxonal degeneration – at least on a group level.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

OPR-041 | Longitudinal changes in the periplaque area of paramagnetic rim lesions may be associated with remyelination failure

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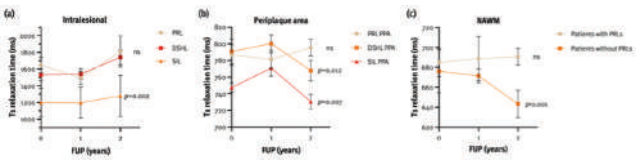
Background and aims: Paramagnetic rim lesions (PRLs) are an emerging imaging biomarker in multiple sclerosis (MS) associated with a more severe disease course.

Methods: In this prospective longitudinal study, quantitative MRI metrics of PRLs, lesions with diffuse susceptibility-weighted imaging (SWI)-hypointense signal (DSHLs) and SWI-isointense lesions (SILs), their surrounding periplaque area (PPA) and normal-appearing white matter (NAWM) were measured in people with MS (pwMS) using the multi-dynamic multi-echo (MDME) sequence post-processing software "SyMRI" at baseline, after 1 and 2 years.

Results: In 15 pwMS, 18 PRLs, 31 DSHLs and 63 SILs were identified; four (26.7%) patients had no PRLs. After 2 years, intralesional T1 relaxation times increased significantly only in SILs (1200.7 (172.6) vs. 1278.6 (245.7), $p = 0.002$) but not in PRLs and DSHLs (1648.6 (402.1) vs. 1810.2 (564.6), $p = 0.154$; 1532.5 (402.1) vs. 1741.4 (328.1), $p = 0.086$, respectively). In the PPA, significantly shorter T1 relaxation times were observed for both DSHLs (790.8 (83.2) vs. 767.9 (45.9), $p = 0.012$) and SILs (747.5 (45.7) vs. 730.6 (51.2), $p = 0.007$) but not for PRLs (786.7 (52.9) vs. 795.2 (30.3), $p = 0.591$). Patients with PRLs also showed no shortened T1 relaxation times in the NAWM (685.0 (46.0) vs. 690.7 (18.5), $p = 0.830$) in contrast to patients without PRLs (676.1 (42.9) vs. 643.3 (19.4), $p < 0.001$).



Longitudinal changes in PRLs, DSHLs and SILs, their surrounding PPA and NAWM.

Conclusion: Significantly shorter T1 relaxation times in DSHL PPA and SIL PPA, but not in PRL PPA after 2 years may again point to remyelination failure in and around PRLs. T1-quantification based on MDME in and around lesions may become a useful and applicable routine marker for silent progression in pwMS.

Disclosure: The project is supported by the Multiple Sklerose Forschungsgesellschaft.

OPR-042 | CVS, CL and PRL for the diagnostic and prognostic workup of MS

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Background and aims: The diagnosis of multiple sclerosis (MS) can be challenging in clinical practice. We evaluated the diagnostic performance, alone or in combination, of the central vein sign (CVS), cortical lesions (CL), and paramagnetic rim lesions (PRL), as well as their association with clinical outcomes.

Methods: This multicenter study included: (1) a cross-sectional analysis of CVS (proportion of CVS-positive lesions, or simplified determination of CVS in three/six lesions - Select3*/Select6*), CL, and PRL in 185 MS/100 non-MS cases on 3T-MRI-brain images, including 3D T2-FLAIR, T2*-EPI magnitude and phase, DIR, and MPRAGE; (2) a longitudinal analysis in 61 MS cases of progression independent of relapse and MRI activity (PIRA).

Results: The presence of ≥41% CVS-positive lesions/≥1 CL/≥1 PRL (optimal cut-offs) had 96%/94%/93% specificity, 97%/80%/60% sensitivity, and 0.99/0.88/0.77 area under the curve (AUC), respectively, to distinguish MS from non-MS cases. Select3*/Select6* showed 93%/95% specificity, 97%/89% sensitivity, and 0.95/0.92 AUC. The combination of CVS, CL, and PRL improved the diagnostic performance, especially when Select3*/Select6* were used (93%/93% specificity, 98%/97% sensitivity, 0.99/0.98 AUC; $p = 0.002/p < 0.001$). Both CL and PRL were associated with higher MS disability and severity. After 2 years follow-up, cases with >4 PRL at baseline were more likely to experience PIRA (OR 17.8, 95% CI: 2.2–144.7; $p = 0.007$), whereas no association was observed between other MRI measures and PIRA, including the number of CL.

Conclusion: The combination of CVS, CL, and PRL can improve MS differential diagnosis. CL and PRL also correlate with clinical measures of poor prognosis, with PRL being a predictor of PIRA.

Disclosure: S. Borrelli is supported by the Funds Claire Fauconnier, Ginette Krysztein & José and Marie Philippart-Hoffelt, managed by the King Baudouin Foundation. A. Stölting has the financial support of the Fédération Wallonie Bruxelles - Fonds Spéciaux de Recherche (F.S.R.). C. Vanden Bulcke has the financial support of the Fédération Wallonie Bruxelles - Fonds Spéciaux de Recherche (F.S.R.). D.S. Reich is supported by the intramural Research Program of NIH/NINDS. M. Absinta is supported by research grants from the Conrad N. Hilton Foundation (Marylin Hilton Bridging Award for Physician-Scientists, grant #17313), the International Progressive MS alliance (21NS037), the Roche Foundation for Independent Research, the Cariplo Foundation (grant #1677), the FRRB Early Career Award (grant #1750327), and the National MS Society (NMSS RFA-2203-39,325). P. Maggi research activity is supported by the Fondation Charcot Stichting Research Fund 2023, the Fund for Scientific Research (F.R.S, FNRS; grant #40008331), Cliniques universitaires Saint-Luc "Fonds de Recherche Clinique" and Biogen.

Epilepsy 1

OPR-043 | Neuron-specific Enolase in Status Epilepticus versus Generalized Periodic Discharges after cardiac Arrest (NEXT-CAT)

Morotti Colleoni[1]; M. Pozzi[2]; S. Tagliabue[1]; E. Bianchi[3]; M. Normanno[1]; F. Pasini[1]; G. Cereda[1]; A. Giglio[1]; A. Stabile[1]; G. Pederzoli[1]; S. Diamanti[1]; J. Di Francesco[1]; L. Stanzani[1]; A. Coppo[2]; L. Avalli[2]; C. Ferrarese[1]; G. Foti[2]; S. Beretta[1]
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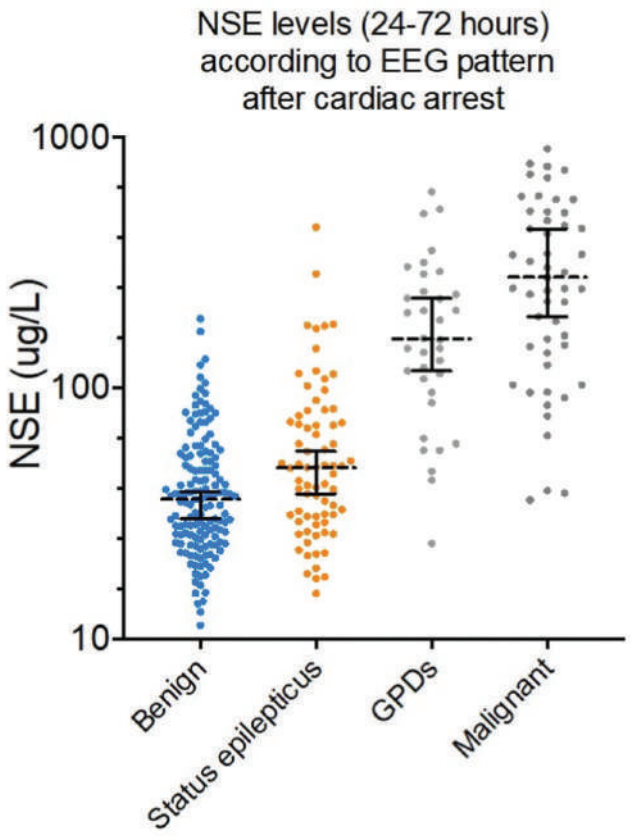
Background and aims: The aim of our study was to analyse the distribution of NSE levels according to specific EEG patterns in post-cardiac arrest patients.

Methods: We conducted a prospective cohort study in patients after cardiac arrest admitted to the ICU, with at least one NSE value between 24 and 72 hours and at least one off-sedation EEG within 72 hours after cardiac arrest. Subjects were categorized in four independent EEG patterns (benign, epileptiform non-GPDs, GPDs, malignant non-epileptiform). Kruskal-Wallis test and Mann–Whitney tests were used to compare the NSE levels distribution among the four EEG patterns and in GPDs versus epileptiform non-GPDs patterns.

Results: We recruited 341 patients from 2011 to 2023. A benign EEG pattern was observed in 161 (47%), an epileptiform pattern in 84 (25%), GPDs in 43 (13%) and a malignant pattern in 53 (15%). The median NSE level were 34 ng/mL for the benign EEG pattern, 45.8 ng/mL for the epileptiform pattern, 144 ng/mL for GPDs and 320.8 ng/mL for the malignant one. The distribution of NSE levels was statistically different among the four EEG patterns ($H = 152.4$, $p < 0.0001$). NSE levels were approximately 100 ng/mL higher in patients with a GPDs pattern, compared to an epileptiform non-GPDs pattern (absolute difference 98.2 ng/mL, 95% CI 66.2–126.7; $p < 0.0001$).



The NSE levels distribution among the four EEG patterns.

Conclusion: The level of the prognostic biomarker NSE is higher in patients after cardiac arrest with GPDs compared to epileptiform activity. A more aggressive therapeutic approach could be justified for patients with epileptiform non-GPDs activity after cardiac arrest.
Disclosure: Nothing to disclose.

OPR-044 | Electroencephalographic and epileptological natural history in metachromatic leukodystrophy: A longitudinal study

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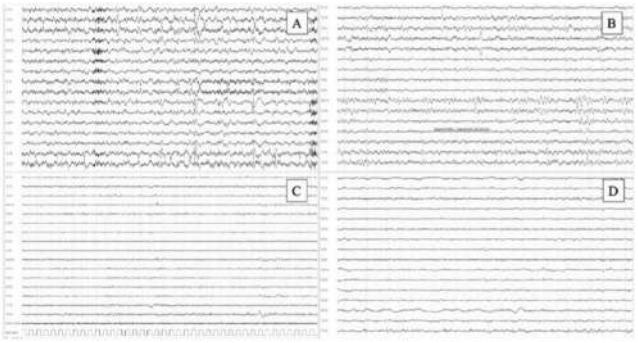
Background and aims: Metachromatic leukodystrophy (MLD) is a lysosomal storage disorder caused by mutations in the ARSA gene. Few data are available on its epileptological history.
Methods: Single-center, retrospective and prospective observational study on MLD patients enrolled in a natural history protocol (January 2000–December 2023). Data including clinical histories, EEG tracings, MRI evaluations and functional scales were collected.

Results: Fifty patients, 25 late infantile (LI), 12 early juvenile (EJ), 7 late juvenile (LJ), 6 adult-onset (AD), were included. Median follow-up was 4 years (IQR: 2–8; range: 1–20), with 360 EEG tracings. Epilepsy was documented in 76% (38/50) of patients: 80% (20/25) of LI, 100% (13/13) of EJ, 50% of AD (3/6) and 43% of LJ (3/7). Epilepsy occurred on average 30 months after disease onset in LI, 35 months in EJ, 108 months in LJ and 109 months in AD. Main seizure types reported were focal and focal-to-bilateral tonic–clonic seizures, often drug-resistant. Status epilepticus was reported in 34% (13/38) of patients, coinciding with epilepsy onset in 4/38. Disease subtypes presented distinct EEG patterns: LI presented rapid background deterioration, frequent seizures, and low-voltage rapid activity bursts. Among Juvenile-onset patients, divergent patterns were observed, with EJ having more similarities with LI group and LJ displaying a slower progression. AD presented disorganized backgrounds with sporadic focal anomalies.

MLD patients (N=50)	LI	EJ	LJ	AD
Patients N	25	12	7	6
Female (n)	14	7	4	3
Years of EEG follow-up (Median, IQR)	3 (1-4)	4 (2-6)	10 (8-14)	8 (4-12)
Age at last FU (Median, IQR)	5 (4-8)	10 (8-17)	25 (20-28)	48 (44-50)
Available tracings (N)	130	103	75	52
MLD onset, months (Median, IQR)	18 (10-25)	56 (48-67)	96 (74-170)	414 (365-487)
Epilepsy (n)	20	13	3	3
Epilepsy onset, Months from MLD onset (Average)	30	35	108	109
Status epilepticus (n)	7	3	2	1
Polytherapy, n (%)	15 (60)	12 (92)	2 (29)	2 (30)
Persistent generalized Seizures (n)	4	2	1	1

Baseline features and demographics of the patients included in the analysis, recapitulating the results section.

Conclusion: Epilepsy represent a significant comorbidity in MLD, especially LI and EJ groups, often presenting with drug-resistant seizures. MLD subtypes present different EEG evolution, hence this could represent a tool to further characterize patients, disease progression and treatment response.



Illustrative EEG epochs of four patients in advanced diseases stages. A (LI), B (EJ), C (LJ), D (AD). Different subtype shows different degrees of background disorganization and focal anomalies.

Disclosure: The study was supported by Telethon Foundation, IRCCS San Raffaele Scientific Institute, GlaxoSmithKline (GSK), and Orchard Therapeutics. The authors have no relevant disclosure related to the present work.

OPR-045 | EpilepsyPOWER a project to favor inclusion of people with epilepsy in workplaces

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Background and aims: Despite good seizure control, unemployment and underemployment are more common among people with epilepsy (pwE), for several reasons. The EpilepsyPOWER is a European project, involving five Countries (Italy, Bulgaria, France, Ireland, Germany), aimed to improve PwE's workplace inclusion.

Methods: For this project, we made a systematic review on epilepsy and employment, selecting 55 articles from 1958 to 2023, analyzing employment rate and determinants of employment/unemployment. We reviewed legislation in involved countries and developed two anonymous surveys asking for PwE's employment condition, and higher education institutions (HEI) general knowledge and attitudes about epilepsy.

Results: For all considered countries, we have not found any specific job legislation. Unemployment rates ranged from similar to twice or three times the general population and above all factors, seizure control and employers' attitudes contributed mostly to unemployment. We collected 567 answers from PwE and 291 from HEI. Unemployment rates were: 7.9% in Italy, 6.7% Ireland, 8.5% France, 15% Germany, 9% Bulgaria; people fully employed: 42.9% in Italy, 53% Ireland, 31.7% France, 40% Germany, 47.9% Bulgaria. In Italy, 24.2% of pwE did not disclose their condition, whereas in Bulgaria 48.5%. HEI individuals correctly defined epilepsy as a neurological disorder, treatable in most cases. Although most respondents have seen a seizure, in some countries, they did not know how to give first aid.

Conclusion: Exploring pwE work conditions and HEI perspectives could help to spread a culture of inclusion and fight marginalization of pwE in workplaces, allowing them to attain correct employment.

Disclosure: Nothing to disclose.

OPR-046 | An internationally derived core outcome set for adult epilepsy treatment trials: The EPSET Project

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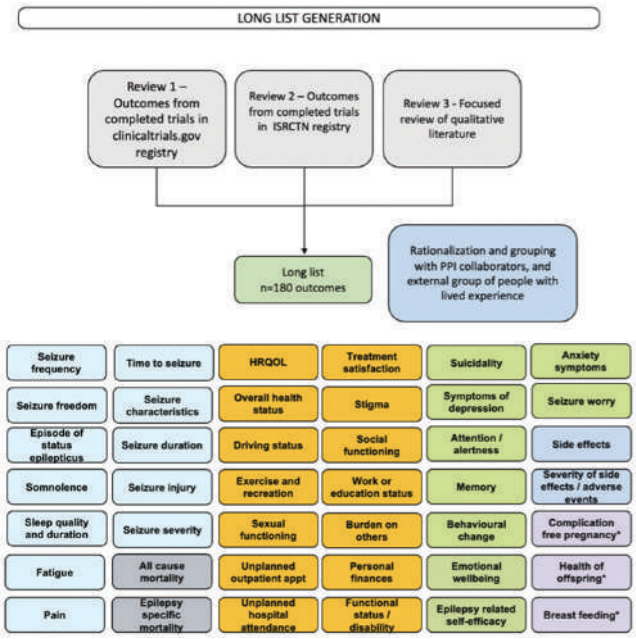
[1]The Walton Centre NHS FT, UK; [2]University of Liverpool, UK; [3]EPSET Project

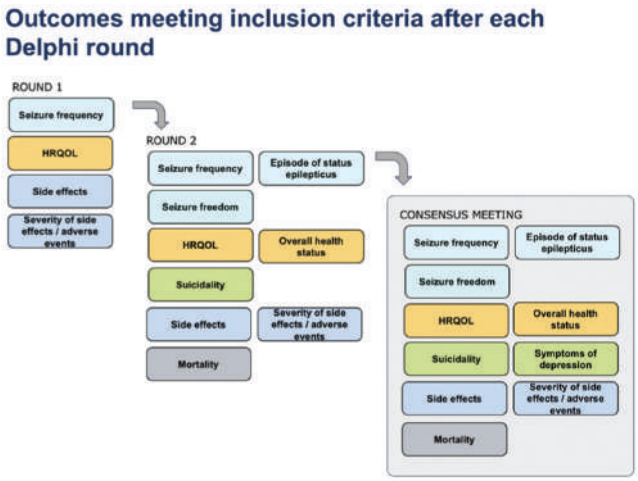
Background and aims: A Core Outcome Set (COS) is a standardised list of outcomes that should be reported as a minimum in all trials. In epilepsy, the choice of outcomes measured varies widely among existing studies, particularly in randomised controlled trials (RCTs). We have developed an internationally derived COS specific to adult epilepsy treatment trials.

Methods: We performed a rapid review of the qualitative literature exploring experiences of people with epilepsy and reviewed outcomes already measured in phase 3 and 4 epilepsy specific RCTs, to generate an outcome long-list. In collaboration with the ILAE Big Data Commission and an international group of healthcare providers, researchers, and people with epilepsy we have performed a grouping and rationalisation process and taken 42 individual outcomes to a two-stage, online Delphi survey followed by consensus meeting.



Long List of Outcomes for EPSET consensus process.

Results: 490 people with epilepsy, their representatives, healthcare professionals and researchers have completed the Delphi surveys in 7 languages, representing the global perspective. Inconclusive outcomes were discussed, and the final outcomes ratified at international online consensus meeting. The ratified COS includes a minimum set of seizure and non-seizure outcomes, that should be measured and reported as a minimum in all future clinical trials.



Outcomes achieving consensus for inclusion in the COS after each Delphi round.

Conclusion: The EPSET Project has identified a COS for adults with epilepsy and derived inter- national consensus. This will ensure that meaningful outcomes are measured in future clinical trials, that the results of trials are relevant to people with epilepsy and facilitate systematic review and meta-analysis.

Disclosure: Nothing to disclose related to the submitted work.

OPR-047 | Heart rate variability exhibits a reduced vagal output in patients with status epilepticus developing Tako-Tsubo

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Background and aims: Tako-tsubo cardiomyopathy (TTC) is an impairment of systolic function, mainly targeting the left ventricle with clinical manifestations closely resembling that of acute coronary syndrome. Although its aetiology has been related to a massive catecholamine release driven by physical and psychological stressors, certain neurologic conditions like status epilepticus (SE) also seem to increase susceptibility to TTC. However, clinical factors linking the SE to TTC are still missing. This study aims to provide reliable criteria to be employed as predictors of TTC in epileptic patients.

Methods: In this study, we examined Heart Rate Variability (HRV) changes in three patients presenting with TTC immediately after an SE. HRV analysis was performed on a 5-minute EKG recording in resting state during and after SE. HRV variability was evaluated according to time and frequency domains and non-linear analysis.

Results: During SE, a leaning towards cardiovagal output reduction was observed, as indicated by decreased RMSSD, HF, and SD1. In addition, an increased LF/HF ratio was also observed, an index that correlates with an overall increased risk of mortality. These imbalances tend to attenuate with SE resolution.

Conclusion: Data from our cohort suggest that HRV variations play a role in predicting cardiac dysfunction (and TTC) in epileptic patients. These data support the notion of a distinct undergoing interplay between sympathetic and cholinergic stimuli on myocardial motility in people with epilepsy.

Disclosure: Nothing to disclose.

OPR-048 | Status epilepticus in patients with brain tumors and metastases: A multicenter cohort study of 208 patients

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Background and aims: Brain tumors and metastases account for approximately 10% of all status epilepticus (SE) cases. This study described the clinical characteristics, treatment, and short- and long-term outcomes of this population.

Methods: This retrospective, multi-center cohort study analyzed all brain tumor patients treated for SE at the university hospitals of Frankfurt and Marburg between 2011 and 2017.

Results: The 208 patients (mean 61.5 ± 14.7 years of age; 51% male) presented with adult-type diffuse gliomas (55.8%), metastatic entities (25.5%), intracranial extradural tumors (14.4%), or other tumors (4.3%). The radiological criteria for tumor progression were evidenced in 128 (61.5%) patients, while 57 (27.4%) were newly diagnosed with tumor at admission and 113 (54.3%) had refractory SE. The mean hospital length of stay (LOS) was 14.8 days (median 12.0, range 1–57), 171 (82.2%) patients required intensive care (mean LOS 8.9 days, median 5, range 1–46), and 44 (21.2%) were administered mechanical ventilation. All patients exhibited significant functional status decline (modified Rankin Scale) post-SE at discharge ($p < 0.001$). Mortality at discharge was 17.3% ($n = 36$), with the greatest occurring in patients with metastatic disease (26.4%, $p = 0.031$) and those that met the radiological criteria for tumor progression (25%, $p < 0.001$).

Conclusion: SE occurrence contributed to a decline in functional status in all cases, regardless of tumor type, tumor progression status, and SE refractoriness, while long-term mortality was increased in those with malignant tumor entities, tumor progressions, and refractory SE.

Disclosure: Nothing to disclose.

Ageing and dementia 2

OPR-049 | CAG repeats within non-pathological range in the HTT gene influence plasma NfL levels in prodromal Alzheimer's disease

C. Crucitti[1]; S. Mazzeo[1]; A. Ingannato[1]; G. Giacomucci[1]; J. Balestrini[1]; V. Moschini[2]; C. Morinelli[2]; G. Galdo[1]; F. Emiliani[1]; D. Frigerio[1]; D. Piazzesi[2]; S. Bagnoli[1]; S. Padiglioni[2]; V. Berti[3]; S. Sorbi[1]; V. Bessi[1]; B. Nacmias[1]

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Background and aims: HTT gene is involved in axon trafficking. It contains a key region of CAG repeats which is responsible, when expanded beyond 39 repeats, of Huntington's disease (HD). Expansions ranging from 27 to 35 are termed as intermediate alleles (IAs). Previous studies showed that increasing repeat length below the HD threshold in HTT confers advantageous changes, stabilizing the interaction with the brain-derived neurotrophic factor. Moreover, CAG repeats seem to affect cognitive performances of patients with Subjective Cognitive Decline (SCD) and Mild Cognitive Impairment (MCI). Here, we aimed to explore the association between CAG repeats, Alzheimer's Disease (AD) CSF biomarkers and plasma neurofilament light chain (NfL) in patients with SCD and MCI.
Methods: We included 95 patients (36 SCD and 59 MCI) who underwent neuropsychological investigation, plasma NfL analysis, CSF biomarkers analysis, Apolipoprotein E (APOE) and HTT genotype analysis. Patients were classified as prodromal AD if they had at least one positive Aβ biomarker and positive p-tau, otherwise they were defined as non-AD.
Results: We tested the association between plasma NfL and CAG repeats: in prodromal AD, this relationship was described by a quadratic model (R^2 0.243, $p=0.009$) as the NfL concentration decreases as the CAG repeat number increases up to 26 repeats (confirmed after age, diagnosis and CAG repeat number adjustment). There was no association in non-AD patients.
Conclusion: The number of CAG repeats, below the IA threshold, may play a role in SCD and MCI modulating the neurodegeneration due to AD, implying the potential of HTT 's involvement in the disease's pathophysiology.
Disclosure: Nothing to disclose.

OPR-050 | Sleep and cognition: Insights from sleep microarchitecture

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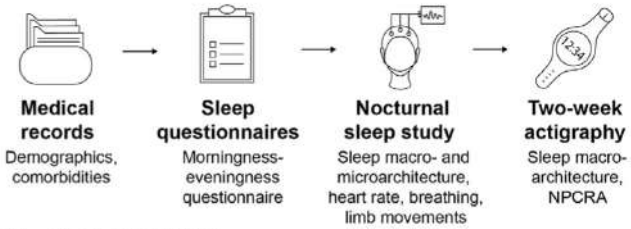
Background and aims: Sleep plays a pivotal role in cognition [Kong, 2023], however, to date little is known about the link between sleep microarchitecture and different cognitive domains [Qin, 2023]. This exploratory analysis aimed to comprehensively investigate this link.
Methods: The "Sleep and cognitive functioning" study included volunteers in good or excellent health condition (Eastern Cooperative Oncology Group grade of 0–1). Demographics, medical history, sleep architecture by polysomnography (electroencephalography [EEG] was recorded either with 6 electrodes or 256 electrodes [high-density EEG, hd-EEG]) and cognition were assessed at study inclusion (Figure 1A). Associations between cognition and sleep microarchitecture were explored using multiple linear regression with adjustment for age and arousal index.

A. Study design



B. Study population

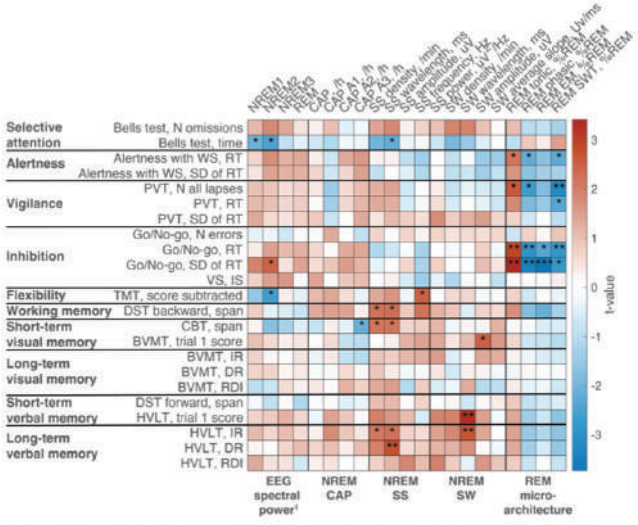
Parameter	Value
Age, years	29.00 [23.00, 35.52]
Female sex	37 (52.1)
MEQ, score	51.00 [46.00, 56.00]
Actigraphy	
Duration of actigraphy, days	14.00 [14.00, 14.00]
Time in bed, minutes	500.91 [457.80, 522.48]
SE, %	82.82 [77.11, 85.39]
Electroencephalography	
Assumed sleep, hours	7.94 [7.55, 8.33]
TRT, hour	8.43 [7.99, 8.95]
TST, hour	7.20 [5.92, 7.81]
SE, %	85.52 [76.89, 90.58]
Arousal index, /h	12.01 [4.25, 20.33]
NREM1, %TST	11.93 [7.81, 17.52]
NREM2, %TST	44.57 [37.56, 49.69]
NREM3, %TST	19.79 [15.40, 24.83]
REM, %TST	21.39 [17.65, 24.10]

Abbreviations: MEQ – Morningness-Eveningness Questionnaire, NPCRA – non-parametric circadian rhythm analysis, NREM – non-rapid eye-movement sleep, PSG –polysomnography, REM – rapid eye-movement sleep, SE – sleep efficiency, TRT – total recording time, TST – total sleep time.

Study design (A) and population (B).

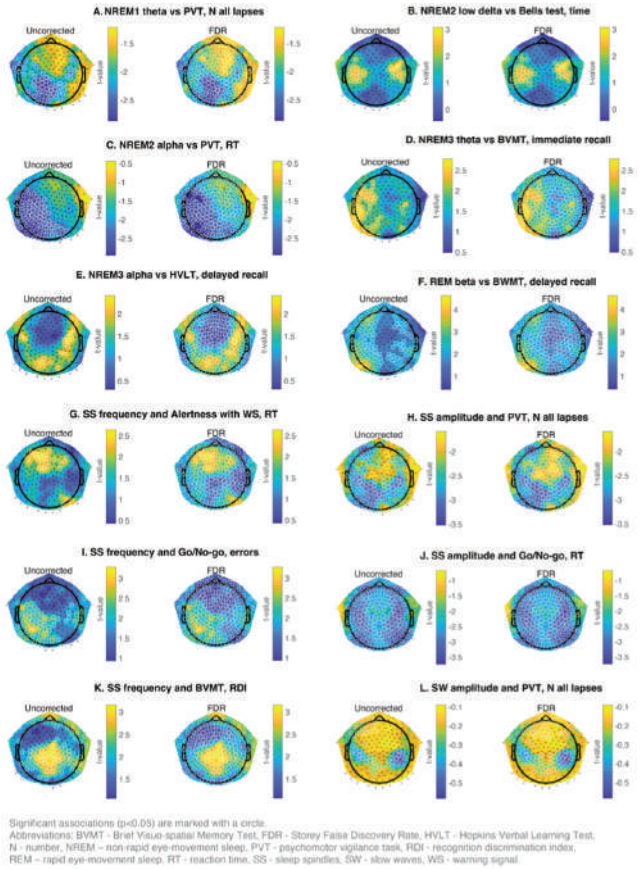
Results: 60 participants were included (median age: 52.7 years old, interquartile range (IQR) [32.9, 64.6]; 55% men; hd-EEG in 52%; Figure 1B). EEG analysis as based on 6 electrodes or their hd-EEG equivalents showed limited associations between cognition and sleep microarchitecture (e.g.,

working and visual memory with high SS density; Figure 2), whereas high-density EEG analysis identified multiple associations of interest with a distinct topography (e.g., visual memory with high EEG spectral power in beta band involving the right posterior region; Figure 3).



* p<0.05, ** p<0.01, *** p<0.001, multiple linear regression. To harmonize the directionality of the effects between different cognitive parameters, the t-values for selective attention, processing speed, attention, and executive functions, except for DST backward span, were multiplied by -1. [1]EEG spectral power is calculated for the band 0.5-40 Hz.
Abbreviations: BVMT – Brief Visuo-spatial Memory Test, CAP – cyclic alternating pattern, CBT – Corsi Block tapping test, DR – delayed recall, DST – digit span test, EM – eye movements,HVLT – Hopkins Verbal Learning Test, IR – immediate recall, IS – interference score, N – number, NREM – non-rapid eye-movement sleep, PVT – psychomotor vigilance task, REM – rapid eye-movement sleep, RDI – recognition discrimination index, RT – reaction time, SD – standard deviation, SS – sleep spindle, SW – slow wave, SWT – saw-tooth wave, TMT – Trail Making Test, VS – Victoria Stroop test.

Associations between cognition and sleep microarchitecture (basic analysis).



Significant associations (p<0.05) are marked with a circle.
Abbreviations: BVMT - Brief Visuo-spatial Memory Test, FDR - Storey False Discovery Rate, HVLT - Hopkins Verbal Learning Test, N - number, NREM – non-rapid eye-movement sleep, PVT - psychomotor vigilance task, RDI - recognition discrimination index, REM – rapid eye-movement sleep, RT - reaction time, SS - sleep spindles, SW - slow waves, WS - warning signal.

Selected associations between cognition and sleep microarchitecture (topographic analysis).

Conclusion: While these results confirm previous findings, they also expand our understanding about the link between sleep microarchitecture and cognition by providing valuable insights for the involvement of specific cortical regions. This knowledge may serve as a basis for targeted interventions to improve sleep-related cognitive function.
Disclosure: European Stroke Research foundation 2021.

OPR-051 | Neurotransmitters circuitry dysfunction in the Alzheimer's disease continuum

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Background and aims: The modulation of neurotransmitters circuitry in Alzheimer's disease (AD) holds promise as a potential focus for pharmacological intervention. We aimed to study the progression of neurotransmitter's networks dysfunction associated to the accumulation of misfolded proteins throughout the AD continuum.
Methods: We enrolled 90AD patients (72.8±7.02 yo) and 42 Healthy Controls (HC, 70±8.53 yo). All patients had a brain [18F] FDG-PET scan and MMSE available. As amyloidosis biomarker, 50 patients performed CSF exam and 40 an amyloid-PET. Patients were divided in two groups based on MMSE score (MMSE <24, $n=24$; MMSE ≥24, $n=66$) to study different disease stages. We performed a voxel-based analysis between AD patients and HC: in the whole group, in MMSE <24 and MMSE ≥24 groups, separately. Using JuSpace toolbox we explored the correlation between [18F]FDG-PET images and PET maps of glutamate (mGluR5), GABA (GABA-a), dopamine (D1, D2, FDOPA), serotonin (SERT, 5HT1a, 5HT1b, 5HT2a, 5HT4), noradrenaline (NAT) and choline (VAChT).
Results: In the whole AD group, the distribution of brain hypometabolism was associated with areas of 5HT2a and mGluR5 density ($p=0.029$, $p=0.034$ respectively). This remained significant in the MMSE <24 group ($p=0.006$). In the whole group, 5HT2a density correlates with a lower MMSE score and greater cerebral amyloid burden.
Conclusion: The spatial pattern of brain hypometabolism in AD is related to the distribution of specific neurotransmitters. We can speculate that areas with elevated expression of receptors involved

may be more susceptible to synaptic damage, as evidenced by brain hypometabolism.

Disclosure: Nothing to disclose.

OPR-052 | Universal prevention of dementia in Italy: A document analysis of the 21 Italian Regional Prevention Plans

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Background and aims: An estimated 40% of dementia cases could be prevented through interventions targeting 12 modifiable risk factors (RFs) at different stages of life. We characterized the subnational population approaches to the prevention of dementia implemented in Italy.

Methods: We conducted a document analysis of the 21 Regional Prevention Plans (RPPs) for 2020–2025. We categorized the dementia-specific preventive interventions according to (i) type of RF targeted, (ii) target age, and (iii) target population. Indirect potential beneficial effects of interventions were defined by critically reviewing published literature on plausible relationships between RFs. Furthermore, we developed and applied to all RPPs a checklist evaluating key elements of situational analysis and prevention planning.

Results: Physical inactivity was the only RF covered by all RPPs, as a direct target of 117/248 interventions for dementia prevention. Smoking was targeted in more than 50% of RPPs, while less than 50% covered alcohol consumption and obesity. Only 25% of RPPs had dementia-specific interventions for social isolation, hypertension, and diabetes. Two RPPs targeted air pollution and only one TBI. No RPP directly covered low education, depression or hearing loss for dementia prevention. Total scores of the checklist ranged from a minimum score of 7 to a maximum of 28/63.

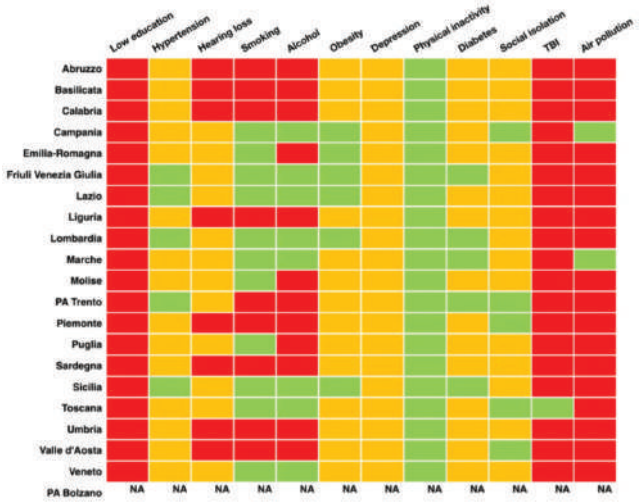
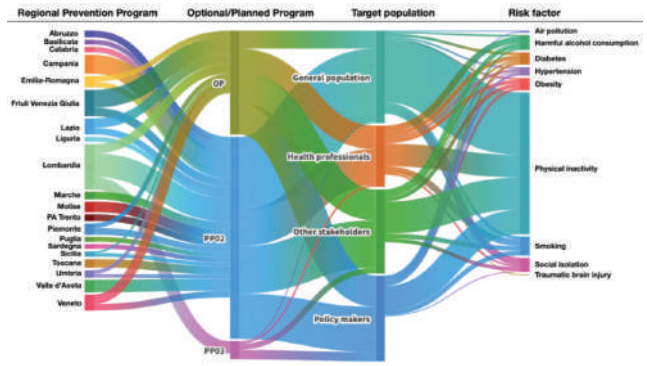
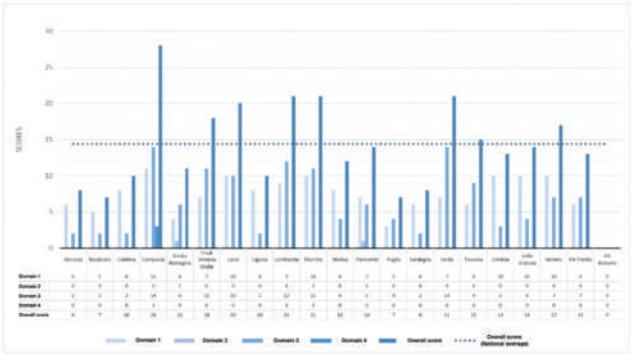


TABLE 1 Subnational coverage of potentially modifiable risk factors for cognitive decline.



Sankey Chart of the dementia-specific preventive interventions.



Checklist scores by RPP.

Conclusion: While interventions on cardiovascular RFs can synergistically affect multiple noncommunicable diseases, their prevalence may suggest that policymakers are not fully aware of RFs more specific to dementia (e.g., social isolation and hearing loss). Therefore, policymakers, public health workers, and dementia experts should closely cooperate for the development of these policies.

Disclosure: Nothing to disclose.

OPR-053 | Neuromodulation of the mediodorsal nucleus during MRgFUS thalamotomy demonstrates a causal role in reward learning

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Background and aims: Evidence from basic neuroscience increasingly supports a specific role for the Medial Dorsal (MD) thalamic nucleus influencing decisions that guide reward-based learning. As common clinical syndromes of impulsivity, apathy and executive dysfunction can be explained by abnormal reward-learning across multiple clinical groups. Neuromodulation target MD nucleus may represent a potential future therapeutic intervention for disorders of cognitive control.

Methods: Thirty-five patient's undergoing MRgFUS thalamotomy for Essential Tremor targeted at ventral intermediate nucleus (Vim) performed pre-and post-operative (<24 hours) cognitive testing using the 4-armed restless bandit task. Outcome measures of task performance included probability of choosing the most rewarding bandit (Prew) and choice perseveration (Pstay). In 23 patients, post-operative masks of (< 24 hours) oedema extension into the MD nucleus were used to analyse the relationship with cortical functional connectivity and it's influence on decision making.

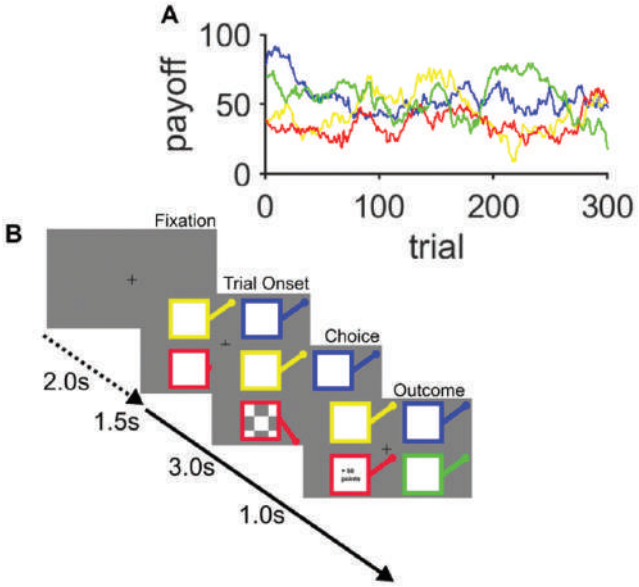

FIGURE 1 Restless bandit reinforcement learning task. (A) example of fluctuating reward payout for each of the four bandits in the task (B) example trial with screenshots of computer graphics.

Results: Post-thalamotomy, patients used a greater proportion of perseverative choices (Pstay) pre: 0.67 ± 0.07, post: 0.75 ± 0.0.05, rmANOVA, $F = 11.05$, $p < 0.001$). Task performance indexed by choices to the best bandit (Prew) was unaffected by thalamotomy (rmANOVA, $F = 3.02$, $p = 0.07$). Cortical functional connectivity with thalamotomy oedema extension into the MD nucleus predicted the extent to which the thalamotomy increased Pstay in individual patients (rho = 0.64, $p = 0.001$).

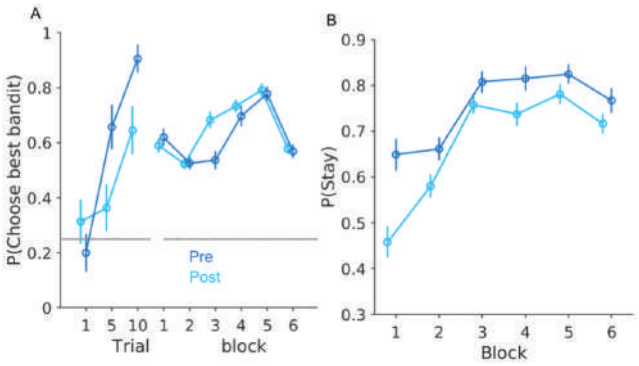

FIGURE 1 Behavioural effects of thalamotomy on task performance. Analysis binned into six- 50 trial blocks (A) probability of choosing the highest value bandit (B) Probability of choosing the same bandit on two consecutive trials (Pstay).

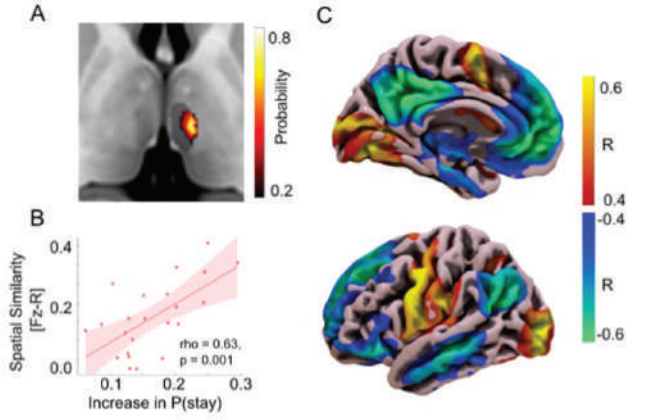

FIGURE 3 (A) Probabalistic analysis of overlap between thalamotomy ($n=23$) oedema (heatmap) with the medialdorsal thalamic nucleus (grey overlay) onto standard brain template in MNI space. (B) R map correlation and (B) cortical connectivity map.

Conclusion: MRgFUS thalamotomy can be used as an opportunity to study cognitive thalamic nuclear function. An experimental design for intra-operative thermal neuromodulation is proposed to causally map the different contributions of the thalamic nuclei to cognitive control.

Disclosure: TG has received honoraria from GE Healthcare Europe. AM has received research funding from Boston scientific, Medtronic and Insightec.

Movement disorders

OPR-054 | **Substantia Nigra and subthalamic nucleus deep brain stimulation for freezing of gait in Parkinson's disease**

C. Ledda[1]; C. Artusi[1]; S. Gallo[2]; D. Rinaldi[3]; C. Campisi[1]; V. Rousseau[4]; C. Thalamas[5]; R. Barbosa[5]; F. Ory-Magne[5]; C. Brefel-Courbon[5]; O. Rascol[6]; A. de Barros[7]; E. Harroch[6]; M. Zibetti[1]; M. Rizzone[1]; A. Romagnolo[1]; G. Imbalzano[1]; L. Lopiano[1]; J. Houeto[8]; M. Fabbri[6]

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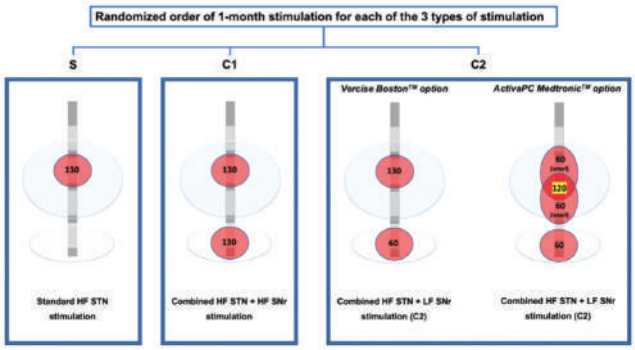
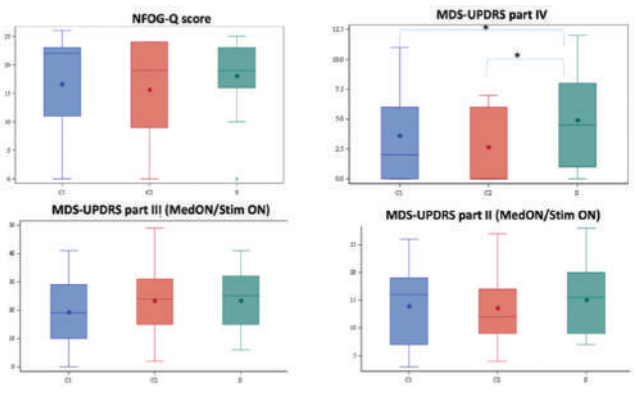
Background and aims: Freezing of gait (FoG) is a debilitating symptom of Parkinson's disease (PD) with limited response to dopaminergic medication and subthalamic deep brain stimulation (STN-DBS). Substantia nigra pars reticulata (SNr) stimulation could improve FoG.

Methods: Two double-blind, cross-over, randomized trials, following an identical protocol were conducted involving STN-DBS treated PD patients with severe FoG. Participants received: standard high frequency (HF) STN-DBS (S), combined HF-STN and SNr stimulation (C1), and combined HF-STN and low-frequency SNr stimulation (C2), for 1 month each in a randomized order. The primary endpoint was the change in the New Freezing of Gait Questionnaire (NFOG-Q) score. Secondary analyses were performed on motor complications, axial symptoms, activities of daily living, psychiatric symptoms, sleep, and patient preference.

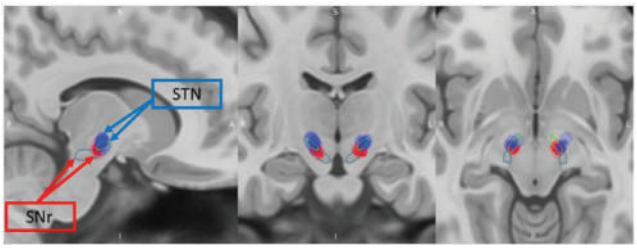


Stimulation method for S, C1, C2.

Results: Fifteen patients received at least one combined stimulation. No statistically significant difference in NFOG-Q scores was found between S, C1, and C2; one-third of patients showed a clinically significant improvement (≥8 points) with combined stimulations. Motor complications improved significantly with C1 and C2 compared to S (C1 vs. S: 3.6 ± 3.8 vs. 4.9 ± 3.8, $p=0.046$; C2 vs. S: 2.7 ± 3.1 vs. 4.9 ± 3.8, $p=0.005$). At the end of the study, 80% of patients chose combined STN-SNr stimulation. All adverse events were manageable.



Scores after one moth of the following stimulation setting: C1, C2, and S.



VTA of the STN and of the SNr for all patient included in the study in the stimulation setting C1/C2.

Conclusion: Our study did not show a statistically significant improvement in NFOG-Q, but one-third of patients experienced a clinically meaningful FoG improvement. Moreover, SNr stimulation was both safe and effective in addressing motor complications., highlighting the importance of further exploration into the effects of combined STN-SNr stimulation.

Disclosure: Nothing to disclose.

OPR-055 | Effectiveness and safety of levodopa-entacapone-carbidopa infusion in Parkinson's disease. A real-world data study

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Background and aims: Levodopa-entacapone-carbidopa intestinal gel (LECIG) infusion is a recently developed device-aided therapy for advanced Parkinson's disease (PD) patients. Our aim was to present real world data (RWD) about the use of LECIG in PD patients from Spain.

Methods: A multicenter observational retrospective study of the first patients to start LECIG in Spain was performed. All neurologists with an experience of at least 2 patients treated until November 1, 2023 were invited to participate. RWD about effectiveness and safety from the medical records (V0, pre-LECIG; V1, LECIG starting; V2, post-LECIG follow-up) with a total of 246 variables was collected.

Results: Fifty-one PD patients (58.8% males; 69.7 ± 9.7 years old) from 15 Spanish centers with a mean disease duration of 13.8 ± 6.2 years were included (Table 1). Fourteen patients (27.5%) were switched directly from levodopa-carbidopa intestinal gel. The mean treatment duration was 140.7 ± 83.7 days (range, 10–302). The mean daily OFF time decreased from 5.1 ± 3 at baseline (pre-LECIG) to 1.9 ± 1.6 (post-LECIG) ($N = 45$; $p < 0.0001$). Global improvement was observed in more than 85% of the patients (Figure 1). No significant change was detected in the levodopa equivalent daily dose from V0 to V2 (Figure 2). Only 2 patients (3.9%) received 24-hour infusion and 11 (21.6%) required more than 1 cartridge per day. Eighteen patients (35.3%) had at least one adverse event related to LECIG and/or the device system. Three patients (5.9%) discontinued LECIG (Table 2).

	N			N	
V0 BASELINE (pre-LECIG)			Entacapone previously (%)	48	66.7
			DAT previously (%):	51	45.1
Age	51	69.7 ± 9.7	- DBS		3.9
Gender (males) (%)	51	58.8	- Apomorphine		9.8
			- LCIG		21.6
Weight (kg)	32	67.1 ± 11.9	- More than 1/other		9.8
Height (cms)	33	164.8 ± 9.8			
BMI	31	24.7 ± 3.1	Treatment for PD (%):	51	
			- Levodopa		100
Civil status (%):	43		- MAO-B inhibitor		60.8
- Married		60.5	- Dopamine agonist		52.9
- Single		16.3	- COMT inhibitor		54.9
- Widowed		11.6	*Entacapone		29.4
- Other		11.6	*Opicapone		25.5
			- Amantadine		23.5
Living style (%)	47		L-dopa daily dose (mg)	46	1093.3 ± 457.2
- With the partner		55.3	DA daily dose (mg)	28	277.3 ± 235.3
- Alone		10.6	LEDD (mg)	45	1537 ± 524.4
- With another family member		8.5			
- Other		25.6	Other treatments (%):	51	
			- Antidepressant		52.9
Comorbidities (%):	51		- Benzodiazepine		52.9
- Arterial hypertension		27.5	- Antipsychotic		25.5
- Diabetes mellitus		11.8	- Anti-dementia		15.7
- Dyslipemia		23.5			
- Atrial fibrillation		3.9			
- Cardiopathy		7.8	**V1 (starting LECIG)**		
- Lung disease		2			
- Polineuropathy		9.8	Type of treatment (%)	51	
			- New start		72.5
Time from diagnosis of PD (years)	51	13.8 ± 6.2	- Switch from LCIG		27.5
Motor fluctuations (%)	50	100			
Time with motor fluctuations (years)	49	7.1 ± 3.9	How LECIG was started (%):	51	
Non-motor fluctuations (%)	51	70.6	- Hospitalization		51
Daily OFF time (hours)	49	5.1 ± 2.9	- On an outpatient basis		49
H&Y – OFF	51	3 [3,4]	Days for full LECIG optimization	51	4.6 ± 5
H&Y – ON	51	2 [2,2.5]	Morning dose (mL)	51	10 [8, 15]
UPDRS – III – OFF	45	41.2 ± 15.9	Infusion rate (mL/h)	50	2.1 [1.8, 2.7]
UPDRS – III – ON	44	18.9 ± 9.8	Extra dose (mL)	51	1.5 [1, 1.8]
Dyskinesia (%)	45	84.4	LECIG monotherapy (%)	50	26
Cognitive impairment (%):	51	35.3	LECIG 24 hours (%)	50	4
- MCI (%)		33.3	LEDD (mg)	44	1403.4 ± 425.8
- Dementia (%)		2			

The results represent % or mean ± SD.

BMI, body mass index; COMT, catechol-O-methyl transferase; DAT, device-aided therapy; DBS, deep brain stimulation; H&Y, Hoehn&Yahr; LCIG, levodopa-carbidopa infusion gel; LECGI, levodopa-entacapone-carbidopa infusion gel; LEDD, levodopa equivalent daily dose; MCI, mild cognitive impairment; UPDRS, Unified Parkinson's Disease Rating Scale.

TABLE 1 Data about sociodemographic aspects, comorbidities, antiparkinsonian drugs and other therapies at baseline (V0) and LECIG starting at V1.

	N
Total AEs, N	36
- Tube obstruction	5
- Stoma infection	4
- Significant weight loss	4
- Orthostatic hypotension / hypotension	4
- Granuloma	3
- Erythema	3
- Dyskinesia impairment	3
- Tube migration	2
- Visual hallucinations / psychosis	2
- B vitamin deficiency	1
- Constipation	1
- Paresthesias in lower extremities	1
- Acute renal insufficiency	1
- Acute urinary retention with urological complication	1
- Acute ischemic stroke	1
Patients with at least one AE, N (%)	19 (37.3)
At least possibly related (LECIG and/or device) AEs, N	33
Patients with at least possibly related (LECIG and/or device) AEs, N (%)	18 (35.3)
Patients with at least one AE leading to discontinuation, N (%)	3 (5.9)
- Serious stoma infection	1
- Acute urinary retention with urological complication	1
- Psychosis	1
Patients with at least one possibly related (LECIG and/or device) leading to discontinuation N (%)	2
Deaths, N (%)	1*

AE, adverse event; LECIG, levodopa-entacapone-carbidopa intestinal gel.

*The patient had a severe stoma infection that required to remove the PEG and stopping LECIG. He was institutionalized and died more than 1 month later related to an acute renal failure.

TABLE 2 Adverse events collected by the neurologist in patients receiving LECIG from V1 (starting LECIG) to V2 (follow-up visit; 140.7 ± 83.7 days, range from 10 to 302).

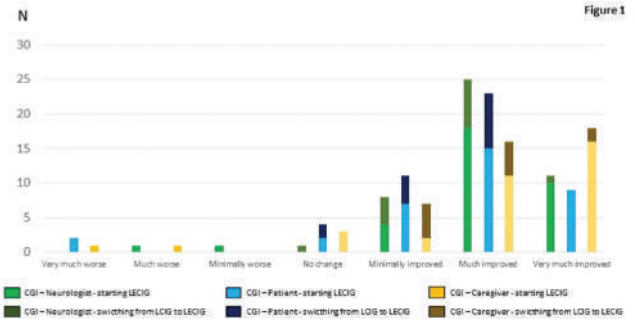

Figure 1. CGI (Clinical Global Impression of change) according to the opinion of the neurologist (N=47); patient (N=49) and caregiver (N=46) at V2 (follow-up visit). Patients who started LECIG appear in light colors and those who switched from LCIG to LECIG appear in dark colors. Improvement was observed in 59.7%, 87.7% and 89.1% of patients, respectively. LECIG, levodopa-entacapone-carbidopa intestinal gel; LCIG, levodopa-carbidopa intestinal gel.

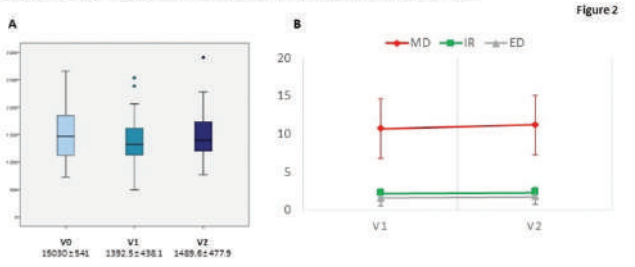

Figure 2. A. LEDD (mg) at baseline (V0; pre-LECIG), V1 (after starting LECIG) and V2 (follow-up visit; 140.9 ± 88 days, range 10 – 302). N = 34. V1 vs V0, p=0.038; V2 vs V0, p=0.489; V2 vs V1, p=0.083. Data are presented as box plots, with the box representing the median and the two middle quartiles (25–75%). B. Change from V1 to V2 in morning dose (mL; N=49; from 10.8 ± 4 to 11.8 ± 3.9; p=0.054), infusion rate (mL/h; N=46; from 2.2 ± 0.6 to 2.3 ± 0.6; p=0.112) and extra dose (mL; N=49; from 1.5 ± 0.6 to 1.7 ± 0.8; p=0.010). Data are presented as mean and standard deviation. P values were computed using the Wilcoxon signed-rank test in A and B. ED, extra dose; IR, infusion rate; LECIG, levodopa-entacapone-carbidopa intestinal gel; LEDD, levodopa equivalent daily dose; MD, morning dose.

Conclusion: LECIG was safe and effective in advanced PD patients.
Disclosure: The authors report no conflict of interest.

OPR-056 | sGFAP – A potential biomarker for disease activity in essential tremor?

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Background and aims: Essential tremor (ET) constitutes a heterogeneous syndrome and possible neurodegeneration has been debated. We recently linked serum-NfL to cognitive decline in ET-patients with short disease duration (DD). Serum-glial fibrillary acidic protein (sGFAP) hitherto remains unstudied in ET.

Methods: Data from 36 ET-patients and 36 age, sex and body-mass-index-matched healthy controls were analyzed. sGFAP was quantified by single-molecule-array in baseline (BL) and follow-up (FU; 5 years) blood samples. ET-patients underwent clinical evaluation (Fahn-Tolosa-Marin-Tremor-Clinical-Rating-Scale-Total-Score, FTM-TS).

Results: BL and FU sGFAP did not differ between groups. In ET-patients, low BL FTM-TS was associated with higher sGFAP-increase during the observational period ($rs = -0.551$, $p = 0.002$). Shorter DD correlated with low BL FTM-TS and trended towards higher sGFAP-increase ($rs = -0.344$, $p = 0.068$). Stratification in DD below/above median (10.7 years) showed higher sGFAP-increase in short DD patients (39.6 vs. 12.6 pg/mL, $p = 0.020$). In short DD patients, high BL sGFAP correlated with high FU FTM-TS ($rs = 0.672$, $p = 0.006$) and FTM-TS-increase ($rs = 0.590$, $p = 0.021$). Stratification of ET-patients according to sGFAP-level below/above median (124.2 pg/mL) revealed that high sGFAP-patients were older at BL (70.0 vs. 60.7 years, $p < 0.001$) and disease onset (62.6 vs. 49.9 years, $p < 0.001$) than low sGFAP-patients. Annual sGFAP-increase correlated with annual FTM-TS-increase in the high ($rs = 0.587$, $p = 0.027$) but not in the low sGFAP-group. In patients with high sGFAP and short DD ($n = 8$), annual sGFAP-increase correlated with annual FTM-TS-increase ($rs = 0.738$, $p = 0.037$).

Conclusion: This study shows elevated sGFAP in elderly, late-onset ET-patients. sGFAP-increase is higher in earlier vs. later disease stages and correlates with worsening motor function, suggesting sGFAP as a possible biomarker of ET disease activity.

Disclosure: Nothing to disclose.

OPR-057 | Modelling pathology progression in Parkinson's disease phenotypes

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Background and aims: Understanding the relationship between phenotypic heterogeneity and the spread of pathology in Parkinson's disease (PD) is challenging. The α-Synuclein Origin site and Connectome (SOC) model postulate that α-synuclein aggregation first localization and spreading determine disease evolution. Accordingly, two PD subtypes were proposed: brain-first-PD, from

central nervous system, and body-first-PD, from peripheral nervous structures. We aim to use the SOC model to differentiate PD phenotypes predicting disease progression.

Methods: 1120 de novo- PD patients, 910 prodromal-cases, and 263 healthy controls were included from the Parkinson's progression markers initiative. Patients and prodromal-cases with REM behavior disorder and/or autonomic symptoms at baseline were classified as body-first, otherwise as brain-first. All subjects underwent longitudinal (12-years) clinical protocol and magnetic resonance imaging.

Results: Body-first-PD (667) demonstrated higher motor burden and complications, worse cognitive evolution, and more severe depression compared to brain-first-PD. Body-first-PD showed bilateral medial and lateral temporal atrophy (amygdala, para-hippocampus, temporoparietal junction), cerebellum and brainstem. Brain-first-PD patients demonstrated circumscribed atrophy of the left hemisphere (angular gyrus, sensory-motor cortex, inferior frontal gyrus). Body-first-prodromal-cases (519) demonstrated similar results to body-first-PD, i.e. greater motor and cognitive impairment, involving the same domains, and grey matter atrophy in lateral temporal areas.

Conclusion: Consistent with the SOC model, the study results indicate that body-first-PD and prodromal-cases had worse disease progression and more severe brain atrophy compared to brain-first. The results underscore the importance of PD patient phenotyping since the prodromal phases. Hence, the application of the model would enable tailored therapeutic approaches and disease prevention interventions in high-risk individuals.

Disclosure: Nothing to declare.

OPR-058 | Thoracic spinal cord stimulation may improve bradykinesia and rigidity in gait impaired Parkinson's disease

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Background and aims: Gait impairment in Parkinson's disease (PD) is debilitating and often resistant to available therapies. Recently, spinal cord stimulation (SCS) has been suggested to be effective. Nevertheless, existing literature on SCS for gait problems is limited and possible mechanisms of action remain to be elucidated. This study is part of the SCS therapy for patients with PD and gait problems (STEP-PD) trial (ClinicalTrials.gov: NCT05110053), and here we aim to evaluate the effect on lower body motor symptoms and gait.

Methods: Fourteen non-demented PD patients with gait impairment were included in the trial. The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) was assessed before surgery and at 6- and 12-month follow-ups. Total motor score, lower body and gait (LBG) subscore, and the sum of lower body bradykinesia and rigidity items (Table 1) were compared using paired t-test. Mean differences with 95% confidence intervals are presented.

Table 1

MDS-UPDRS part III: total motor score	Sum of items 3.1 – 3.18
MDS-UPDRS LBG subscore	Sum of items 3.3d, 3.3e, 3.7a, 3.7b, 3.8a, 3.8b, 3.10, 3.11, 3.12
MDS-UPDRS lower body bradykinesia and rigidity	Sum of items 3.3d, 3.3e, 3.7a, 3.7b, 3.8a, 3.8b

TABLE 1 Details of the Movement Disorder Society-Unified Parkinson Disease Rating Scale (MDS-UPDRS) scores presented. LBG, lower body gait.

Results: Thirteen patients were treated with active SCS for 6 months and eight patients were treated for 1 year. While the total motor score improved slightly after both 6 months (−2.85 points [−7.07;1.38]) and 12 months (−5.63 points [−14.03;2.78]), the LBG subscore improved by −3.38 points (−4.83;-1.93), $p = 0.0003$, after 6 months and −5.25 points (−8.93;-1.57), $p = 0.0118$, after 12 months. Furthermore, lower body bradykinesia and rigidity improved by −2.31 points (−3.75; −0.86), $p = 0.0046$, after 6 months and −3.88 points (−7.17; −0.58), $p = 0.027$, after 12 months.

Conclusion: SCS may ameliorate lower body bradykinesia and rigidity in gait-impaired PD patients. Furthermore, our results suggest that extended treatment duration could yield a greater improvement.

Disclosure: KM's institution (Aarhus University Hospital) has received travel support from Boston Scientific.

Motor neurone diseases 2

OPR-059 | Role of brain 2-[18F]FDG-PET for the differential diagnosis between ALS and ALS-mimics

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Background and aims: The combination of brain and spinal cord 2-[18F]FDG-PET has shown a 81.5% accuracy in discriminating ALS and ALS-mimics in a published study. We investigated the potential role of brain 2-[18F]FDG-PET as a single marker to discriminate ALS and ALS-mimics.

Methods: Our dataset included 663 ALS cases and 40 patients referred for suspected ALS but for whom an alternative diagnosis was made (ALS-mimics) who underwent brain 2-[18F]FDG-PET at diagnosis at the ALS Centre of Turin between 2009 and 2019. We randomly collected 40 ALS cases and calculated Laplacian scores in this group. This is an algorithm for the selection of features, which correspond to the voxels. It constructs a nearest neighbour graph. Laplacian score seeks those features that respect this graph structure. We retained the top features and performed feature extraction form the two groups (ALS and mimics). Then, we randomly split the sample composed of ALS and mimics in a training set (80%) and a test set (20%). The training set was used to train the classifier (Support Vector Machine) and the test set was used to evaluate the performance of the model. The procedure was randomly repeated 10 times for internal validation.

Results: SVM showed 85% specificity and 81% sensitivity on the test set, with an error rate of 17%. The classification was based on three cerebellar clusters, situated in left anterior lobe, right uvula and right culmen.

Conclusion: Our data support the possible role of brain 2-[18F]FDG-PET as a single diagnostic marker to discriminate ALS and ALS-mimics.

Disclosure: Nothing to disclose.

OPR-060 | Morphometric analysis of spinal motor neuron degeneration in sporadic amyotrophic lateral sclerosis

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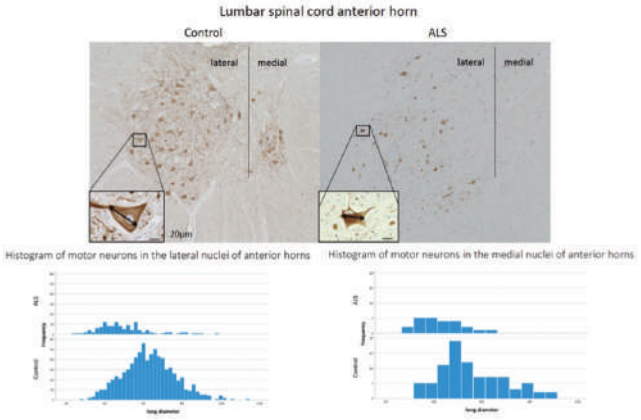
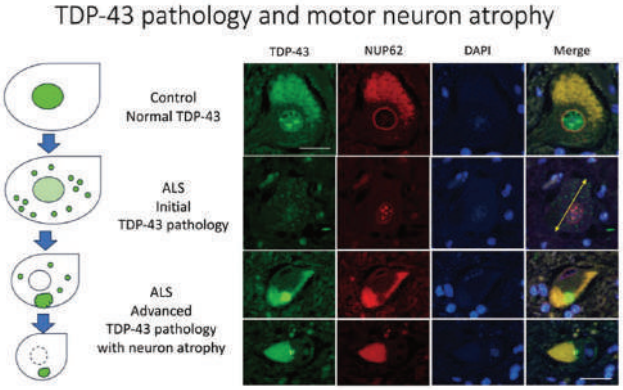
Background and aims: To clarify the relationship between TDP-43 pathology and spinal anterior horn motor neuron (AHMN) atrophy in sporadic amyotrophic lateral sclerosis (SALS).

Methods: The subjects were 8 SALS and 12 disease controls. Formalin-fixed specimens of lumbar spinal cord samples were paraffin-embedded and sectioned at the level of the fourth lumbar spinal cord with a thickness of 4 μm. Using a microscope (BZ-X800), the long diameter of neurons with nucleoli was measured in spinal AHMNs stained with anti-SMI-32 antibody. AHMNs were divided into medial and lateral nuclei for statistical processing. Among spinal AHMNs double-fluorescently stained with TDP-43 and anti-nucleoporin p62 (NUP62) antibodies against the nuclear membrane, we also measured the long diameter of AHMNs with TDP-43 in both the nucleus and cytoplasm, which are considered as initial lesions of TDP-43 pathology.

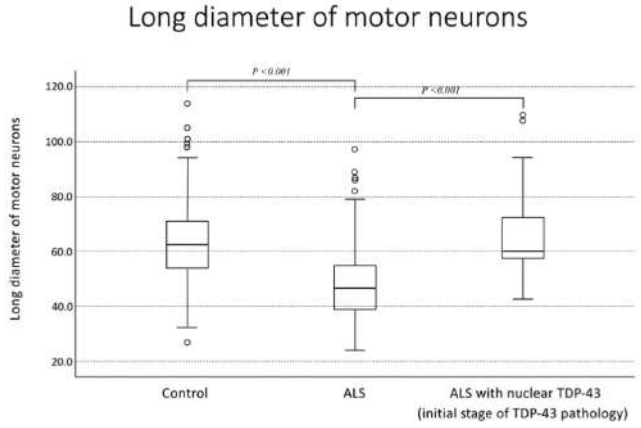
Results: The long diameter of the lumbar spinal AHMNs in SALS was smaller in the medial nucleus (42.54 ± 9.33 micrometer, $n = 24$) and the lateral nucleus (49.41 ± 13.86, $n = 129$) than in controls (medial nucleus 55.84 ± 13.49, $n = 85$, $p < 0.001$; lateral nucleus 62.39 ± 13.29, $n = 756$, $p < 0.001$, Mann–Whitney test). All 21 motor neurons with early TDP-43 pathology were in the lateral nucleus, and their long diameter (67.60 ± 18.3) was not significantly different from controls.



Histogram of spinal motor neurons.



TDP-43 pathology and motor neuron atrophy.



Long diameter of motor neurons.

Conclusion: Motor neuron atrophy in SALS does not occur at the initial stages of TDP-43 pathology, and TDP-43 pathology has already progressed in the atrophic motor neurons.

Disclosure: Nothing to disclose.

OPR-061 | Genome-wide directional effects of transcription factor binding on Amyotrophic Lateral Sclerosis

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Background and aims: The transcription factor (TF) c-myc has been shown to be elevated in many neurological disorders, including neurodegenerative diseases. We observed an increased activity of c-myc in astrocytes in TDP-43 mice models of Amyotrophic Lateral Sclerosis (ALS), being related to a reduction in survival, probably due to the release of an altered protein cargo by astrocytes. The aim of our study was to test the role of TFs in the pathogenesis of ALS.

Methods: We used signed LD profile (SLDP) regression to test the activity of TFs in large case–control GWAS of both ALS and frontotemporal dementia (FTD) [1,2]. SLDP regression is a validated method used to identify genome-wide directional effects of signed functional annotations on polygenic disease risk [3]. We ran SLDP regression using the 382 available TF annotations for both ALS and FTD gene data sets. Results were significant at a per-trait FDR <5%. A positive association implies a greater binding of the TFs, leading to greater expression; likewise, a negative association implies a lower binding of the TFs, leading to lower expression.

Results: We used GWAS summary statistics obtained from 12.577 ALS patients (vs. 23.475 healthy controls) and 3.526 FTD patients (vs. 9.402 healthy controls). We detected 38 and 14 significant associations respectively in ALS and FTD (Tables 1 and 2). Particularly, genetic variants determining a greater binding of c-myc were associated with an increased risk of ALS, but not FTD.

TF	z	p
Nrsf	3,37580524	0,000736
Nrsf	3,31819873	0,000906
Nrsf	3,27596932	0,001053
Nrsf	3,26335888	0,001101
Sp1	3,12155278	0,001799
Nrsf	2,99952605	0,002704
Max	2,98649007	0,002822
Foxp2	2,93254149	0,003362
Jund	2,86584334	0,004159
Corest	2,66455613	0,007709
Hnf4	2,64088411	0,008269
Cmyc	2,59986662	0,009326
Mxi1	2,5741042	0,01005
Pol2s2	2,5159857	0,01187
Etoh	2,50198258	0,01235
cfos/Tam	2,47968092	0,01315
Chd2	2,47670891	0,01326
Sin3	2,4059607	0,01613
Ctcfsc5916	2,36172765	0,01819
Pol2	2,31670146	0,02052
cfos/Tam	2,27128055	0,02313
Pol2	2,24341602	0,02487
Cmyc	2,23011213	0,02574
Mxi1	2,21880491	0,0265
Pol24	2,2103627	0,02708
Pmisc	2,1731371	0,02977
Gm1	2,13354554	0,03288
Fosl2	2,11805984	0,03417
Elf1	2,09153648	0,03648
Max	2,07875364	0,03764
Pol2	2,07625903	0,03787
Ubtf	2,07238018	0,03823
Ctcf	2,06661973	0,03877
Pol2	2,06260681	0,03915
Rfx	2,05935754	0,03946
Pol2	2,04141092	0,04121
Ctcf	2,02487696	0,04288
Etoh	1,99963215	0,04554

TABLE 1 SLDP regression for ALS gene data set. Significant associations obtained from 12.577 ALS patients (vs. 23.475 healthy controls) are shown. We detected 38 significant positive associations at per-trait FDR <5%.

TF	z	p
Egr1	3,32036446	0,000899
Maz	2,7341055	0,006255
Maz	2,62428929	0,008683
Mafk	2,56965445	0,01018
Pol2	2,55759092	0,01054
Nrsf	2,39988998	0,0164
Znf	-2,34967122	0,01879
Chd2	2,23131909	0,02566
Sin3	2,19393615	0,02824
Elf1	2,18484791	0,0289
Pol2	2,1288098	0,03327
Nrsf	2,10824272	0,03501
Pol2	2,04090772	0,04126
Pol2	2,02439039	0,04293

TABLE 2 SLDP regression for FTD gene data set. Significant associations obtained from 3.526 FTD patients (vs. 9.402 healthy controls) are shown. We detected 14 significant associations at per-trait FDR <5%, Only 1 of these associations was negative.

Conclusion: An increased activity of c-myc could be a specific pathogenetic mechanism in ALS, leading to premature motor neurons death.

Disclosure: Nothing to disclose.

OPR-062 | Early-onset amyotrophic lateral sclerosis (EO-ALS): A different phenotype with a higher resilience?

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder with a mean age of onset around 60 years. Evidence from the literature suggests the existence of a distinct clinical phenotype associated with earlier age at onset (EO-ALS). Here we aim to define the clinical phenotype of EO-ALS in comparison to late-onset ALS (LO-ALS).

Methods: We studied a cohort of 1165 ALS patients, divided in two groups: EO-ALS (onset 20–45 years), and LO-ALS (onset >45 years). Clinical phenotype, survival outcome measures and serum biomarkers were compared in the two groups Significant *p*-value was set at <0.05.

Results: We found that EO-ALS patients had significant predominance of males (72.5% vs. 60.9%, $p=0.010$), familial ALS (15.3% vs. 9.5%, $p=0.037$), spinal-onset (82.4% vs. 70.7%, $p=0.047$), progressive muscular atrophy phenotype (11.7% vs. 3.9%, $p=0.00009$). In the EO-ALS group, 1.5% had a cerebellar-ALS-plus phenotype ($p=0.00004$). Interestingly, a lower progression rate (median: 0.47 vs. 0.61, $p=0.011$) and prolonged survival (median values: 117.3 vs. 49.7 months, $p<0.001$) were observed in EO-ALS as well as a longer diagnostic delay (17.8 vs. 12.5 months, $p<0.001$). Finally, in EO-ALS serum GFAP was lower (median: 84.02 vs. 122.36 pg/mL, $p=0.011$), and CPK was higher (median: 262 vs. 160 U/L, $p<0.001$).

	EO-ALS				LO-ALS				
	n	%	mean (SD)	median (min-max)	n	%	mean (SD)	median (min-max)	p-value
Sex									0.010*
F	36	27.5			404	39.1%			
M	95	72.5			630	60.9%			
Familial									0.037*
FALS	20	15.3			98	9.5			
SALS	110	84.0			933	90.2			
Age at onset (y)			37.8 (± 6.1)				62.9 (± 9.4)		
Diagnostic delay (m)				17.18 (0.3 - 450.3)				12.5 (0.6 - 154.9)	< 0.001*
Site of onset									0.047*
Bulbar	22	16.8			255	24.7			
Spinal	108	82.4			772	74.7			
Phenotype									
Classic	64	50			535	52.1			0.65271 (B)
Bulbar	19	14.8			222	21.6			0.07508 (B)
UMN-p	15	11.7			86	8.4			0.20767 (B)
PLS	4	3.1			55	5.4			0.28014 (B)
PMA	15	11.7			40	3.9			0.00009 (B)*
Flail arm	7	5.5			36	3.5			0.26700 (B)
Flail leg	4	3.1			32	3.1			0.99202 (B)
Respiratory	0	0			21	2.0			0.10310 (B)
PUMNS			10.8 (± 8.6)	11 (0 - 29)			9.8 (± 7.1)	9 (0 -29)	0.448
LMNS			5.1 (± 3.4)	4 (0 - 14)			4.6 (± 3.2)	4 (0 - 14)	0.257
MRC sum score			49.0 (± 11.2)	52 (12 - 60)			51.0 (± 8.8)	53.5 (6 - 60)	0.252
Cerebellar-ALS-plus	2	1.5			2	0.2			0.00004 (B)*
ALSFRS-R				39 (4 - 47)				40 (5 - 84)	0.892
ΔFS				0.47 (0.01 - 7.43)				0.61 (0.03 - 8.88)	0.011*
Survival (m)				117.3 (3.5 - 450.6)				49.7 (1.3 - 271.9)	< 0.001*
GFAP (pg/mL)				84.02 (36.77–113.67)				122.36 (44.00 – 447.65)	0.011*
CPK (U/L)				262 (31 - 1795)				160 (16 – 3768)	< 0.001*

EO-ALS early-onset amyotrophic lateral sclerosis; AO-ALS adult-onset amyotrophic lateral sclerosis; *F* female; *M* male; *FALS* familial ALS; *SALS* sporadic ALS; *UMN-p* upper motor neuron predominant; *PLS* primary lateral sclerosis; *PMA* progressive muscular atrophy; *PUMNS* Penn Upper Motor Neuron Score; *LMNS* Lower Motor Neuron Score; *ALSFRS-R* Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; *ΔFS* progression rate calculated with the formula [(48 – ALSFRS–R score)/disease duration expressed in months]; *GFAP* glial fibrillary acid protein; *CPK* creatine phosphokinase; *y* years; *m* months; *B* Bonferroni-adjusted p value; * significant p-value.

TABLE 1 Demographic and clinical characteristics of the study cohort, classified into the two main groups.

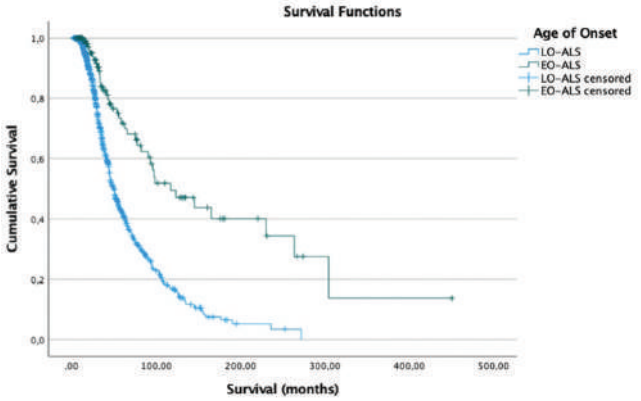

FIGURE 1 Kaplan–Meier plots of survival probabilities for EO-ALS (green line) and LO-ALS (blue line). Median values: 117.3 months for YO-ALS and 49.7 months for AO-ALS. +: censored cases.

Conclusion: Findings from our study indicate that EO-ALS is associated with prolonged survival, suggesting that different pathogenetic mechanisms or enlarged motor neurons reserve might be at play in this group of patients. Compared to previous studies, we did not confirm the previously reported higher frequency of the upper motor neuron predominant phenotype in the EO-ALS group.

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OPR-063 | Longitudinal progression of subcortical structural damage in amyotrophic lateral sclerosis

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Background and aims: Converging evidence suggests an early involvement of subcortical structures in the course of neuropathological progression of amyotrophic lateral sclerosis (ALS). Our aim was to explore the longitudinal evolution of structural damage to subcortical and hippocampal structures in a cohort of incident ALS patients.

Methods: Twenty-four patients with ALS and 34 healthy controls underwent at least two longitudinal clinical evaluations and brain MRI scans on a 3T scanner (median follow-up time = 0.96 years). Segmentation of subcortical and hippocampal structures was obtained. ANOVA models were performed between groups at baseline. Linear mixed effect models were used to test longitudinal trajectories of atrophy.

Results: At baseline, ALS patients showed significant bilateral reduction of hippocampal volumes compared with controls (left: $p = 0.05$; right: $p = 0.038$), and a trend toward significance for atrophy in the right thalami ($p = 0.08$). Baseline volumes of the basal ganglia were comparable between patients and controls. Longitudinally, ALS patients showed a significant reduction of grey matter volumes of the left pallidum ($p = 0.01$) and right putamen ($p = 0.02$).

Conclusion: Our results suggest a different temporal involvement of hippocampal and subcortical structures in the course of ALS, with an early involvement of hippocampi and thalami followed by a subsequent progression of damage to the basal ganglia. We highlight the importance of subcortical structural alterations for a more comprehensive understanding of ALS, supporting the use of MRI for tracking disease progression. Funding. This study was supported by: European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease; Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

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MS and related disorders 2

OPR-064 | Relevance of paramagnetic rim and cortical lesions in MS at diagnosis: Exploring the clinical practice biomarker toolkit

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Background and aims: In multiple sclerosis (MS), imaging biomarkers aid the disease characterization at the time of diagnosis and support the appropriate treatment choice. The presence of paramagnetic rim lesions (PRLs) and cortical lesions (CLs) is not routinary evaluated in clinical practice. In this study, we investigated the association between a broad range of imaging biomarkers available and the clinical disability in MS patients at diagnosis.

Methods: 45 RRMS (mean disease duration: 9.6 months) underwent brain and spinal cord 3 T-MRI and OCT. Susceptibility-weighted imaging (SWI) and double inversion recovery (DIR) sequences were used to manually segment respectively PRLs and CLs. Neuroimaging metrics extracted are shown in Table 1. Regression models assessed the relationship of the lesion and atrophy metrics with physical disability (Expanded Disability Status Scale [EDSS]) and cognitive impairment (Symbol Digit Modalities Test [SDMT]).

Results: PRL and spinal cord lesion volume and count most strongly predicted EDSS. Only CL volume and count were significantly associated with SDMT score at diagnosis. In a regression model including non-rim WML and PRL volume (or count), only the latter was significantly associated with EDSS along with spinal cord volume (or count). In the same model with the two WML phenotypes grouped together, the WML volume (or count) did not reach the significance.

	MS	Non-PRL MS	PRL MS	Non-PRL vs PRL p-value
Subjects, n (%)	41	23 (56%)	18 (44%)	
Age, years, mean (SD)	39.9 (12.1)	39.4 (12.2)	40.5 (12.9)	0.788[a]
Female, n (%)	26 (63%)	14 (61%)	12 (67%)	0.804[b]
Education, years, mean (SD)	14.3 (3.7)	14.8 (4.1)	13.4 (3.0)	0.246[a]
EDSS, median (IQR)	1.5 (1.0)	1.5 (1.0)	1.5 (0)	0.173[c]
SDMT, mean (SD)	54.7 (12.8)	56.8 (13.3)	51.5 (12.1)	0.507[a]
Disease duration, years, mean (SD)	0.49 (0.90)	0.48 (0.94)	0.53 (0.87)	0.863[a]
Disease duration, months, mean (SD)	9.61 (11.33)	10.04 (12.26)	9.47 (10.49)	0.863[a]
Non-rim lesion load (mm^3), mean (SD)	5663 (5104)	3554 (4007)	8251 (5317)	**<0.001**[c]
Non-rim lesion count, mean (SD)	45.3 (34.6)	35.8 (28.3)	58.5 (39.6)	0.055[c]
PRL load (mm^3), mean (SD)	347 (752)	-	816 (987)	-
PRL count, mean (SD)	0.75 (1.4)	-	1.76 (1.68)	-
CL load (mm^3), mean (SD)	280 (541)	140 (157)	486 (787)	0.265[c]
CL count, mean (SD)	3.2 (6.3)	1.6 (1.1)	5.6 (9.4)	0.201[c]
WM volume, mean (SD)	0.316 (0.021)	0.319 (0.017)	0.310 (0.024)	0.305[c]
Cortical Thickness (mm), mean (SD)	4.39 (0.15)	4.43 (0.14)	4.32 (0.15)	**0.019**[a]
Thalamic volume, mean (SD)	0.0046 (0.0005)	0.0046 (0.0004)	0.0043 (0.0005)	**0.048**[a]
Cerebellar volume, mean (SD)	0.0892 (0.0077)	0.0908 (0.0076)	0.0867 (0.0075)	0.108[a]
Cerebellar lesion load (mm^3), mean (SD)	118 (255)	58 (164)	126 (162)	**0.015**[c]
C2-C3 CSA (mm^2), mean (SD)	69.3 (6.6)	69.9 (5.8)	68.4 (7.7)	0.318[a]
Spinal cord lesion load (mm^3), mean (SD)	144.4 (253.8)	109.5 (180.1)	191.7 (328.4)	0.219[c]
Spinal cord lesion count, mean (SD)	1.2 (1.5)	0.9 (1.4)	1.6 (1.6)	0.145[c]
pRNFL thickness, µm, mean (SD)	98.34 (10.92)	98.86 (12.64)	97.29 (8.59)	0.538[d]
GCIPL volume, mm^3, mean (SD)	1.98 (0.17)	1.99 (0.19)	1.96 (0.15)	0.497[d]
INL volume, mm^3, mean (SD)	0.95 (0.05)	0.95 (0.05)	0.96 (0.06)	0.753[d]

TABLE 1 Demographics, clinical and radiological characteristics.

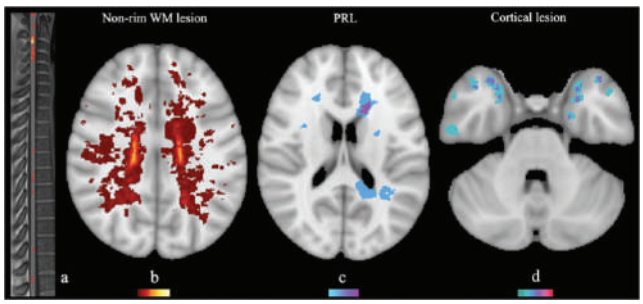

FIGURE 1 Probability maps of the spinal cord (a), non-rim white matter (b), paramagnetic rim (d), and cortical lesions (d).

	Adjusted for age, gender				Adjusted for age, gender, education		
	Unstadardized Beta	P-value	R^2		Unstadardized Beta	P-value	R^2
Expanded disability status scale (EDSS)				**Symbol digit modalities test (SDMT)**			
PRL volume	0.001	**<0.001**	0.388	PRL volume	-0.002	0.467	0.293
PRL count	0.429	**0.001**	0.315	PRL count	-1.222	0.368	0.298
Non-rim lesion volume	4.17e-5	0.240	0.081	Non-rim lesion volume	-0.001	0.066	0.349
Non-rim lesion count	0.006	0.244	0.081	Non-rim lesion count	-0.064	0.238	0.311
Total WM lesion volume	4.71e-5	0.132	0.103	Total WM lesion volume	-0.001	0.054	0.355
Total WM lesion count	0.007	0.202	0.087	Total WM lesion count	-0.064	0.231	0.312
CL volume	-8.91e-5	0.800	0.048	CL volume	-0.008	**0.035**	0.368
CL count	-0.004	0.893	0.046	CL count	-0.650	**0.028**	0.374
WM volume	-13.14	0.130	0.104	WM volume	91.72	0.295	0.306
Cortical thickness	0.408	0.790	0.048	Cortical thickness	7.721	0.622	0.289
Thalamic volume	-398.5	0.341	0.069	Thalamic volume	1834	0.669	0.288
Cerebellar volume	-10.63	0.667	0.051	Cerebellar volume	85.95	0.759	0.286
Cerebellar lesion volume	<0.001	0.696	0.050	Cerebellar lesion volume	-0.007	0.322	0.303
C2-C3 CSA	-0.039	0.166	0.095	C2-C3 CSA	0.117	0.689	0.287
Spinal cord lesion volume	0.003	**<0.001**	0.406	Spinal cord lesion volume	-0.004	0.621	0.287
Spinal cord lesion count	0.415	**0.001**	0.317	Spinal cord lesion count	-0.923	0.486	0.292
pRNFL thickness	0.003	0.827	*	pRNFL thickness	0.162	0.214	*
GCIPL volume	-0.614	0.466	*	GCIPL volume	17.45	0.064	*
INL volume	-1.760	0.518	*	INL volume	6.962	0.802	*

TABLE 2 Relationship between neuroimaging biomarkers and clinical disability. Multivariate linear regression models.

Conclusion: PRLs and spinal cord lesions describe the best association with physical disability in MS patients at diagnosis. CLs best correlate with cognitive performance. SWI and DIR sequences and the assessment of PRLs and CLs might add pivotal information at the first MS patient assessment.

Disclosure: Nothing to disclose.

OPR-065 | Evaluation of neuronal and glial serum biomarkers in patients with MOGAD: the MULTIMOGAD study

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Background and aims: The role of serum biomarkers to evaluate MOGAD prognosis is limited. We aim to characterize serum neuroglial biomarkers and analyze their usefulness to predict relapses and disability in MOGAD.

Methods: Retrospective longitudinal study included MOGAD and age-matched multiple sclerosis (MS) patients with serum samples obtained within 3 months from disease onset. Clinical and laboratory data were collected. Serum neurofilament light-chain (sNfL) and glial fibrillary acidic protein (sGFAP) levels were determined using Simoa. A descriptive comparison between MOGAD and MS groups was performed. Within MOGAD group, Spearman test was built to assess correlations between baseline serum biomarkers and disability at sampling, as well as Cox and linear regression analyses to predict time to second relapse and disability, respectively.

Results: Eighty-nine MOGAD and 32 MS patients were included. In MS, female were more predominant ($p=0.020$), had lower EDSS at onset ($p=0.046$), and higher presence of oligoclonal bands ($p=0.001$). Baseline sNfL levels were higher in MOGAD compared to MS ($p=0.018$). In MOGAD patients, sNfL (rho 0.289; $p=0.008$) and sGFAP (rho 0.32; $p=0.003$) correlated with EDSS at sampling. sGFAP levels were associated with EDSS at last follow-up in univariate ($p=0.017$), but lost significance in multivariate analysis. In multivariate Cox analysis, higher baseline sNfL values increased the risk of having a second relapse in MOGAD patients presenting with optic neuritis (hazard-ratio 5.88 [95% CI 1.56; 22.20]; $p=0.009$).

Characteristics	Whole (n=121)	MOGAD (n=89)	MS (n=32)	p-value
Baseline				
Sex female; No. (%)	73 (60.3)	48 (53.9)	25 (78.1)	0.020
Age at onset; years, median (IQR)	36.2 (27.8-46.2)	36.2 (27.3-50.5)	35.8 (28.1-41.4)	0.252
Topography at onset; No. (%) ON SC Brainstem Encephalic ON + SC Encephalic + SC Other	 59 (48.8) 35 (28.9) 8 (6.6) 2 (1.7) 4 (3.3) 3 (2.5) 10 (8.3)	 46 (51.7) 24 (26.9) 2 (2.3) 2 (2.3) 4 (4.5) 3 (3.4) 8 (9.0)	 13 (40.6) 11 (34.4) 6 (18.8) 0 (0) 0 (0) 0 (0) 2 (6.25)	
EDSS at onset; median (IQR)	2.0 [1.0-3.0]	2.5 [1.5-4.0]	2.00 [1.0-3.0]	0.046
Oligoclonal bands; No. (%)	41/99 (41.4)	16/69 (23.2)	25/30 (83.3)	<0.001
Pleocytosis; No. (%)	39/88 (44.3)	36 (51.4)	3/18 (16.7)	0.009
Acute treatment at the first episode, No. (%)	97/110 (88.2)	78/78 (100)	19/32 (59.4)	<0.001
Acute treatment pre-sampling[a]; No. (%)	71/97 (73.2)	56/78 (71.8)	15/19 (79)	0.773
Time to sampling; months, median (IQR)	0.76 (0.33-1.54)	0.62 (0.23-1.74)	0.85 (0.64-1.46)	0.285
Follow-up				
Follow-up; years, median (IQR)	2.5 (0.8-7.0)	1.82 (0.85-4.34)	7.52 (4.30-11.57)	<0.001
Chronic treatment during follow-up; No. (%)	70 (57.9)	49 (55.1)	21 (65.6)	0.404
Proportion of time under chronic treatment; (%) median (IQR)	28.3 (0-84.8)	38.7 (0-82.7)	18.8 (0-86)	0.682
Presence of relapses; No. (%)	42 (34.7)	28 (31.5)	14 (43.8)	0.279
ARR; mean (SD)	0.21 (0.44)	0.24 (0.51)	0.09 (0.13)	0.740
EDSS at last follow-up; median (IQR)	1.00 (0.00-2.00)	1.00 (0.00-2.00)	1.25 (1.00-2.00)	0.046

TABLE 1 Demographic and clinical characteristics.

	Final EDSS	
Variables	Univariate β (95% CI); p-value	Multivariate β (95% CI); p-value
Age at onset	0.03 (0.01; 0.05); 0.006	0.05 (0.03; 0.07); <0.001
Female	-0.13 (-0.84; 0.57); 0.712	
EDSS at onset	0.30 (0.16; 0.45); <0.001	0.27 (0.13; 0.42); <0.001
Topography (SC)	1.09 (0.32; 1.86); 0.006	0.73 (-0.03; 1.49); 0.060
Brainstem	0.92 (-0.44; 2.29); 0.183	
Encephalic	2.07 (0.59; 3.56); 0.007	0.98 (-0.37; 2.33); 0.153
Other	0.42 (-0.78; 1.63); 0.487	
Oligoclonal bands	-0.05 (-0.98; 0.88); 0.917	
Pleocytosis	0.42 (-0.35; 1.20); 0.281	
Relapsing course	0.68 (-0.06; 1.43); 0.073	
Chronic treatment after first event	0.55 (-0.16; 1.26); 0.128	
Follow-up years	-0.00 (-0.01; 0.01); 0.596	
sNfL z-score	0.26 (-0.02; 0.55); 0.073	0.11 (-0.15; 0.38); 0.404
sGFAP	0.51 (0.09; 0.92); 0.017	-0.02 (-0.43; 0.40); 0.928
High sNfL + High sGFAP	1.45 (0.59; 2.30); 0.001	0.46 (-0.34; 1.27); 0.256

TABLE 2 Univariate and multivariate regression models assessing the association of baseline sGFAP and sNfL levels with EDSS at last follow-up in MOGAD patients.

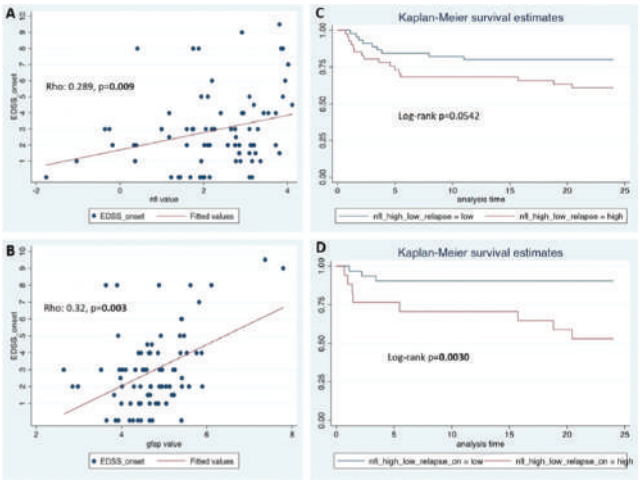

FIGURE 1 Correlation analyses between EDSS at sampling and baseline sNfL (A) and sGFAP (B). Kaplan–Meier survival curves comparing time to relapse between MOGAD patients with high or low sNfL levels in the whole cohort (C) and in the subgroup of ON (D).

Conclusion: In MOGAD patients, the neuro-axonal and astrocytic damage is related with disability at sampling. Neuro-axonal damage predicts a relapsing disease course in the subgroup of patients with optic neuritis.

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OPR-066 | Profiling and modelling cellular senescence in progressive multiple sclerosis brains

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Background and aims: Senescent cells accumulate in age-related diseases. Whether these cells actively contribute to the tissue dysfunction leading to progressive MS is unknown. Here, we investigate the spatial distribution of senescent cells in MS brains, and we model post-inflammatory senescence using 3D hiPSC-derived organoids.

Methods: We performed single-nucleus RNA-sequencing (snRNAseq) on 31 samples of cortex and white matter (WM) from progressive MS cases ($n=10$, mean age = 49) and controls ($n=4$, mean age = 54); SenMayo gene set was applied to the snRNAseq datasets to identify senescent cells. As validation, multiplex immunofluorescence (26 primary antibodies, including the senescence marker p16INK4A+) was performed on 7 MS-tissue blocks. To model inflammation-induced senescence, we exposed 3D hiPSC-derived organoids to the CSF (10% for 24 h) from MS patients and processed by scRNAseq.

Results: In the snRNAseq datasets, endothelia were the most prominent cells featuring senescence signatures in all WM lesion stages (3-fold change [FC] increase) and MS cortex (2.3-FC). Compared to control brain, senescent microglia were twice as abundant at the chronic active lesion (CAL) edge and MS cortex; senescent astrocytes predominated in the lesion core (2-FC), CAL edge (2.6-FC), and MS cortex (2-FC). Consistently, MS brains displayed a higher number of p16INK4A+ cells compared to control, enriched within areas with chronic inflammation and at the ventricular ependyma. Using organoids, we observed that the short-term inflamed-CSF exposure promoted microglial senescence (4.2-FC relative to untreated organoids).

Conclusion: Inflammation-associated cellular senescence is pronounced in progressive MS and might potentially exacerbate tissue dysfunction, with key translational implications.

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OPR-067 | Factors influencing postpartum activity in multiple sclerosis patients: A prospective study and intervention strategy

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Background and aims: Postpartum relapses in multiple sclerosis (MS) patients significantly impact family planning decisions, often leading to cautious reproductive choices. Neurologists frequently advise these individuals on managing their condition during and after pregnancy. Objective: to analyze the factors influencing postpartum disease activity in MS patients. Additionally, we assessed the effectiveness of a proactive strategy designed to reduce postpartum relapses.

Methods: We conducted a prospective longitudinal study involving pregnant women with MS, starting in 2015. We collected and analyzed demographic, clinical, and radiological data before pregnancy, during pregnancy, and in the postpartum period. We implemented a specific strategy to minimize postpartum relapses, including initiating treatment after delivery for active patients and conducting cranial MRI scans 2 months postpartum.

Results: The study included 128 women, with a mean age of 35 years (range 25–47). Pre-pregnancy, 28.3% had experienced relapses in the 2 years leading up to pregnancy, and similar proportions exhibited new T2 lesions (28.3%) and gadolinium-enhancing lesions (21.6%). During pregnancy, 10% experienced relapses, with 7% having clinical relapses and 22% developing new T2 lesions within 6 months postpartum. Notably, 41.4% of patients received DMT treatment within 15 days postpartum, leading to reduced postpartum relapses. Significant correlations were found between postpartum relapses and relapse history, number of relapses, and gadolinium-enhancing lesions.

Conclusion: This study highlights the importance of a targeted postpartum management strategy in reducing MS relapses. The proactive approach, involving early DMT treatment and postpartum MRI scans, effectively reduced postpartum relapses, demonstrating the potential for improved outcomes in MS patients considering pregnancy.

Disclosure: nothing to disclose related to the abstract.

OPR-068 | Disconnection of cerebellar motor areas and motor impairment in multiple sclerosis

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Background and aims: The cerebellum is often affected in patients with multiple sclerosis (MS). It contains two motor representations: the anterior (ACMA, lobules I–V) and posterior (PCMA, lobule VIII) cerebellar motor areas. We assessed atrophy and T2-hyperintense lesion loads in these areas and their association with motor impairment.

Methods: Eighty-nine MS patients and 65 healthy controls (HC) underwent a functional assessment (gait function and hand dexterity) and structural MRI acquisition at 3.0 T. Cerebellar lobules were segmented using the SUIT atlas. Between-groups comparisons and age/sex-corrected partial correlations were assessed.

Results: Compared to HC, ACMA and PCMA were atrophic in MS ($p < 0.001$), with similar reductions between the two areas. More than 60% of MS patients had lesions in either motor lobule. ACMA volume was lower than PCMA in HC and MS ($p < 0.001$), whereas T2-hyperintense lesion load was higher in ACMA than PCMA in MS ($p = 0.040$). Patients with lesions in both areas had worse motor performance than those without lesions in either area ($p < 0.001$ for all). Patients with lesions only in the ACMA or PCMA had similar motor abilities. In patients, lower ACMA and PCMA volumes correlated with worse left-hand dexterity ($p < 0.001$), whereas higher T2-hyperintense lesion load in both ACMA and PCMA correlated with worse performance in all motor tests (r range = −0.358; −0.445, $p <= 0.001$ for all).

Conclusion: The non-homogeneous distribution of lesions suggests an increased susceptibility of the ACMA to focal demyelinating lesions. Considering correlation analyses, disconnection of cerebellar motor areas, rather than localised lobular atrophy, seems to better explain motor impairment in MS.

Disclosure: F. Romanò, B. Signoracci and E. Pagani have nothing to disclose. P. Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi, and research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). M. Margoni reports grants and personal fees from Sanofi Genzyme, Merck Serono, Novartis and Almiral. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

Neuroimmunology 1

OPR-069 | Neurologic, psychiatric and sleep investigations after initial treatment of anti-LGI1 encephalitis: A prospective study

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Background and aims: Anti-LGI1 encephalitis responds well to immunotherapy, but the symptoms that remain after treatment have not been well described. We aimed to characterize the clinical features of these patients over more than 1 year after initial immunotherapy.
Methods: This prospective cohort study included individuals with anti-LGI1 encephalitis who received immunotherapy within the past year and sex and age matched healthy participants (HP). At study entry, at 6 months (not in HP), and at 12 months, participants underwent neuropsychiatric and video-polysomnography (VPSG) assessments.
Results: Between 2019 and 2022, 24 (57%) patients with anti-LGI1 encephalitis and 18 (43%) healthy participants were recruited. At study entry (median 88 days [IQR 67–155] from initial immunotherapy), all 24 patients had one or more symptoms: cognitive (83%), psychiatric (83%), insomnia (58%), REM sleep behaviour disorder (50%), faciobrachial dystonic seizures (FBDS 38%), and focal onset seizures (29%). FBDS were unnoticed in 17% and focal onset seizures in 21%. VPSG alterations included disruption of sleep structure (79% patients; 0 HP; $p=0.013$]), excessive fragmentary myoclonus (63% patients; 22% HP; $p=0.039$) and myokymic discharges (38% patients; 0 HP; $p=0.0051$). These findings led to additional immunotherapy in 63% of the patients, resulting in improvement or resolution in all cases, however at 12 months 65% remained with cognitive deficits.
Conclusion: Unsuspected but ongoing clinical and video-polysomnography alterations are common in patients with anti-LGI1 encephalitis during the year that follows initial immunotherapy. Recognition of these alterations is important because they are treatable, can be used as outcome measures in clinical trials, and may influence cognitive outcome.
Disclosure: Nothing to disclose.

OPR-070 | Clinical characterization and long-term outcome of children and adults with anti-AMPAR encephalitis

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Background and aims: Anti-α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (anti-AMPAR) encephalitis manifest with limbic encephalitis (LE) associated with cancer. The full clinical spectrum, prognostic factors and outcome are not well established, especially in children. We compared clinical features of children and adults and characterized the long-term outcome of anti-AMPAR encephalitis.
Methods: Clinical information of adults and children with anti-AMPAR encephalitis were reviewed from medical records.
Results: Eighty-four patients with AMPAR antibodies were included (13 children, 71 adults). Patients with other concomitant neuronal antibodies were excluded. Overall, 62% of patients presented with LE (7 children, 45 adults, $p=0.539$). Compared to adults, children experienced more frequently prodromal symptoms ($p=0.035$), movement abnormalities ($p=0.032$) and cerebellar symptoms ($p=0.025$). Brain MRI was abnormal in 68% of patients, restricted to mesio-temporal lobes (50%) or associated with extratemporal abnormalities (34%). Exclusive involvement of extratemporal areas (16%) was more frequent in children than adults (44% vs. 11%, $p=0.035$). Tumours were found only in adults (56%, mainly lung cancer and thymoma). A follow-up >24 months was available for 34 patients (4 children, 30 adults): 64% showed neurological sequelae, including cognitive (83%), psychiatric (33%), sleep (11%), and movement (6%) disorders. Twenty-two patients (65%) had a good outcome (modified Rankin scale [mRS] < 2) whereas 12 (35%) a bad outcome (mRS > 2). At multivariate analysis, failure to respond to first-line immunotherapy was the only predictor of bad outcome (OR 8.8, 95% CI 1.3–59.5, $p=0.025$).
Conclusion: Children with anti-AMPAR encephalitis present distinct clinical and radiological features compared to adults. Despite most patients respond to immunotherapy, neurological sequelae are frequent.
Disclosure: M. Spatola receives research support from La Caixa Foundation and Spanish National Research Institute (Carlos III).

OPR-071 | Brain MRI changes and their impact on cognition in the post-acute stage of anti-NMDA receptor encephalitis

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Background and aims: We aimed to characterize the course of alterations in brain grey matter (GM) volumetry and diffusion-based white matter (WM) connectivity and their association with cognitive performance during the post-acute stage of anti-NMDAR encephalitis (NMDARe).

Methods: NMDARe patients were prospectively studied at 4, 8, 12 and 12–24 months from disease onset with paired cognitive and MRI assessments that quantified whole brain volume, regional GM changes, and structural integrity of WM connectivity. Differences between NMDARe patients and healthy controls (HC), similarly studied, in the longitudinal follow-up were analyzed using multilevel linear mixed-effect models.

Results: Twenty-one post-acute NMDARe patients and 19 HC were included. Compared with HC, patients showed similar global brain volume, but specific regional changes: atrophy of the middle frontal cortex, and enlargement of bilateral hippocampus and right amygdala, mainly during the first 8 months, which improved over time. NMDARe patients showed differences in 76/2020 (3.8%; $p<0.05$, family-wise error rate) WM connections, following two distinct dynamic patterns: reduced connectivity in 63/76 (83%) connections, involving bilateral cingulate, parietal cortex and deep GM, which improved rapidly (first 8 months), and increased connectivity in 13/76 (17%) connections, mainly subcortical areas, which stabilized over time. Regional atrophy and decreased WM connectivity largely explained variability in working memory (87%) and learning and memory (86%) outcomes.

Conclusion: The first 8 months of post-acute NMDARe were dominated by regional vulnerability to damage and rapid MRI improvements. In subsequent months (8–24), MRI changes slowed and mild residual volumetric and connectivity abnormalities persisted alongside protracted cognitive deficits in NMDARe patients.

Disclosure: J.D. holds patents for the use of NMDAR as autoantibody tests. GS received speaker fees from Angelini Pharma. SL received compensation for consulting services and speaker honoraria from Biogen Idec, Novartis, TEVA, Genzyme, Sanofi and Merck. S.L. received compensation for consulting services and speaker honoraria from Biogen Idec, Novartis, Janssen, Merck and Bristol-Myers Squibb, and holds grants from the Instituto de Salud Carlos III. E.S. received travel reimbursement from Merck and Sanofi-Aventis S.A. The rest of the authors declare no conflicts of interest related to this work.

OPR-072 | How to retreat patients with anti-MAG polyneuropathy after a course of rituximab? A comparison between two regimens

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Background and aims: Rituximab represents an effective therapy in anti-MAG polyneuropathy. However, a well-established retreatment strategy is currently lacking. We aim to compare two different retreatment protocols, upon clinical relapse vs. upon memory B cell reappearance, to evaluate whether they could be associated with an increased long-term disability.

Methods: We retrospectively evaluated 29 patients who were responsive to an initial cycle of rituximab (375/mg/m^2/week for 4 weeks), and retreated according to two different protocols: full course at the time of clinical relapse ($n=20$), or a single infusion of rituximab (375 mg/m^2) whenever the frequency of reemerging CD27+ memory B cells exceeded 0.05% in the first 2 years and 0.1% thereafter ($n=9$). The scores obtained in the validated clinical scales INCAT, MRC, ISS scales were evaluated at baseline, after 9 months and at the last follow-up visit.

Results: Comparing the scores obtained in the three clinical scales between baseline and the last follow-up, we found that patients treated upon relapse disclosed a progressively more disabling clinical course, whereas none of the patients treated upon memory B cells reappearance had a significant clinical decline compared to baseline (statistical data not presented for shortness).

Conclusion: Our findings reveal that patients treated upon clinical relapse exhibit greater levels of long-term disability than patients treated upon CD27+ lymphocyte reappearance, suggesting that the latter protocol may be an effective maintenance treatment strategy in patients with anti-MAG polyneuropathy.

Disclosure: Nothing to disclose.

OPR-073 | Detailed characterization and evolution of brainstem tau pathology in anti-IgLON5 disease

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Background and aims: Anti-IgLON5 disease is a newly identified rare form of autoimmune disorder characterized by anti-IgLON5 antibodies that, via an as-yet-unidentified mechanism, are associated with a brainstem-dominant tau pathology. Recent research indicates that the tau pathology may develop in a time-dependent manner, being absent or mild at early disease stages and very prominent after years of disease progression. This study aimed to precisely characterize the different tau phosphorylation steps and establish a sequence of markers at the different severity stages in an autopsy cohort.

Methods: We used immunohistochemistry to analyze the medullary region of 14 autopsy cases of anti-IgLON5 disease with different severity grades of tau pathology and varying disease durations, from 6 to 180 months. We used 13 antibodies for different tau phosphorylation sites. The presence and severity of tau pathology were assessed semi-quantitatively and compared to one PSP case and two neurologically healthy controls.

Results: We identified different tau phosphorylation sites in anti-IgLON5 disease and were able to determine a sequence of phosphorylation steps based on the disease duration. The development of cytoplasmic tau pathology seems to occur only in later disease stages, whereas alterations of the nuclear envelope were evident in the early stages.

Conclusion: Different tau phosphorylation steps occur during the progression of anti-IgLON5 disease. The establishment of a sequence of pathological disease markers adds support to the hypothesis that tauopathy might indeed be a time-dependent phenomenon. Furthermore, it may aid in the neuropathological identification of cases with mild pathology, and provides insight into the earliest stages of tauopathy.

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OPR-074 | High relapse rate influences the long-term clinical outcome in anti-CASPR2 encephalitis

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Background and aims: Anti-contactin-associated protein-like 2 (CASPR2) encephalitis is a young disease entity, and information on long-term clinical outcome and relapse rate are limited. We aim to describe long-term clinical outcome, relapse rate and treatment efficacy to guide treatment decisions.

Methods: In this nationwide observational cohort study, patients with a confirmed diagnosis of anti-CASPR2 encephalitis were included. Clinical data were collected at diagnosis and during follow-up, both retrospectively and prospectively. In all patients, written informed consent was obtained.

Results: Forty-four patients with anti-CASPR2 encephalitis were included (42/44 [95%] male; median age at onset 65 years, range 40–86). The median follow-up time was 46.5 months, range 7–113. Relapses were present in 23/44 patients (52%). Compared to the initial disease episode, patients experienced similar but fewer symptoms during the relapse(s). However, peripheral symptoms occurred newly during a relapse in five patients. The median time to relapse was 11 months (range 3–58). At relapse, one patient was tapering prednisone, eight patients had maintenance immunotherapy, three had received Rituximab induction therapy, while 11 patients had no immunotherapy anymore. VGKC RIA titre fluctuations in serum correlated well (84%) with relapse and remission. Nine patients (24%) suffered multiple relapses. In 10 patients, a tumour was present, of which two were only discovered during a relapse.

Conclusion: The relapse rate in anti-CASPR2 encephalitis is much higher than previously anticipated, which provides a clear rationale for prolonged immunotherapy. VGKC RIA titres in serum can guide monitoring for relapses and disease course. It is recommended to repeat tumour screening when patients relapse.

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CSL Behring. JdV is local investigator for the CIELO satralizumab in anti-NMDAR and anti-LGI1 encephalitis (Roche).

Neuro-ophthalmology/Neuro-otology

OPR-075 | Idebenone treatment for Leber hereditary optic neuropathy: Time to clinically relevant recovery in the LEROS study

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Background and aims: LHON is a mitochondrial disease resulting in bilateral vision loss. In LEROS, a Phase IV, open-label interventional study (NCT02774005), visual acuity (VA) outcomes following 24 months of idebenone treatment were compared to an external matched Natural History (NH) cohort. Eyes treated with idebenone had significantly higher rates of clinically relevant recovery (CRR) from baseline at 12 and 24 months compared to the NH control group. Here, we present the cumulative percentage of eyes with a CRR from baseline (KM-estimate) by disease phase and primary mtDNA mutation as a function of treatment duration.

Methods: LEROS included patients with LHON aged ≥12 y and with a disease onset ≤5 y prior. Eyes were stratified by time since symptom onset: subacute/dynamic (≤1 y) and chronic (>1 y). CRR was defined as an improvement from "off-chart" VA to at least 1.6 logMAR, or a ≥0.2 logMAR improvement if "on-chart".

Results: The intention-to-treat (ITT) population included 196 patients. The KM-estimate of a CRR from baseline increased from 18.4% of eyes at Month 6 to 47.3% at Month 24 with idebenone treatment in the subacute/dynamic phase, and from 18.2% to 29.1% in the chronic phase. Improvement of visual acuity was also observed in sub-analyses by mtDNA mutation in both subacute/dynamic and chronic eyes (Table 1).

	Month 6	Month 12	Month 18	Month 24
Subacute/dynamic eyes (≤1 year after onset of symptoms)				
Overall	18.4% [13.3, 25.1]	34.9% [28.0, 43.1]	38.8% [31.5, 47.2]	47.3% [38.4, 57.1]
m.11778G>A	13.0% [7.4, 22.3]	25.5% [17.2, 36.9]	28.6% [19.8, 40.4]	37.7% [26.7, 51.4]
m.3460G>A	14.4% [6.3, 31.2]	33.4% [20.0, 52.3]	33.4% [20.0, 52.3]	33.4% [20.0, 52.3]
m.14484T>C	30.7% [19.1, 46.9]	53.9% [39.4, 69.8]	60.0% [45.0, 75.5]	80.0% [56.6, 95.5]
Chronic eyes (>1 year after onset of symptoms)				
Overall	18.2% [13.2, 24.7]	26.7% [20.6, 34.1]	28.2% [21.9, 35.7]	29.1% [22.7, 36.9]
m.11778G>A	17.5% [11.8, 25.6]	22.2% [15.6, 30.9]	23.2% [16.5, 32.1]	24.6% [17.6, 33.8]
m.3460G>A	13.2% [5.1, 31.4]	26.0% [13.2, 47.4]	26.0% [13.2, 47.4]	26.0% [13.2, 47.4]
m.14484T>C	31.2% [15.4, 56.8]	61.2% [39.5, 83.2]	70.9% [46.9, 91.0]	70.9% [46.9, 91.0]

TABLE 1 Kaplan–Meier estimates of cumulative CRR [95% CI] from baseline.

Conclusion: Longer duration of idebenone treatment (beyond 1 y) further improved visual outcomes regardless of LHON disease phase. This improvement was most pronounced for eyes with the m.14484T>C mutation.

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OPR-076 | Abstract withdrawn

OPR-077 | Zebra or Horse: Diagnostic process, misdiagnosis, and bias in suspected idiopathic intracranial hypertension

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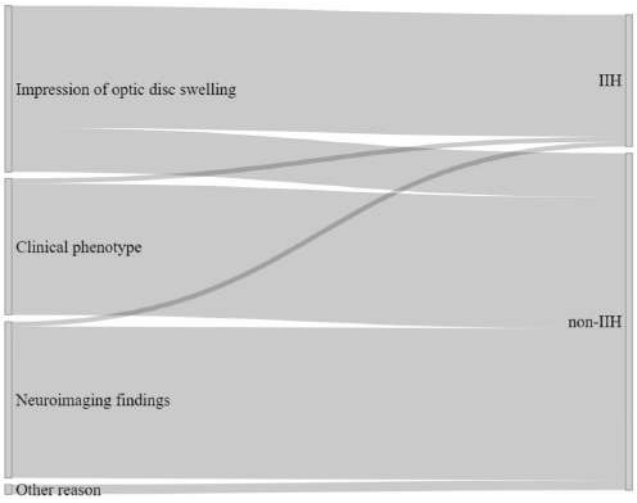
Background and aims: Misdiagnosis of Idiopathic Intracranial Hypertension (IIH) is prevalent and potentially harmful. We evaluate the diagnostic process in IIH and the impact of National Guideline (NG) on IIH management.

Methods: Retrospective observational study of patients referred to the Danish Headache Center bysuspected IIH,Jan 2020 to Sep 2022. We retrieved data on diagnostic work-up (DW) and duration, causes for suspecting IIH, and mismanagement, and compared outcomes by final diagnosis (confirmed versus disproven IIH (non-IIH)) and by period before and after the NG. Level of significance was Bonferroni-corrected to $p < 0.002$.

Results: 124 patients were referred. We excluded IIH relapse ($n = 22$) and secondary intracranial hypertension($n = 6$) leaving 96 patients with suspected new-onset IIH. We confirmed IIH in 28% and disproved IIH in 72% Confirmed IIH was discovered by optic disc swelling in 93%. Neuroimaging indicating intracranial hypertension ($n = 1$) and clinical phenotype ($n = 1$) aided little in finding true cases, but often elicited IIH suspicion suggesting anchoring bias with premature closure. False-positive misdiagnosis affected 9%, false-negative misdiagnosis affected 2%. DWU was significantly more comprehensive and faster in confirmed IIH compared to non-IIH. Mismanagement dropped by implementation of the NG (from 44% to 20%, $p = 0.022$), whereas diagnostic accuracy remained low (38% before vs. 21% after, $p = 0.11$).



Causes for initial IIH suspicion and final diagnosis.

Conclusion: Optic disc swelling is the main determinant leading to correct IIH diagnostics. Ophthalmic evaluation is urgent and decisive in suspected IIH and should guide DWU to mitigate unnecessary investigations. Neuroimaging and clinical phenotype have little diagnostic value and introduce bias. A national guideline optimizes the diagnostic process.

Disclosure: N. S. Hansen received funding from the Novo Nordic Foundation during the conduction of the work. J. J. Korsbæk received funding from the Lundbeck Foundation, Rigshospitalet-Glostrup and Odense University Hospital. S. Hamann received funding from the VELUX Foundation. R. Jensen gave lectures for Pfizer, Eli-Lilly, ATI, Merck, TEVA, Novartis, Lundbeck and Allergan. Investigator in clinical trials with ATI, Eli-Lilly, Novartis and Lundbeck; received research funding from University of Copenhagen, Rigshospitalet, ATI, Lundbeck Foundation, The Medical Society in Copenhagen, Novo Nordisk Foundation and Tryg Foundation.

OPR-078 | OCT in multiple sclerosis: beyond the optic neuritis versus non-optic neuritis universe

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Background and aims: When using optical tomography studies(OCT) in multiple sclerosis(MS) eyes are usually classified as having had clinical optic neuritis(ON), subclinical ON, or as otherwise normal. We believe such approach undermines the importance of further including and classifying eyes with signs indicative of retrochiasmal/chiasmal disease(RCD/CD).

Methods: Objectives. To analyze eyes with OCT, evidence of RCD/CD in a large database of MS patients. Methods. Eyes of MS patients examined with OCT were classified as normal, with clinical ON(diagnosed >6 months prior), subclinical ON(>7 micra inter-eye retinal nerve fiber layer[RNFL] thickness difference and/or > 4 micra inter-eye ganglion cell layer[GCL] thickness difference), subclinical or clinical CD(bilateral and congruent nasal GCL loss), subclinical or clinical RCD(bilateral and congruent homonymous GCL loss) and subclinical (non-localizing) involvement (color and/or statistical RNFL/GCL map abnormalities not fulfilling criteria above).

Results: We included 273 eyes. 177(64.8%) of our MS patients had OCT abnormalities, 32.9% of which were subclinical. Eyes had evidence of ON only ($n = 86$, 31.5%), RCD/CD ($n = 36$, 13.1%), and non-localizing findings ($n = 55$, 20.1%). When comparing between normal, ON, and RCD/CD eyes, disease duration in the right eye was different between groups ($p = 0.020$), being greater in RCD/CD ($p = 0.019$) and ON ($p = 0.029$), than in normal eyes. Disease duration in the left eye was near-significantly different between groups ($p = 0.076$), being greater in RCD/CD ($p = 0.037$) than in normal eyes. Relapse rate in the 2 years prior in the right eye, was near-significantly different between groups ($p = 0.086$), being greater in RCD/CD ($p = 0.036$) than in ON eyes.

Conclusion: Our work supports the use of OCT for identifying MS-related damage of chiasmal and retrochiasmal pathways.

Disclosure: Nothing to disclose.

OPR-079 | Clinical features, video-oculographic profile, and treatment in spinocerebellar ataxia type 27B (SCA27B)

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Background and aims: Spinocerebellar ataxia type 27B (SCA27B) is a late-onset, autosomal-dominant disorder caused by a GAA-repeat

expansion in the FGF14 gene and characterized by oculomotor abnormalities. This study aims to detail the oculomotor profiles of SCA27B patients and assess the efficacy of 4-aminopyridine.

Methods: Eight genetically confirmed SCA27B patients underwent clinical and video-oculographic examinations using EyeSeeCam. Six received 4-aminopyridine to evaluate its effect on nystagmus.

Results: The cohort consisted of six males and two females, mean age 69 ± 10.3 years, with disease duration of 6.6 ± 3 years. All displayed oculomotor abnormalities at both clinical and instrumental examination; half reported diplopia. Video-oculography showed reduced smooth pursuit gain in all tested patients (6/6), but normal saccade metrics (8/8). Nystagmus was present in all, predominantly downbeat (7/8) and gaze-evoked (3/8), with normal vestibulo-ocular reflex gains (8/8). Treatment with 4-aminopyridine led to both subjective and objective improvement in 5/6 cases, which was significant in three patients (see Figure) and mild in two. Only one patient had no benefit.

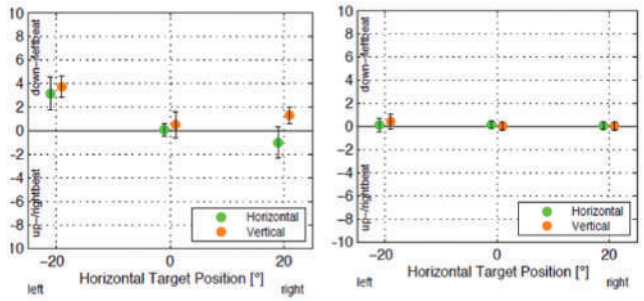

FIGURE 1 Gaze Holding assessment before and after treatment with 4-aminopyridyne shows complete disappearance of nystagmus.

Conclusion: SCA27B patients exhibit primarily vestibulocerebellar impairments, with significant smooth pursuit and nystagmus abnormalities but no saccadic or vestibulo-ocular reflex alterations. 4-aminopyridine was effective in treating nystagmus in most patients, highlighting the potential of targeted therapy in SCA27B management. Further research is needed to optimize treatment strategies.

Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder

OPR-080 | Efgartigimod in non-AChR myasthenia gravis: a 24 months experience

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Background and aims: The neonatal Fc receptor (FcRn) inhibitor Efgartigimod (EFG) has been approved for treatment of generalized Myasthenia Gravis (gMG) with anti-AChR antibodies. We investigated the efficacy of EFG in non-AChR gMG along a clinical follow-up of 2 years.

Methods: We treated 13 patients with gMG without anti-AChR antibodies: 5 MuSK+, 2 LRP4+ and 6 triple-negative (confirmed by live CBA). EFG was administered according to the GENERATIVE protocol (consisting of a Fixed period of 2 treatment cycles of 4 infusions at weekly intervals, followed by a Flexible period during which EFG was given in case of clinical worsening) starting from November 2021. Outcomes were evaluated by means of the MG-ADL, QMG, and MGC scores.

Results: The mean follow-up was 14.5 ± 6.7 months. Meaningful improvement was observed with the clinical scores adopted (MG-ADL: −5.5 ± 3.64; MGC: −8.5 ± 6.54; QMG: −4.84 ± 4.92). The number of cycles/year was 3.9 ± 0.99. The interval between cycles was 8.9 ± 3.8 weeks. MG-ADL improvement greater than 5 points was recorded in 49% of patients. 46% of patients required hospitalization during the 2 years before treatment with EFG; during EFG none of the patients was hospitalized or required immunomodulation. No major side effects or infusion related reactions occurred.

Conclusion: EFG was effective in non-AChR gMG and modified significantly the course of the disease. Our experience strengthens the role of FcRn inhibition as a new effective tool in the management of MG without anti-AChR antibodies, as demonstrated by RCT in AChR-associated gMG. A longer follow-up will be available at the time of the meeting.

Disclosure: C. Antozzi received funding for travel, meeting attendance, or Advisory Board participation from Biogen, Sanofi, Alexion, Momenta, argenx, UCB and Janssen R. Frangiamore received funding for meeting attendance and speaking from argenx, UCB and Alexion. L. Maggi received funding for travel, meeting attendance or Advisory Board participation from Sanofi Genzyme, Roche, Alexion, AmicusTherapeutics and Biogen. S. Bonanno received funding for travel, meeting attendance or Advisory Board participation from Sanofi Genzyme, Biogen and Roche. F. Vanoli received funding for travel or meeting attendance from Alexion Pharmaceuticals and argenx R. Mantegazza received funding for travel, meeting attendance or Advisory Board participation from Alexion, Argenx, Biomarin, Catalyst, Sanofi, Regeneron and UCB A. Pinna and R. Arnaboldi are employees of argenx Italy F. Andreetta and E. Rinaldi have nothing to disclose.

OPR-081 | A real-life comparison of eculizumab and efgartigimod in generalized myasthenia gravis patients

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Italy; [5]*Neurology Unit, Department of Medicine, Surgery and Dentistry, University of Salerno, Salerno, Italy*; [6]*GENESIS Department, Federico II University, Naples, Italy*

Background and aims: Eculizumab (ECU) and Efgartigimod (EFGA) are approved for the treatment of generalized Myasthenia Gravis (gMG). Objective of our study is to describe their clinical response in a real-life setting.

Methods: We included patients receiving either ECU or EFGA as part of our clinic practice and retrospectively collected data on the MG activities of daily living (MG-ADL), quantitative MG scale (QMG), MG deterioration/crises, adverse events, and prednisone use.

Results: We enrolled 63 patients, 32 treated with ECU and 31 with EFGA (Table 1). Median follow-up was 234 days. Both treatments were well tolerated. Patients treated with EFGA were more likely to suspend treatment (HR 3.732; CI 1.041, 13.385; $p=0.043$; Figure 1A). Main reason was MG deterioration, patient choice, adverse event. ECU decreased the MG deterioration/crises rate more than EFGA (OR 0.545, CI 0.363, 0.818; $P=0.003$; Figure 1B). By week 24, MG-ADL decreased by −6.5 points for ECU and −5.0 for EFGA ($p=0.188$; Figure 2A); the QMG decreased by −8.0 for ECU and −2.9 for EFGA ($p=0.003$; Figure 2B). Mean prednisone reduction at follow-up was −21.3 mg for ECU and −8.1 mg for EFGA ($p=0.026$). Speed of CS reduction was −13.1 mg/month for ECU and −3.2 mg/month for EFGA ($p=0.001$).

Table 1. Baseline Demographics

Variable	Eculizumab (n=32)	Efgartigimod (n=31)	Total (n=63)
Gender (F/M)	18/14	22/9	40/23
Ab-AChR+	32	22*	54
Age	60.6±15.5	51.9±14.4	56.3±15.5
Previous Py use	30	30	60
Previous CS use	30	26	56
Previous NSIST = 0	9	6	15
Previous NSIST ≥1	23	25	48
Previous NSIST ≥2	11	8	19
Previous NSIST ≥3	2	3	5
Previous IVIG	22	20	42
Previous PLEX	8	9	17
Follow-up days (median)	247.5 (30-3141)	253 (28-681)	253 (28-3141)
MG-ADL	11.0±3.4	9.9±4.2	10.5±3.8
QMG	17.8±6.1	15.3±5.2	16.5±5.8

AChR-Ab+ = anti-acetylcholine receptor antibody positive; PY = Pyridostigmine; CS = Corticosteroids; NSIST = Non-steroidal Immunosuppressants; MG-ADL = Myasthenia Gravis Activities of Daily Living scale; qMG = Myasthenia Gravis quantitative scale. * 6 patients treated with Efgartigimod were seronegative, and 3 were Ab-MuSK+.

TABLE 1 Patient demographics.

Conclusion: Eculizumab and Efgartigimod proved to be both effective treatments in a real world setting as they reduced MG-ADL and QMG in difficult to treat gMG patients. Patients treated with ECU were less likely to suspend treatment or show a deterioration/crisis. Prednisone sparing effect and reduction speed was higher with Eculizumab.

Disclosure: F.S. received public speaking honoraria from Alexion, argenx, Biogen, Genpharm, Madison Pharma, Mylan, Novartis, Roche, Sanofi, Teva, Viatris, Zai Lab; he also received compensation for Advisory boards or consultation fees from Alexion, Almirall, argenx, AstraZeneca, Avexis, Biogen, Dianthus, Forward Pharma, Lexeo Therapeutics, Novartis, Reata, Sandoz, Takeda; he is PI in clinical trials for Alexion, argenx, Immunovant, Novartis, Prilenia, Sanofi.

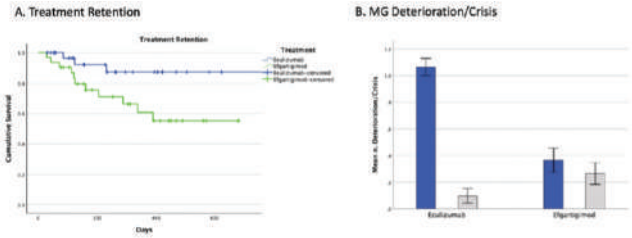

FIGURE 1 Treatment retention and MG deterioration/crisis during treatment.

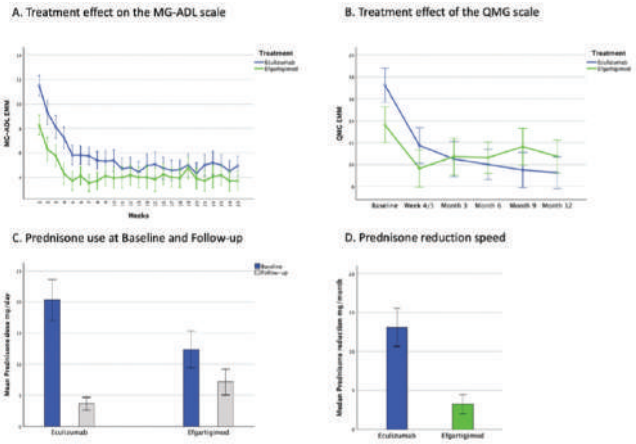

FIGURE 2 Treatment effect of MG-ADL, QMG, and Prednisone reduction.

OPR-082 | Childbirth and neonatal outcomes in a nationwide myasthenia gravis cohort

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Background and aims: Myasthenia Gravis (MG) muscle weakness can complicate childbirth. Transient neonatal myasthenia gravis (TNMG) can result from maternofetally transferred autoantibodies. Our aim was to estimate the risks at childbirth in a maternal MG-cohort.

Methods: A cohort study using nationwide data from the Medical Birth Registry of Norway. Maternal MG was identified by MG-diagnosis or pyridostigmine-use, in current or prior pregnancy. All MG-exposed and unexposed singleton live births in Norway 1999–2022 were compared. Main outcomes were mode of delivery (caesarean section (CS) vs. vaginal, emergency CS vs. vaginal, elective

CS, and operative vaginal vs. non-operative vaginal), induction of labour, TNMG-rate and neonatal ward admission. Odds ratios (OR) with robust standard errors adjusted for year of birth, maternal age, parity and co-habitation were calculated.

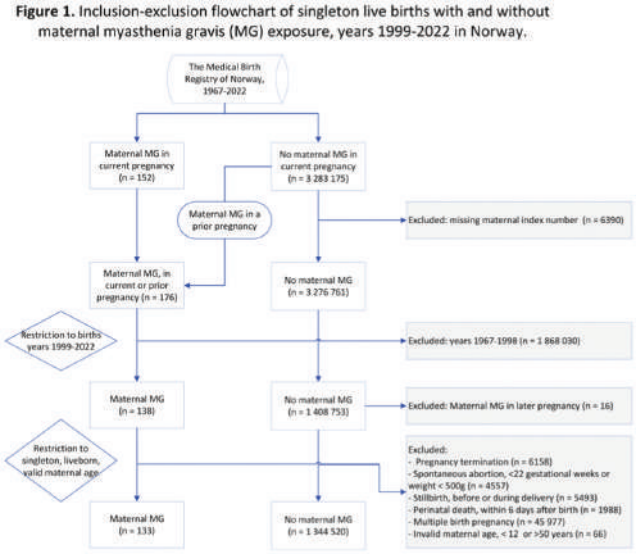

FIGURE 1 Inclusion–exclusion flowchart of singleton live births with and without maternal myasthenia gravis (MG) exposure, years 1999–2022 in Norway.

Results: 133 MG-births and 1,344,520 unexposed births were included. Maternal MG did not significantly increase the risk for CS (aOR 1.32, 95% CI: 0.87–1.99). Elective CS (1.90, 1.10–3.30) and induced labour (1.56, 1.05–2.33) were more common with MG. The emergency CS rate was 10% for both groups (0.97, 0.54–1.76). Among MG-exposed children, five (4%) had TNMG and 38% were admitted to neonatal ward, compared to 10% of unexposed (5.47, 3.85–7.77).

Table 1. Obstetrical and neonatal outcomes among all singleton live births with and without maternal MG exposure in Norway 1999-2022.

	Maternal MG	No maternal MG		
Outcome	N (%)	N (%)	OR (95% CI)	aOR[1] (95% CI)
CS total[2]	27/ 133 (20.3)	204 862/ 1 344 520 (15.2)	1.42 (0.93 - 2.16)	1.32 (0.87 - 1.99)
Elective CS	15/ 133 (11.3)	75 510/ 1 344 520 (5.6)	2.14 (1.25 - 3.65)	**1.90 (1.10 - 3.28)**
Emergency CS	12/ 118 (10.2)	128 768/ 1 268 426 (10.1)	1.00 (0.55 - 1.82)	0.97 (0.54 - 1.76)
Operative vaginal delivery[3]	14/ 106 (13.2)	124 896/ 1 139 658 (11.0)	1.24 (0.70 - 2.17)	1.31 (0.73 - 2.34)
Induction of labour	34/ 133 (25.6)	240 766/1 344 518 (17.9)	1.57 (1.07 - 2.32)	**1.56 (1.05 - 2.33)**
Admission to neonatal ward	49/ 129 (38.0)	131 750/ 1 298 806 (10.1)	5.43 (3.80 - 7.74)	**5.47 (3.85 - 7.77)**
TNMG	5/133 (3.8)	0	NA	NA

Abbreviations: MG; myasthenia gravis; N, number; aOR, adjusted odds ratio; CI, confideoce interval; CS, Caesarean section; TNMG, transient neonatal myasthenia gravis; NA, not applicable

[1] Adjusted for maternal age, year of birth, parity, mother's co-habitation status
[2] Elective, emergency or unspecified C-section
[3] Use of vacuum or forceps

TABLE 1 Obstetrical and neonatal outcomes with and without maternal MG exposure among all singleton live births in Norway 1999–2022.

Conclusion: The risks for elective CS and induced labour were increased, but not for emergency CS, suggesting that pregnancy planning helps avoid complications in MG-women. Few MG-exposed children had TNMG, but 38% were admitted to a neonatal ward. All children of mothers with MG should be observed in-hospital for minimum 2–3 days as TNMG symptoms often develop with delay.

Disclosure: N.E. Gilhus has received financial support from UCB, Argenx, Janssen, Merck, Roche, Alexion, Immunovant, Huma, Denka, Grifols, and Dianthus. Bjørk, M H. has received speaker honoraria and/or served on scientific advisory boards for Teva, Eisai, AbbVie, Pfizer, Novartis, Lundbeck, Angelini Pharma, Jazz pharmaceuticals, and Lilly during the last 5 years. None of the assignments concerned treatment of Myasthenia Gravis. Lindroos, JLV; Cohen, JM; Danielsson, KC; Hikmat, O; Hoff, JM: Nothing to disclose.

OPR-083 | Automatic method for jitter estimation in electromyographic signals

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Background and aims: Neurophysiological jitter measurement using concentric needle electrodes is a laborious and difficult task, because potentials from several fibers may appear in the recordings due to the large recording areas of these electrodes. This work presents an automatic method that estimates jitter from motor unit potential (MUP) trains recorded using single-fiber or concentric needle electrodes.

Methods: MUP intervals likely being formed by only one muscle fiber potential are detected. Then jitter measurement is performed between pairs of these intervals. 132 electromyographic signals were recorded from 8 patients with disorders of the neuromuscular junction or different neuropathies, using a Keypoint system and facial-concentric electrodes. These signals were decomposed into several MUP trains using DQEMG software. Jitter was then estimated manually, using a home-made graphical interface (Figure 1A,B) and using the automatic method (Figure 1C,D).

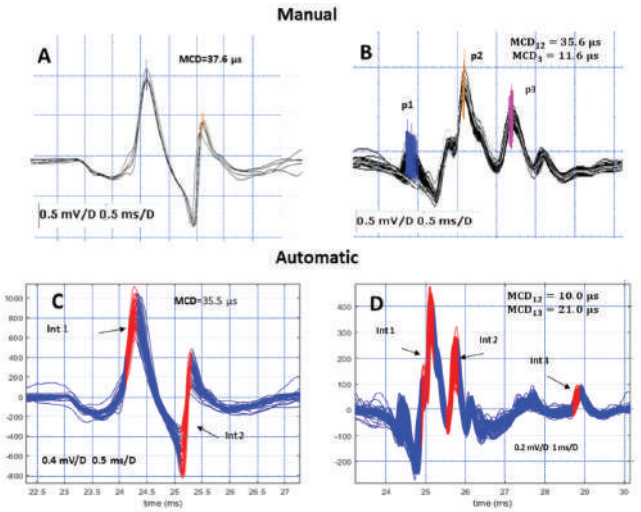

FIGURE 1 Examples of MUP trains analyzed by the manual method, with marked negative peaks and the obtained MCD values (A, B). The same MUP trains analyzed with the automatic method, with highlighted valid intervals and MCD values (C, D).

Results: From 96 MUP trains valid for the analysis, 102 automatic and 84 manual jitter measurements were obtained. Comparative analysis (Figure 2) yielded a mean of jitter differences of 1.74 µs, a mean of absolute differences of 2.73 µs and values of −2.62, −0.35, 2.53 and 7.56 µs for the 5th, 25th, 75th and 95th percentiles of the jitter differences distribution, respectively.

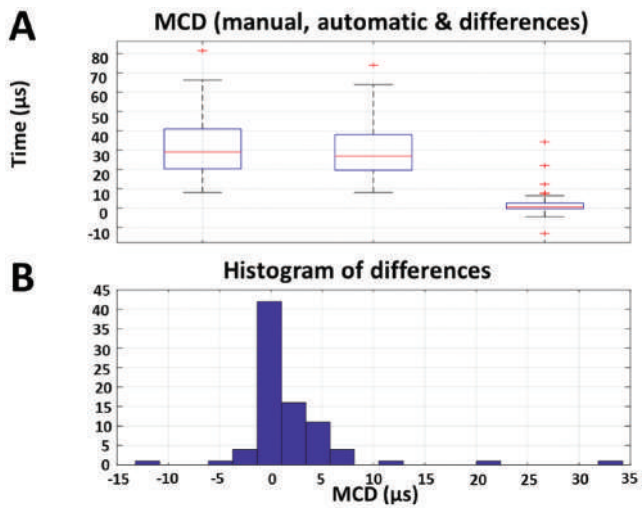

FIGURE 2 Boxplots of MCD values obtained by manual and automatic methods and of the difference in MCD values (A). Histogram of the difference in MCD values (B).

Conclusion: Although more extensive tests are still required, these results suggest that the proposed automatic jitter estimation method may be a valuable technique for clinical practice.

Disclosure: This work has been funded by the Department of Health of the Government of Navarra (project GN2022/29) and by the Spanish Ministry of Science and Innovation (project PID2022-136620OB-I00).

Epilepsy 2

OPR-084 | The lifetime outcomes of antiseizure medication in patients with mesial temporal lobe epilepsy and hippocampal sclerosis

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Background and aims: To evaluate the lifetime seizure frequency in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (mTLE-HS).

Methods: We studied 118 patients with mTLE-HS followed at UNICAMP. We reviewed the seizure frequency, age, duration of epilepsy, dosages and type of antiseizure medications (ASM) used. Patients were split into 3 groups: seizure-free (no seizures in the last 2 years or more of follow-up), fluctuating (seizure-freedom periods of 1 year or longer) or pharmacoresistant (never had a seizure-free period of more than 1 year). Pharmacoresistant patients did not undergo surgery either because they refused it or had contraindications. Patients who underwent surgery were not included in this study.

Results: The mean age was 56.13 years and mean follow-up was 20.25 years (range 3–47, SD 9.83). 35.6% ($n=42$) had right-TLE, 50% ($n=59$) left-TLE and 14.4% ($n=17$) bilateral-TLE. Thirty-six (30.5%) were seizure-free, 39 (33.05%) had a fluctuating course and 43 (36.45%) were pharmacoresistant. There were no differences among groups in relation to the age they became seizure-free, age of epilepsy onset, epilepsy duration, epilepsy family history, number of ASM used over the years or number and type of ASM in use at the last follow-up ($p>0.074$). The most common ASM was carbamazepine.

Conclusion: Three clinical evolution patterns were observed among patients with mTLE-HS who did not underwent surgery: pharmacoresistant, fluctuating seizure control/pharmacoresistant, and seizure-free. We found no significant differences in the main clinical features among groups. Further studies are necessary to define the factors that could predict these three outcome profiles.

Disclosure: Grants: CEPID - FAPESP: "The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN)" 2013/07559–3; CNPQ 315953/2021–7; Conflicts of interest: Fernando Cendes participated in advisory board for Takeda Pharmaceuticals, Libbs, Eurofarma; Clarissa Yasuda participated in advisory board for Eurofarma. Received honoraria for writing educational material for Torrent and Libbs.

OPR-085 | Exploring the long-term effects of COVID-19 in patients with epilepsy: A multicenter Italian observational study

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Background and aims: A growing evidence in the literature support that patients recovered from COVID-19 may develop novel neurological and psychiatric symptoms lasting from weeks to months. This condition, labeled as "long COVID", can be observed more frequently in patients with chronic diseases. The aim of this study is to identify the long-term effects of COVID-19 in people with epilepsy (PwE).

Methods: PwE aged >18 who accessed to three epilepsy centers in the center of Italy during the first pandemic wave between March 2020 and December 2021 were enrolled. According to a documented clinical and laboratory SARS-CoV-2 infection, patients were divided into two groups: COVID+ and COVID-. Epilepsy features (i.e., seizure frequency, treatment), and neurological and psychiatric symptoms were collected at baseline and at 6- and 12-month follow-up visits in both groups.

Results: 39 patients in COVID+ group (17/22 M/F, age: 40.6 ± 18.6 years, 33 focal epilepsy, 6 generalized epilepsy) and 91 patients in COVID- (42/49 M/F, age: 42.9 ± 19.7 years, 69 focal epilepsy, 22 generalized epilepsy) met the inclusion criteria. At 6-month, COVID+ group showed a need for antiseizure medication dose adjustment compared to COVID- group ($p < 0.0001$). An increased diagnosis of psychiatric (i.e., anxiety and depression) and neurological (i.e., cognitive) symptoms was observed in the COVID+ group at both 6- and 12-month ($p < 0.0001$). At 12-month, up to 40% of patients in the COVID+ group revealed an increased seizure frequency ($p = 0.002$).

Conclusion: These findings suggest that PwE with previous SARS-CoV-2 infection may develop psychiatric and neurological long-lasting effects.

Disclosure: Nothing to disclose.

OPR-086 | Evolution into electrical status epilepticus during sleep in patients with self-limited focal epilepsies

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Background and aims: Self-limited focal epilepsies of childhood (SeLFE), while predominantly considered benign, are known to potentially manifest with electrical status epilepticus during sleep (ESES) in a minority of patients.

Methods: The medical records of individuals diagnosed with one of the SeLFE syndromes according to the ILAE 2022 diagnostic criteria, who have been followed in our center between 1989–2023, were retrospectively analyzed. At least two awake and sleep EEGs were performed during a minimum 2-year follow-up. ESES is considered as spike and wave discharges occupying ≥50% of NREM sleep with symmetrical or mildly asymmetrical bilateral or unilateral hemispheric distribution.

Results: Among 144 patients with SeLFE, 57(39.6%) were diagnosed with self-limited epilepsy with centrotemporal spikes (SeLECTS); 65(45.1%) with self-limited epilepsy with autonomic seizures (SeLEAS); and 22 (15.3%) with childhood occipital visual epilepsy (COVE). The mean age of seizure onset was 7.6 years, 5.6 years, 8.5 years, respectively. Twelve (8.3%) evolved into ESES (5 from SeLECTS, 6 from SeLEAS, 1 from COVE). Time elapsed between onset of first seizure and evolution into ESES ranged from 5.2 to 75 months (mean: 26.8±19.8), 6.2–42.8 months (mean: 20.1±14.7 for patients with SeLECTS; 5.2–75.0 months (mean: 32.7±24.5) with SeLEAS, and 25.0 months with COVE). All except one patient had also cognitive or behavioral regression and one patient was diagnosed with Landau–Kleffner syndrome.

Conclusion: The most recent definition of ILAE highlights that SeLFEs are no longer recognized as "benign" epilepsies. Even with a low incidence rate, clinicians should always be cautious about the risk of ESES development in these syndromes.

Disclosure: Nothing to disclose.

OPR-087 | Thalamic atrophy and parahippocampal cortical surface area may distinguish clinical response in temporal lobe epilepsy

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Background and aims: To correlate response to antiseizure medication (ASM) with cortical surface area (CSA) and subcortical volumes (SV) in patients with mesial temporal lobe epilepsy with hippocampal sclerosis (mTLE-HS).

Methods: 111 patients with mTLE-HS who did not undergo surgery because they refused it, had contraindications, or had good seizure control with ASM (mean follow-up of 21.8 years) were categorized in three groups: pharmacoresponsive (seizure-free in the last 2 years or more), fluctuating-response (seizure-freedom periods of 1 year or longer) and pharmacoresistant (never had a seizure-free period of more than 1 year). T1-weighted MRIs (1 × 1 × 1 mm) were processed with Freesurfer-6.0. We analyzed the following regions of interest for CSA: inferior, middle and superior temporal gyrus, parahippocampal gyrus and insula. Volumes of thalamus, hippocampus and

amygdala, along with the CSA from each ASM response-groups were compared with 112 controls.

Results: Groups were balanced for age, sex, and side of HS. Each ASM response-group had 37 patients. Compared with controls, ipsilateral hippocampal volumes were reduced in all groups ($p < 0.0001$) without difference among groups. There was no difference in the contralateral hippocampal volumes among groups. Volumes of ipsilateral and contralateral thalami were reduced in the pharmacoresistant group ($p < 0.003$), and the contralateral thalamus was reduced in pharmacoresponsive and fluctuating-response groups ($p < 0.006$). Amygdala was reduced in the pharmacoresponsive group ($p = 0.03$). Ipsilateral parahippocampal CSA was reduced in the pharmacoresistant group ($p = 0.013$). Other CSA did not differ among groups.

Conclusion: Bilateral thalamic atrophy and reduced ipsilateral parahippocampal CSA appears to distinguish pharmacoresistant mTLE-HS from those with better response to ASM.

Disclosure: CEPID - FAPESP: "The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN)", grant 2013/07559–3; CNPQ 315953/2021–7.

OPR-088 | Real-world data on continuous deep brain stimulation of the anterior nucleus of the thalamus for drug-resistant epilepsy

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Background and aims: This study aimed to evaluate the efficacy and safety of bilateral deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) in patients with drug-resistant epilepsy (DRE), focusing on continuous stimulation settings.

Methods: A retrospective review was conducted on eight patients with focal DRE who underwent bilateral ANT-DBS. Clinical and seizure data were collected, and stimulation parameters were adjusted to maximize clinical benefit. Patients were followed for a mean of 51 months, and changes in seizure frequency were assessed.

Results: Continuous ANT-DBS demonstrated a significant (>50%) reduction in seizure frequency for all patients, with a mean reduction of 68%. The most severe seizure type showed the greatest response to stimulation. None of the patients achieved seizure freedom, but all experienced a transient post-implantation seizure-free period. Psychiatric adverse events were reported in 50% of patients, primarily depression, but they were manageable.

Case	Age, sex	Etiology	Seizure types	Localization	Seizure reduction	Adverse events	Follow-up
1	43, male	Unknown	FAS, FIAS	NOT LOCALIZED	99%	No	11.5 y
2	33, female	Anti-GAD encephalitis	FAS, FIAS	TEMPORAL (BILATERAL)	90%	Depression	8 y
3	22, male	HSV 1 encephalitis	FAS, FIAS, FBTCS	TEMPORAL (BILATERAL)	79%	Depression (worsened)	3.5 y
4	40, male	Unknown	FIAS, FBTCS	MULTIFOCAL	99%	No	3.5 y
5	57, female	Unknown	FIAS	MULTIFOCAL	67%	No	2.5 y
6	24, male	Unknown	FIAS	FRONTAL, INSULA	71%	Apathy	2 y
7	46, male	Immune	FAS, FBTCS	MULTIFOCAL	14%	No	1,75 y
8	52, female	Type I FCD	FAS, FIAS	FRONTAL	22%	No	1 y

TABLE 1 Summary of results. FAS, focal aware seizure; FIAS, focal impaired awareness seizure, FBTCS, focal to bilateral tonic–clonic seizure.

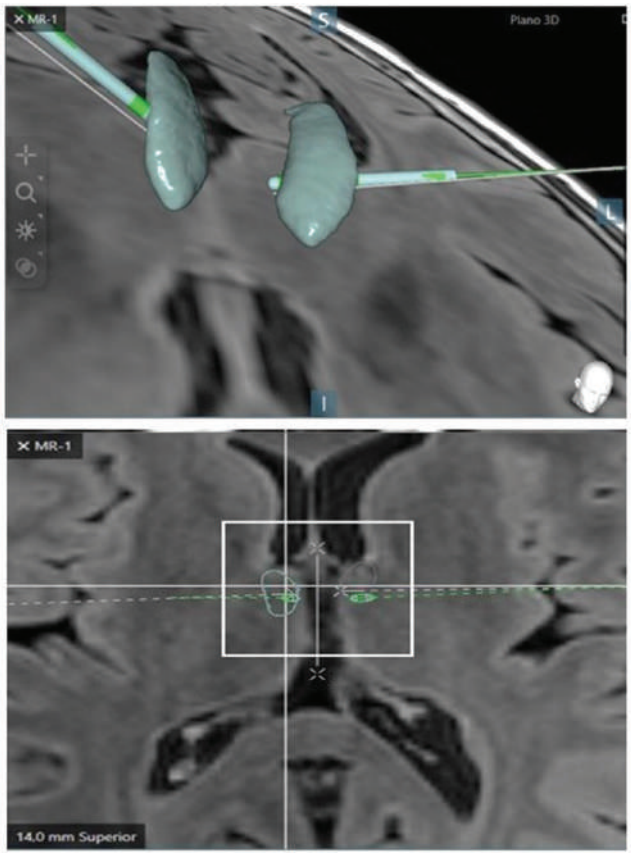

Image 1 and 2. MRI reconstruction of DBS implantation: 3D (top) and axial planes (bottom).

Conclusion: This study highlights the effectiveness of continuous ANT-DBS in reducing seizures for patients with DRE who are not candidates for resective surgery. The findings suggest that continuous stimulation may offer a valuable alternative to intermittent settings. The study underscores the importance of precise electrode placement and a network-focused approach in selecting DBS targets. Overall, ANT-DBS presents a safe and promising option for improving the quality of life in patients with drug-resistant epilepsy.

Disclosure: Nothing to disclose.

Autonomic nervous system diseases

OPR-089 | Abnormal dopamine transporter imaging in pure autonomic failure – A follow-up study

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Background and aims: Abnormal dopaminergic transporter imaging in pure autonomic failure (PAF) is a potential biomarker of central nervous system involvement as described in our pilot study of 10 PAF patients. In this follow-up study, we evaluated the prevalence of abnormal 123I-Ioflupane dopamine transporter SPECT (DaTSCAN) in a larger, prospective cohort of patients with PAF and assessed the rate of phenoconversion to more widespread alpha synucleinopathies.
Methods: Consecutive PAF patients underwent a multimodal assessment including cardiovascular autonomic function testing performed with the Finapres NOVA and DaTSCAN, as part of the Queen Square Autonomic Prodromal Project (QSA-PRODROMAL).
Results: 70 patients with PAF with a median disease duration of 6 (IQR 3–10) years were identified. 22 developed a more widespread synucleinopathy (7 Parkinson's disease, 4 dementia with Lewy bodies, 2 multiple system atrophy-cerebellar [MSA-C], 9 multiple system atrophy-parkinsonian). All phenoconverters had an abnormal DaTSCAN, apart from 2 patients who converted to MSA-C. In patients who underwent DaTSCAN while still retaining a PAF phenotype, the median lag between imaging and phenoconversion was 8 IQR (4–16) months. 48 patients retained a PAF phenotype at last follow-up and 4 of them had an abnormal DaTSCAN. These had a clinical REM sleep behaviour disorder. There were no differences in demographics, autonomic function, or plasma catecholamine spillover between PAF patients with normal or an abnormal DaTSCAN.
Conclusion: DaTSCAN is a biomarker of subclinical central nervous system involvement in PAF and can predict phenoconversion to more widespread alpha-synucleinopathies in patients with a prodromal phase of up to 9 years.
Disclosure: The authors have nothing to disclose.

OPR-090 | The role of plasma norepinephrine level in differential diagnosis of alpha-synucleinopathies

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Background and aims: The alpha-synucleinopathies, including Parkinson's Disease (PD), Dementia with Lewy Body (DLB), Multiple System Atrophy (MSA) and Pure Autonomic Failure (PAF), differ for specific configurations of abnormal alpha-synuclein aggregation across the nervous system. The variation in autonomic dysfunction observed in these conditions is attributed to the differing degrees of involvement of Autonomic Nervous System at central or peripheral level or both. This results in different patterns of plasma level of the neurotransmitter norepinephrine (NE), that could help to differentiate alpha-synucleinopathies.
Methods: We collected blood samples for NE measurement during supine rest (at 20th and 25th min) and at 10th min of the orthostatic phase or at the occurrence of orthostatic intolerance during Head-Up Tilt Test (HUTT), from 331 subjects (61 controls, 72 PD/DLB; 147 MSA, 51 PAF).
Results: Preliminary results showed a significant higher increment of plasma NE during HUTT in PD/DLB (mean ± SD; 155.9 ± 130.2 pg/mL) compared to MSA (82.9 ± 101.4 pg/mL) in absence of a significant difference in supine NE levels (PD/DLB, 250.3 ± 137.7 pg/mL; MSA, 259.5 ± 160.5 pg/mL). Comparisons with the other groups and cut-off values evaluation are ongoing.
Conclusion: Our findings suggest that plasma NE patterns could potentially differentiate alpha-synucleinopathies in the early stages of the diseases, representing a biomarker for differential diagnosis.
Disclosure: Nothing to disclose.

OPR-091 | Cardiovascular autonomic signature of hereditary transthyretin amyloidosis

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Background and aims: Autonomic dysfunction is a fundamental hallmark in the neurological presentation of hereditary transthyretin amyloidosis (ATTRv). Despite its diagnostic significance, there is a notable lack of instrumental studies examining the cardiovascular autonomic involvement in ATTRv individuals.
Methods: To characterized cardiovascular autonomic functions in a single-center cohort of subject with ATTRv through standardized cardiovascular reflex tests (CRTs) including head-up tilt test (HUTT), Valsalva maneuver (VM), deep breathing, cold face test and handgrip test (Finapres Medical System). For comparative analysis, an equivalent number of healthy controls (HC) with similar age and sex distributions were recruited.

Results: The cohort included 65 ATTRv subjects (age 59.77 (14.56), 42% female). During HUTT, ATTRv subjects displayed decreased BP and HR responses compared to HC; with four patients experiencing orthostatic hypotension. All indexes of VM were reduced in ATTRv compared to HC (overshoot: 20 vs. 41 mmHg; phase IIb-IIa: 6 vs. 15 mmHg; Valsalva ratio: 1.33 vs. 1.75). BP responses to cold face and hand grip tests were also attenuated in ATTRv compared to HC. Additionally, the inspiration/expiration ratio during deep breathing was reduced in ATTRv subjects. Among ATTRv cohort, 23 subjects were asymptomatic with no neurological or cardiological involvement. ATTRv carriers differed from HC, exhibiting significantly lower BP responses during HUTT and reduced overshoot at VM, indicating early autonomic involvement in ATTRv.

Conclusion: This study represents the largest investigation into autonomic cardiovascular regulation in ATTRv. CRT documented cardiovascular autonomic impairment in ATTRv subjects. Additionally, ATTRv carriers displayed early autonomic dysfunction, preceding the onset of neurological and cardiological manifestation. These findings provide crucial insights for earlier diagnosis and timely intervention.

Disclosure: Nothing to disclose.

OPR-092 | The catastrophic nature of vasovagal syncope in cardiovascular self-organized criticality

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Background and aims: The recent elucidation of self-organized criticality dynamics within the cardiovascular system (CV-SOC) presents a potential explanatory framework for the occurrence of vasovagal syncope. Self-organized criticality, a universal theory governing natural systems, posits the spontaneous emergence of unexpected large events, termed catastrophes. This study investigates the hypothesis that vasovagal syncope represents a catastrophic manifestation within the CV-SOC. To test this hypothesis, we conducted assessments of CV-SOC preceding an orthostatic challenge.

Methods: Thirty-five healthy volunteers underwent an orthostatic test involving lower body negative pressure (LBNP, −50 mmHg) in the supine position to simulate orthostatic fluid shifts. Tolerance to the test was defined as completion without symptoms or no blood pressure dropping below 80 mmHg. Beat-by-beat heart rate was recorded in the supine position for 20 min 2 days before LBNP to determine the slope of the distribution of long bradycardia (aL), a descriptive CV-SOC index. We compared subjects classified as orthostatic intolerant and tolerant.

Results: Nineteen subjects were intolerant, and 16 were tolerant (10 and 6 female, respectively). Despite similar heart rates between groups (67 ± 2 and 65 ± 2 bpm for intolerant and tolerant, respectively), the aL index significantly differed (0.14 ± 0.01 and 0.18 ± 0.01, T test, $p < 0.01$) between tolerant and intolerant subjects.

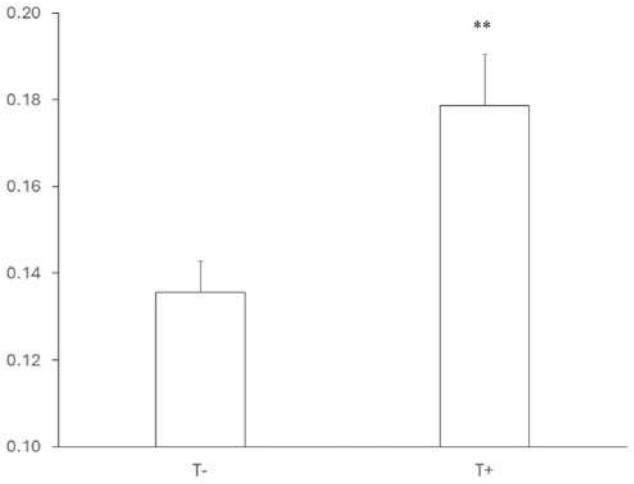

Fig. Slope of the statistical distribution of bradycardia occurrence (no unit) as index of self-organized criticality dynamics in healthy subjects non-tolerant and tolerant to an orthostatic test (T− and T+, respectively). **: $p < 0.01$, unpaired *T* test.

Conclusion: This study not only affirms the self-organized criticality nature of cardiovascular dynamics but also provides compelling evidence linking vasovagal syncope to this inherent nature. Vasovagal syncope, within this framework, emerges as a catastrophic event within the self-organized criticality dynamics of the cardiovascular system.

Disclosure: The VIVALDI study was funded by the European Space Agency (ESA), and the French National Center of Space Studies (Centre National d'Études Spatiales, CNES, funding n° 4800001118.

OPR-093 | Intracranial baroreflex: A review

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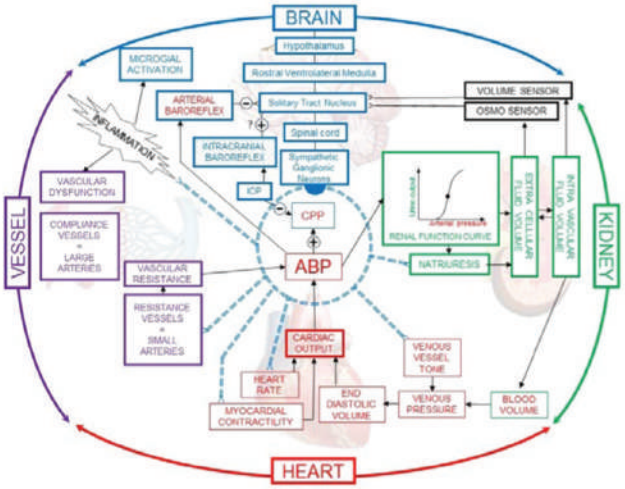
Background and aims: In 2018, two independent teams demonstrated that intracranial pressure (ICP) influences the level of sympathetic activity. A modest physiological increase in ICP leads to an increase in directly recorded sympathetic nerve activity in mice, sheep and humans. This novel regulatory mechanism represents an intracranial baroreflex, bridging ICP and the autonomic nervous system (ANS). Over the last 6 years, data have been published to investigate the role of intracranial baroreflex in physiology and pathology.

Methods: We analysed the literature published on the intracranial baroreflex in the last 6 years to provide an up-to-date review and highlight the most important facts.

Results: 1. Astrocytes seem appear to function as intracranial baroreceptors and may play a role in ANS control. 2. Modest ICP

increase induced by head-down tilt increases sympathetic activity. 3. Intracranial baroreflex is attenuated in an ovine model of renovascular hypertension. 4 Acute ICP rise was associated with a significant increase in heart rate variability and baroreflex sensitivity.

Conclusion: The effect of ICP on the ANS and the concept of a physiological intracranial baroreflex are now supported by convergent and independent data. Intracranial and extracranial (i.e. arterial) baroreflexes behave in opposition, with excitatory and inhibitory effects on the sympathetic activity, respectively. We propose an integrated physiological scheme of ABP regulation, including intracranial and extracranial baroreflexes, which may be involved in the fine-tuning of ABP. However, the exact role of the intracranial baroreflex in the pathophysiology of sympathetic overactivity and hypertension requires further investigation.



Intracranial baroreflex in ABP regulation.

Disclosure: no.

OPR-094 | Cutaneous phosphorylated-synuclein: An early diagnostic biomarker for pure autonomic failure

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Background and aims: Pure autonomic failure (PAF) is a predominantly peripheral alpha-synucleinopathy, presenting with progressive autonomic failure in the absence of other neurological features. Atypical presentations may lead to diagnostic uncertainty. We studied whether cutaneous phosphorylated-synuclein (p-syn) could distinguish between PAF, multiple system atrophy (MSA), and non-synucleinopathy related autonomic failure, and its correlation with quantitative markers of autonomic failure.

Methods: Patients underwent autonomic questionnaires, cardiovascular autonomic testing (Finapres) and bilateral distal leg skin biopsies. We noted whether p-syn was present in nerves supplying autonomic adnexa, including sweat glands, blood vessels, arrector pili muscles, and subepidermal fibres, dermal fibres and nerve fascicles (maximum autonomic subscore 3 and total p-syn score 6 for each sample, average calculated for both sides).

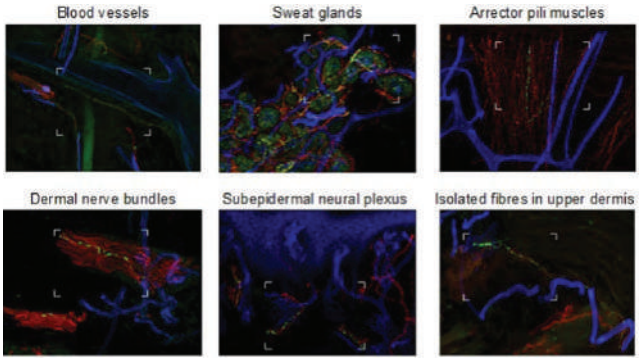

FIGURE 1 Summary of structures used for calculating autonomic p-syn subscore (3 structures in top panel) and total p-syn score (all 6 structures). Figure adapted from Nolano 2022, with permission from IOS Press.

Results: Thirty-six individuals were studied (11 PAF, 13 MSA, 12 non-synucleinopathy related autonomic failure). P-syn was present in 22/22 (100%) PAF biopsies, 19/26 (73%) MSA biopsies, and 0/22 (0%) non-synucleinopathy biopsies. Total p-syn score was significantly higher in PAF (median 4.5) compared to MSA (median 1, $p < 0.001$). Autonomic p-syn subscore correlated with quantitative markers of autonomic failure related to impaired control of total peripheral resistance, including orthostatic intolerance ratio on tilt (rho = 0.63; $p = 0.0004$) and blood pressure recovery time following Valsalva manoeuvre (rho = 0.44; $p = 0.03$), as well as patient-reported orthostatic intolerance (rho = 0.57; $p = 0.006$).

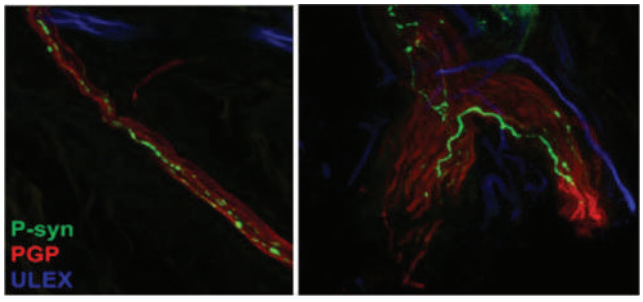

FIGURE 2 Confocal images of cutaneous p-syn deposits from a patient with PAF. P-syn is seen to co-localise along nerve fibres, marked with PGP (protein G peptide), running within dermal nerve bundles.

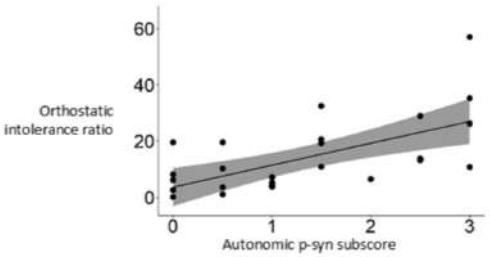

FIGURE 3 Cutaneous autonomic p-syn score correlated with orthostatic intolerance ratio on tilt (change in systolic blood pressure in mmHg divided by time tolerated on tilt in minutes, to a maximum of 10 min).

Conclusion: Cutaneous p-syn was abundant in PAF and represents a promising early diagnostic biomarker to help distinguish between predominantly peripheral and central alpha-synucleinopathies, and non-synucleinopathy related autonomic failure. P-syn deposition on autonomic nerves may impair control of total peripheral resistance giving rise to symptomatic orthostatic hypotension.

Disclosure: This study was supported by the Italian Ministry of Health "Ricerca Finalizzata 2013" – project code PE-2013-02359028. SK was supported by the Guarantors of Brain Entry Fellowship. MPL and VI are supported by NIHR UCL Biomedical Research Centre.

Neuroimmunology 2

OPR-095 | Diagnostic and prognostic biomarkers in immune checkpoint inhibitor-related encephalitis

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Background and aims: Diagnostic and prognostic biomarkers are lacking in immune checkpoint inhibitors (ICI)-related encephalitis. We aimed to characterize the clinical features of ICI encephalitis patients, and identify diagnostic biomarkers and outcome predictors.

Methods: This retrospective study included all patients with possible or definite ICI-encephalitis whose samples and clinical data were studied in the Lyon Neurological Hospital (2015–2023). Response to treatment was defined as CTCAE (v5.0) grade <3. S-100 calcium-binding protein, neurofilament light chain (NfL) and glial fibrillary acidic protein levels were measured in 27 definite ICI-encephalitis patients and 16 controls.

Results: Seventy-six patients were identified, including 67 (88%) with definite ICI-encephalitis (median age, 67 years, 66% male). A focal syndrome was observed in 43/67 patients (64%; limbic encephalitis, rapidly-progressive cerebellar ataxia, and/or brainstem encephalitis), while 24 (36%) had meningoencephalitis, a non-focal syndrome with frequent altered mental status (92%) and pleocytosis (100%). Meningoencephalitis patients had less frequent abnormal brain MRI findings (33% vs. 62%, $p=0.025$), PNS-related antibodies (4% versus 84%, $p<0.001$), and neuroendocrine cancers (4% versus 49%; $p<0.001$) than focal encephalitis patients. Serum NfL > 273.5 pg/mL discriminated definite ICI-encephalitis patients from controls with sensitivity of 88% and specificity of 81%. Focal ICI-encephalitis patients responded less to treatment (15%) than ICI-meningoencephalitis patients (72%, $p<0.001$), and PNS-related antibodies were negatively associated with treatment response (adjusted OR 0.05; 95% CI [0.01; 0.21]). Thirty-two patients (48%) died during the study period (median 7 months of follow-up).

Conclusion: Analysis of serum NfL facilitates the diagnosis of ICI-encephalitis, and focal encephalitis and PNS-related antibodies are associated with worse treatment response.

Disclosure: Nothing to disclose.

OPR-096 | Outcome and risk of relapse in GABAAR encephalitis

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Background and aims: Autoimmune encephalitis with antibodies against γ-aminobutyric acid type A receptor (GABAAR) is characterized by prominent seizures and multifocal brain lesions. Limited data are available on relapse risk and long-term outcome. The study aim was to report clinical course and outcome of patients with GABAAR encephalitis.

Methods: Clinical information was obtained retrospectively from medical records. Patients were included if GABAAR antibodies were

identified by 2 techniques (rat brain tissue and live cell-based assays) in serum or cerebrospinal fluid.

Results: Nineteen patients with GABAAR encephalitis were included, 3 (16%) children and 16 (84%) adults. At onset, 17 (89%) patients developed seizures, evolving to status epilepticus in 12 (63%), alone or accompanied by other neurological symptoms, most commonly cognitive disturbances (74%). Tumor (mainly thymoma) was found in 11 (58%) patients. Brain MRI showed cortico-subcortical T2/FLAIR abnormalities in 15 (79%) patients and isolated cerebellar lesions in 2 (11%). Immunotherapy resulted in clinical improvement in 14/16 (88%) patients. Nine (47%) patients had clinical relapses (median 1, range 1–3 relapses), manifesting with seizures in 7 (78%). Older age was associated with clinical relapses ($p = 0.0206$). After a median follow-up of 19 months (range 1–59), 4 (21%) patients were dead, 6 (32%) completely recovered, and 9 (47%) partially recovered. Cognitive disturbances were the most frequent neurological sequelae (5/9, 56%). Overall, 10/11 (91%) patients were seizure-free at last follow-up, 9/10 (90%) on antiseizure medications.

Conclusion: In GABAAR encephalitis, relapses are not rare, often manifesting with seizure recurrence. Half of the patients are left with residual neurological deficits, mainly cognitive disturbances.

Disclosure: C. Papi receives support from European Academy of Neurology; M. Spatola receives research support from La Caixa Foundation and Spanish National Research Institute (Carlos III).

OPR-097 | Ataxia and movement disorders in autoimmune encephalitis and paraneoplastic neurological syndromes

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Background and aims: Movement disorders (MD) are well-recognized symptoms of autoimmune encephalitis (AIE) and paraneoplastic neurological syndromes (PNS). Although a large variety of MD has been described in different antibody-associated syndromes, the frequency of MD remains unknown for most antibodies. This knowledge is important to aid in early diagnosis and develop rational antibody testing strategies.

Methods: We reviewed a large cohort of all known Dutch patients with antibody-associated AIE/PNS ($n = 927$) to describe associated movement disorders (MD) and (cerebellar) ataxia. The most common antibodies were LGI1 ($n = 182$, 19.6%), NMDAR ($n = 166$, 17.9%), high-titer GAD65 ($n = 122$, 13.2%) and Hu ($n = 114$, 12.3%). Sensory ataxia and faciobrachiodystonic seizures were not considered MD.

Results: MD were present in 337/901 (37.4%) and were the first and/or predominant symptom in 193/297 (65.0%) and 214/297 (72.1%), respectively. Ataxia was by far the most common ($n = 159$, mainly Yo and GAD65), followed by stiff-person syndrome ($n = 50$, mainly GAD65 and GlyR) and chorea ($n = 35$, mainly NMDAR, IgLON5 and CV2). AIE/PNS associated with antibodies against Yo and Tr presented (almost) exclusively with MD (more specifically ataxia, in 29/30 and 4/4, respectively), while the lowest MD frequency was observed with GABAbR (7/59, 11.9%) and LGI1 (5/182, 2.7%).

Conclusion: MD are common in AIE and PNS, occurring in over a third of the patients. Their frequency varies greatly between subtypes. MD can be the first, predominant and even the only manifestation of these disorders. AIE and PNS should be in the differential diagnosis of new-onset MD, especially in the case of cerebellar ataxia and chorea.

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OPR-098 | Demographic and HLA-related specificities in LGI1-antibody encephalitis

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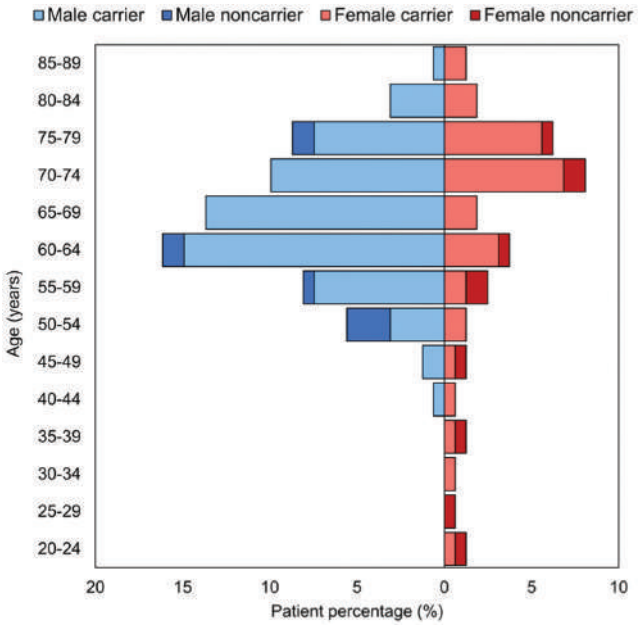
Background and aims: Patients with autoimmune encephalitis with leucine-rich glioma-inactivated 1 (LGI1) antibodies typically are older men and very often carry HLA-DRB1*07:01. Herein, we aimed to investigate clinical and prognostic features according to patients age, sex, and HLA carrier status.

Methods: Retrospective chart review of 224 patients with isolated LGI1-antibody positivity in serum and/or cerebrospinal fluid registered at the French Reference Center database. After computing percentiles of age distribution, patients were divided into three age subgroups: old, ≥79 years; typical, 52–78 years; young, ≤51 years. Poor outcome was defined as modified Rankin scale (mRS) >2.

Results: Among 224 patients, 148 (66%) were male, and 179 (80%) belonged to the typical age subgroup. In three-way comparisons, female sex ($p=0.003$) and temporal lobe seizures ($p<0.001$) were more common in the younger subgroup ($n=20$, 9%), while older patients ($n=25$, 11%) presented more frequently facio-brachial dystonic seizures ($p=0.034$) and had higher mRS both at nadir ($p<0.001$) and last follow-up ($p=0.001$). Non-DRB1*07:01 carriers ($n=19/161$, 12%) were more frequently female ($p=0.044$, Figure 1) and had poorer outcome ($p=0.021$). In a multivariate analysis, older age (odds ratio [OR]:1.12, 95% confidence interval [CI]: [1.05; 1.19]; $p=0.001$), female sex (OR: 3.4, 95% CI [1.07; 10.87]; $p=0.039$), and higher mRS at nadir (OR: 5.43, 95% CI [2.86; 10.3]; $p<0.001$) were independently associated with poor outcome, while carrying DRB1*07:01 was protective (OR: 0.04, 95% CI [0.007; 0.22]; $p<0.001$).



Population pyramid of the 161 patients with available HLA-DRB1*07:01 carrier status.

Conclusion: Clinical manifestations differ among age subgroups, whereas poor outcome is associated with certain demographic (older age and female sex) and genetic (non-DRB1*07:01 carrier status) features.

Disclosure: Macarena Villagrán-Garcia is supported by a research grant from Fundación Alfonso Martín Escudero (Spain).

OPR-099 | Predictors of annualized attack rates in AQP4-IgG+ NMOSD patients treated with rituximab or classical immunosuppression

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Background and aims: Aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG+ NMOSD) primarily manifests with attacks of optic neuritis or myelitis. Immunosuppression can prevent attacks but may be associated with risks, e.g. infections. We compared the efficacy and risk of rituximab and classical immunosuppressive agents in AQP4-IgG+ NMOSD patients.

Methods: We compared annualized attack rates (AAR), infection rates (IR, infections per time) and laboratory parameters during rituximab (RIX), azathioprine (AZA), mycophenolate mofetil (MMF) and methotrexate (MTX) treatment cycles in a multicentric, retrospective cohort from the German Neuromyelitis Optica Study Group (NEMOS) registry.

Results: We analyzed 570 treatment episodes in 251 patients. Mean AAR during RIX treatment episodes was significantly lower than with AZA (0.24 vs. 0.61, $p<0.001$, Mann–Whitney U). The IR did not differ between RIX ($N=238$) and all other treatment episodes ($N=332$, 0.38 versus 0.44, $p=0.81$, Mann–Whitney U). We identified the IR, leukocyte count and IgM serum concentration as predictors for (higher) AAR. Time from diagnosis to treatment and sex showed no effect. During rituximab treatment episodes, higher neutrophil and B cell counts, and higher IgM serum concentration were associated with higher AAR.

Conclusion: Rituximab is associated with lower AAR, but not with higher infection rates than classical immunosuppressives. Whether the IR constitutes a risk factor for attacks needs to be evaluated prospectively.

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Sleep–wake disorders

OPR-100 | Topography of NREM oscillations is associated with circadian preference and rhythmicity

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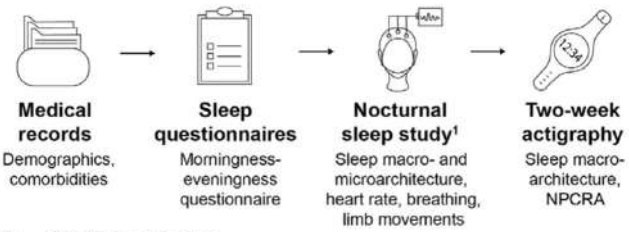
Background and aims: Homeostatic and circadian processes play a pivotal role in sleep regulation. However, little is known about the association of NREM oscillations with circadian rhythm characteristics accessed within clinical routine. This exploratory analysis aimed to comprehensively address this link.

Methods: This analysis is based on the pooled data from two observational studies and includes volunteers in good or excellent health condition (Eastern Cooperative Oncology Group grade of 0–1). Clinical history, circadian parameters (i.e., Morningness-Eveningness Questionnaire and actigraphy) and NREM sleep architecture (i.e., sleep spindle [SS] and slow wave [SW] density and morphology according to 256-electride electroencephalography) were assessed at study inclusion (Figure 1A). Association between NREM architecture as dependent variables and circadian parameters as independent variables were explored using multiple linear regression with adjustments for age and arousal index.

A. Study design

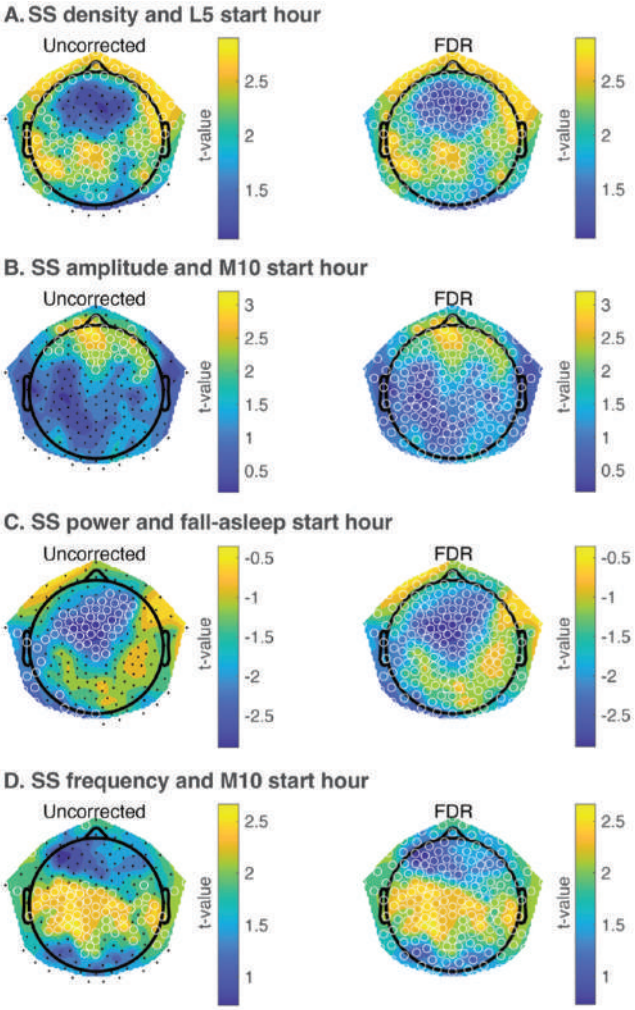


B. Study population

Parameter	Value
Age, years	29.00 [23.00, 35.52]
Female sex	37 (52.1)
MEQ, score	51.00 [46.00, 56.00]
Actigraphy	
Duration of actigraphy, days	14.00 [14.00, 14.00]
Time in bed, minutes	500.91 [457.80, 522.48]
SE, %	82.82 [77.11, 85.39]
Electroencephalography	
Assumed sleep, hours	7.94 [7.55, 8.33]
TRT, hour	8.43 [7.99, 8.95]
TST, hour	7.20 [5.92, 7.81]
SE, %	85.52 [76.89, 90.58]
Arousal index, /h	12.01 [4.25, 20.33]
NREM1, %TST	11.93 [7.81, 17.52]
NREM2, %TST	44.57 [37.56, 49.69]
NREM3, %TST	19.79 [15.40, 24.83]
REM, %TST	21.39 [17.65, 24.10]

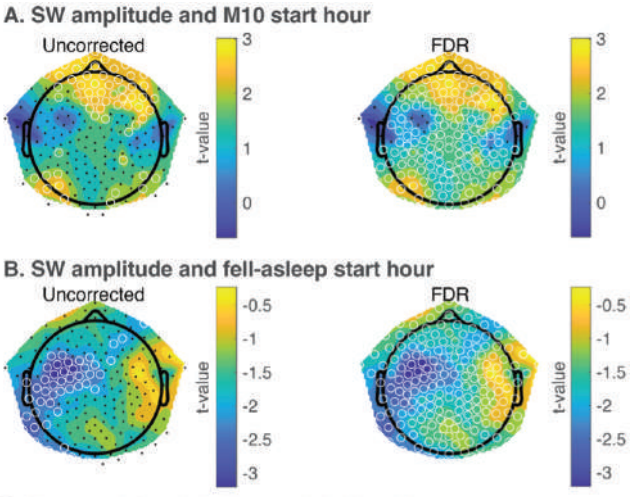
Abbreviations: MEQ – Morningness-Eveningness Questionnaire, NPCRA – non-parametric circadian rhythm analysis, NREM – non-rapid eye-movement sleep, PSG –polysomnography, REM – rapid eye-movement sleep, SE – sleep efficiency, TRT – total recording time, TST – total sleep time.

Results: Data of 71 participants was analyzed (age: median 29.0 interquartile range (IRQ) [23.0, 35.5] years old; 52% women; Figure 1B). SS were prevalently associated with circadian parameters (Figure 2; e.g., high SS density in posterior and pre-frontal regions vs. late L5 hour), whereas only limited associations between SW and circadian parameters were identified (Figure 3; e.g., high frontal SW amplitude vs. late M10 hours).



Significant associations (p<0.05) are marked with a circle.
Abbreviations: FDR - Storey False Discovery Rate, L5 - least five active hours, M10 - maximal ten active hours, SS - sleep spindles.

Selected associations between circadian parameters and sleep spindles.



Significant associations (p<0.05) are marked with a circle.
Abbreviations: FDR - Storey False Discovery Rate, M10 - maximal ten active hours, SW - slow waves.

Selected associations between circadian parameters and slow waves.

Conclusion: Circadian rhythm is associated with NREM oscillations in a domain- and topography-specific manner, with evening preference being linked to favourable electroencephalographic markers. This knowledge may serve as a basis for targeted interventions for sleep–wake disorders.

Disclosure: European Stroke Research foundation 2021 and Interfaculty Research Cooperation grant of the University of Bern "Decoding sleep".

OPR-101 | The impact of physical exercise and ketogenic diet on narcolepsy: A randomized, controlled trial

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Background and aims: Narcolepsy treatment involves pharmacological and non-pharmacological therapies. This trial aimed to evaluate the efficacy of two specific non-pharmacological treatments for narcoleptics: regular physical activity and ketogenic diet, respectively.
Methods: In a 10-week trial on adults with type 1 narcolepsy (NT1), three groups were studied: regular physical activity, ketogenic diet, and control. Assessment included clinical data, treatments, Power Walking Test, and pre/post questionnaires. The sport group adhered to a training plan, keto group followed a high-fat, low-carb diet, and controls maintained routine. Questionnaires covered sleep, life quality, well-being, fatigue, recovery, and stress.
Results: In total, 60 patients (41 female, mean age: 34 years) with NT1 were randomized; 44 completed the study. ESS improved from 13.9 to 11 points ($p < 0.009$) in the sports group, and 16.3 to 13.2 points ($p < 0.005$) in the keto group. For controls, no significant change was found. PSQI improved from 9.3 to 6.6 points ($p < 0.005$) in the sports group only. Quality of life measures (WHO-5) improved from 12.3 to 15.8 points ($p < 0.027$) in the sports groups, and from 9.3 to 13.4 points ($p < 0.013$) in the keto group. Stress levels were reduced from 13.6 to 10.3 ($p < 0.007$) in the sports group.
Conclusion: Regular physical training or a ketogenic diet effectively reduce daytime sleepiness in narcolepsy. Quality of quality, well-being, and physical aspects of life quality are also improved by regular physical training in particular. These treatments offer a convenient, cost-effective, and efficient therapeutic option alongside pharmacological measures.

Disclosure: No disclosures.

OPR-102 | Widespread white matter axonal loss in narcolepsy type 1

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Background and aims: Narcolepsy type 1 (NT1) is a debilitating neurological disorder marked by hypocretin deficiency (or orexin), causing excessive daytime sleepiness and cataplexy. Brain imaging studies have suggested global white matter irregularities in NT1, with unknown underlying histopathological correlates. Consistent with expected hypocretin projection patterns, the cerebellum was least affected. In a globally unique sample of human NT1 postmortem brain tissue, we assessed axonal and myelin integrity through immunohistochemical microscopy.

Methods: Postmortem brain sections from four NT1 donors and 10 controls were assessed for axonal density, axonal injury and myelin integrity. Regions of interest included subregions of the midbrain, corpus callosum, cortical regions (anterior cingulate and occipital cortex), and the cerebellum as a control region (Figure 1). Manual axon count and staining intensity assessed axonal density. Area percentage immunoreactivity of phosphorylated neurofilament chains evaluated axonal injury. Myelin integrity was assessed using staining intensity analyses.

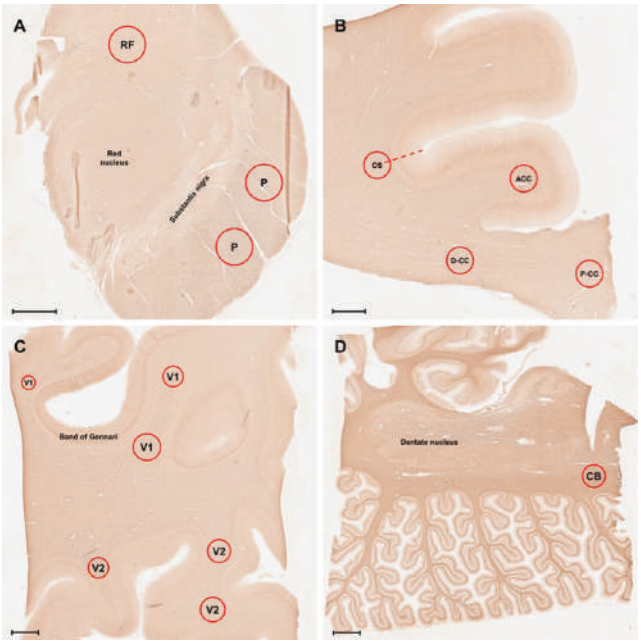

FIGURE 1 The regions of interest: (A) reticular formation and pyramidal tract, (B) proximal and distal corpus callosum, anterior cingulate gyrus and cingulate sulcus, (C) primary and secondary visual cortices, (D) cerebellum. Scale bar is 2 mm.

Results: Significantly reduced axonal density was observed in NT1 compared to controls in the reticular formation, pyramidal tract, corpus callosum and anterior cingulate gyrus (Figure 2). No significantly different axonal density was seen in the cerebellum nor in the axonal staining colour intensity, axonal injury and myelin integrity measures, except for lower secondary visual cortex myelin density in NT1.

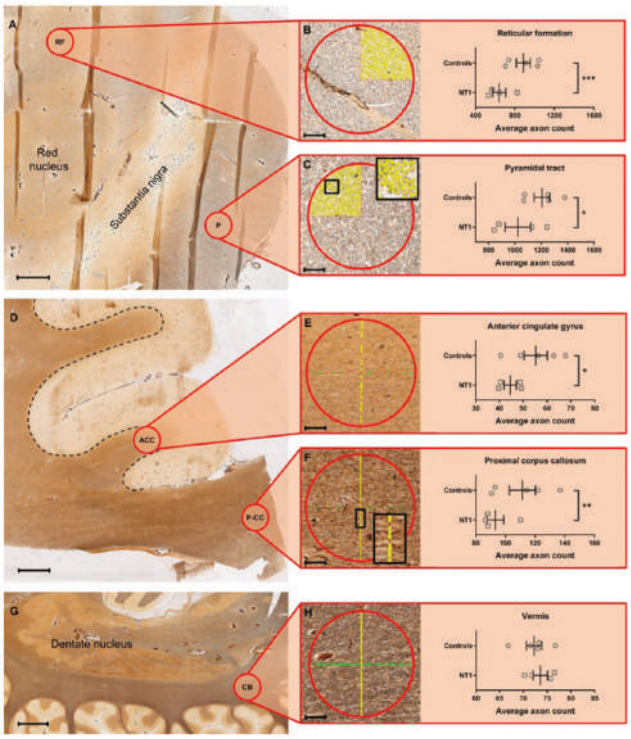

FIGURE 2 Axon counting results: (A–C) reticular formation (RF) and pyramidal tract (P), (D–F) proximal corpus callosum (P-CC), anterior cingulate gyrus (ACC), (G, H) cerebellum (CB). Scale bar is 2 mm for A, D, G and 100 μm for B, C, E, F, H.

Conclusion: In NT1, there is widespread lower axonal density within and outside the ascending reticular activating system. These results align with prior in-vivo brain imaging reports and typical hypocretin projection patterns, and may contribute to the pathophysiology of NT1, possibly stemming from hypocretin deficiency and/or chronic sleep–wake alterations.

Disclosure: Nothing to disclose.

OPR-103 | Sleep-related hypermotor epilepsy vs. disorders of arousal: Diagnostic interobserver reliability of homemade videos

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Background and aims: Video-polysomnography is the reference standard for diagnosing Sleep-related Hypermotor Epilepsy (SHE)1. However, it entails high hospitalization costs and it is not exempt from the possibility of failing to capture rare events. Homevideo recording (HVR) can help the diagnosis of SHE2 but its diagnostic value remains uncertain. This study aims to assess the reliability of HVR in distinguishing between SHE and NREM Disorders of arousal (DOA) among neurologists with different clinical expertise.

Methods: We selected HVRs (performed by caregivers in real-world setting) capturing 20 typical sleep-related events from 10 patients with SHE and 10 with DOA. Thirteen experts and 20 general neurologists were invited to classified each HVR as "SHE", "DOA" or "unknown", based on seizure semiology. The experts was then asked to discuss each case, providing agreed key semeiological features for diagnosis. Baseline interobserver reliability (IR) among raters, and among general neurologists before and after experts' discussion, was calculated using Kappa statistics.

Results: The global raw agreement was 74.9% ("moderate" IR, Kappa 0.54). Agreement among experts was 75.3% ("moderate" IR, Kappa 0.55). Among general neurologists agreement improved from 74.5% at baseline to 83.8% after training, corresponding to IR "moderate" (Kappa 0.54) and "substantial" (Kappa 0.69), respectively.

Conclusion: Baseline reliability of HVR for diagnosing SHE versus DOA was found globally moderate. Educational training, focused on behavior patterns, enhanced agreement among non-expert neurologists. These data highlight HVR as a reliable diagnostic tool in most cases for differentiating SHE from other paroxysmal non-epileptic manifestations, thereby reducing health care costs and disparities.

Disclosure: Nothing to disclose.

OPR-104 | Cerebrospinal-fluid orexin levels: A possible biomarker for early identification of neurodegenerative disorders?

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Background and aims: Orexin system mainly regulates sleep–wake cycle, but there is also growing evidence of its impairment in neurodegenerative diseases(NDs). In this study, we investigated cerebrospinal-fluid(CSF) orexin levels in patients with different NDs compared to non-demented controls. We included patients

with mild or moderate–severe Alzheimer's disease(mAD, msAD), behavioral variant of Frontotemporal Dementia(bv-FTLD), non-fluent primary aphasia(NFPA) and idiopathic normal pressure hydrocephalus(iNPH).

Methods: Patients and controls underwent between 2012 and 2015 a neurological assessment and a lumbar puncture for CSF biomarker analysis. We evaluated 76 AD(mAD = 45, msAD = 31), 34 FTLD(bv-FTLD = 12, NFPA = 22), 13 iNPH patients and 91 controls. CSF orexin levels were also correlated with β-amyloid42(Aβ42), total-tau(t-tau), phosphorylated-tau(p-tau) and clinical data.

Results: CSF concentrations of Aβ42, t-tau, p-tau and orexin were significantly different comparing all groups ($p < 0.001$). The highest CSF orexin levels were found in the iNPH (263.31 ± 56.89). NFPA (210.86 ± 61.99) and msAD (173.04 ± 19.76) showed higher CSF orexin concentrations compared to controls (145.18 ± 27.01) ($p < 0.001$). CSF orexin levels were similar between Bv-FTLD (190.12 ± 100.84), mAD (130.76 ± 21.70) patients and controls. Considering the correlation analysis, only in the controls the CSF levels of Aβ42 and t-tau correlated with orexin ($p = 0.014$; $p < 0.001$). Only in the mAD and msAD groups, Mini Mental State Examination scores correlated with CSF orexin levels ($r = -0.54$; $p < 0.001$; $r = -0.92$; $p < 0.001$; respectively).

Conclusion: This study documented significant differences in CSF orexin levels in NDs patients, with the highest levels in iNPH. Our findings highlight the possibility to add orexin to the CSF biomarker panel for the early identification of NDs causing cognitive impairment and dementia.

Disclosure: Nothing to disclose.

OPR-105 | Burden of illness study among patients with central disorders of hypersomnolence in France, Germany and Italy

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Background and aims: Narcolepsy type 1 (NT1) and 2 (NT2) and idiopathic hypersomnia (IH), are rare, chronic neurological disorders with a high disease burden; however, no studies have attempted to establish the relationship between patient burden and disease severity.

Methods: This cross-sectional, observational, anonymous online/email survey assessed patient burden for participants with NT1, NT2, and IH. Questions included demographics, work-force participation, disease symptoms, daily activities, coping strategies, resource consumption, and quality of life (QoL: EQ-5D-5L). Disease severity was assessed with a visual analog scale (VAS; range 0–10) and three validated instruments (Epworth Sleepiness Scale [ESS], Narcolepsy Severity Scale [NSS-CT], and Idiopathic Hypersomnia Severity Scale [IHSS]). Participants were recruited via clinical sites, patient associations, and registries across Europe.

Results: This interim analysis included 487 participants with complete disease severity data from the first three countries reaching enrolment targets. Mean (range) age was 37 (18–89) years. Mean (range) ESS scores were above normal for NT1/NT2 (15.0 [0–24]) and IH (13.2 [0–22]); self-reported disease severity ranged from 6.2 to 6.9 (VAS). Mean (range) NSS-CT scores were higher (greater severity) for NT1 (20.1 [0–47]) and NT2 (15.2 [1–34]) vs. IH (13.1 [0–40]); IHSS scores were higher (greater severity) for IH (32.4 [5–48]) vs. NT1 (27.0 [4–49]) or NT2 (28.7 [8–44]). Excessive sleepiness and daily naps were reported by 71% and 73%. 82% of participants were treated. Among 66% working participants, 70% reported disease affecting their work negatively. QoL was inversely related to disease severity.

Conclusion: These results illustrate the effect of narcolepsy/IH disease severity on patient-reported quality of life.

Disclosure: YD: Received funds for seminars, board engagements and travel to congresses from Avadel, Bioprojet, Idorsia, Jazz, Orexia, and Takeda GP: Received honoraria for board engagements from Bioprojet, Idorsia, Jazz, Orexia, and Takeda. UK: Honoraria for board engagements and scientific lectures from Bioprojet, Jazz and Takeda. SC: Employee of Takeda Development Center Americas, Inc., and stockholder of Takeda Pharmaceutical Company Ltd LJ: Consultant to EHE GmbH GK: President of EHE GmbH and project manager of this study on behalf of Takeda.

Neuroimaging in neurodegeneration

OPR-106 | Motor reserve impact on nigrostriatal vulnerability and motor severity in Parkinson's disease

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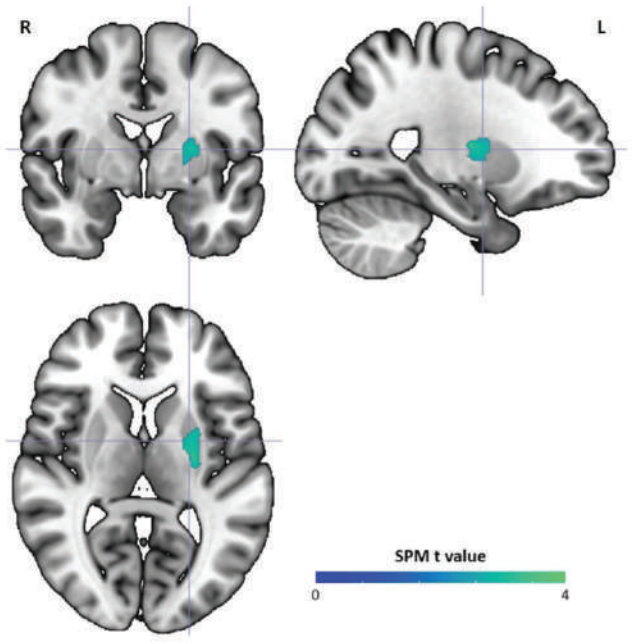
Background and aims: Increasing evidence supports beneficial effects of lifelong physical activities on cognition or mobility. Recently, motor reserve (MR) has been associated with a greater ability to cope with

normal or pathological motor-skill decline. This study investigated the possible impact of MR on dopamine binding and motor severity in early-diagnosed patients with Parkinson's Disease (PD).

Methods: Drug-naïve PD patients underwent cognitive and motor assessment- and 123I-FP-CIT-SPECT imaging. Gait parameters were evaluated in normal, fast and dual-task conditions using Mobile Health Technologies (MHT) in supervised setting. Motor Reserve Index questionnaire (MRIq) was administered and individuals were categorized into high-MR or low-MR. The relationship between MR and dopamine binding was assessed using a voxel-wise regression model. Clinical differences between high and low-MR patients were assessed using two-sample t-test, whereas differences in gait parameters were explored using a MDS-UPDRS-III, sex and height-adjusted ANCOVA model.

Results: Forty drug-naïve PD patients entered the study (age 68.35 ± 7.5). MR was negatively correlated with dopamine binding in left putamen and pallidum in the voxel-wise model. High vs.. low-MR PD had similar demographics, motor, and cognitive severity. Only in motor dual-task conditions, high-MR vs. low-MR PD showed lower step-time ($p = 0.002$), motor cost ($p < 0.001$), step-time variability ($p = 0.045$), and higher step-length ($p = 0.045$).



Voxel-wise regression showing negative correlation between MRIq and dopamine binding.

Conclusion: MR emerged as important modulator of dopamine nigrostriatal circuitries at onset of PD, with an impact on motor impairment and performances assessed by MHT. These mechanisms might explain the heterogeneity of progression and response to treatments in early disease phases and need to be verified in ongoing longitudinal studies.

Disclosure: Nothing to disclose.

OPR-107 | Nerve ultrasound in Friedreich's Ataxia

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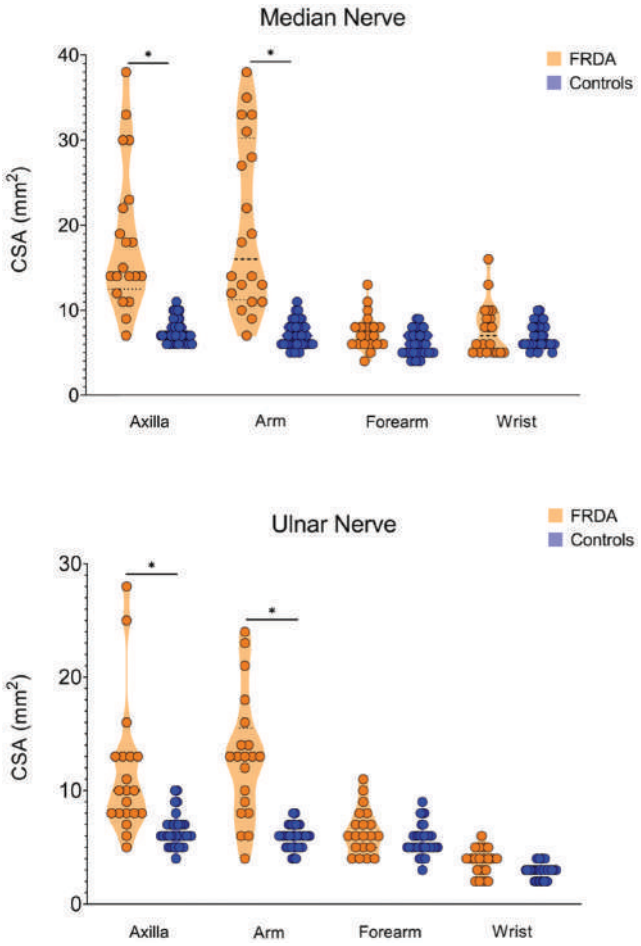
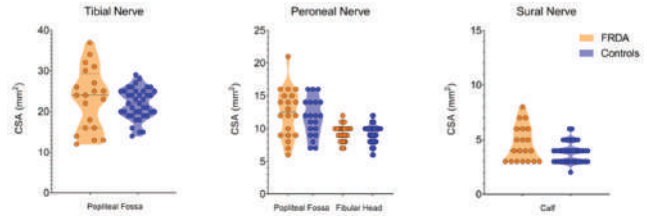
Background and aims: Friedreich's Ataxia (FRDA) is the most common hereditary ataxia, it is caused by GAA expansion of the FXN gene. Frataxin mutations lead to a damage of the Peripheral Nervous System producing a sensory neuropathy. The mechanism underling this manifestation is still a matter of debate. It is thought to be a ganglionopathy but alterations along the nerve have also been observed. In this study, we tested the usefulness of nerve ultrasound in the assessment of peripheral neuropathy in FRDA.

Methods: We prospectively enrolled 9 consecutive FRDA patients (39.3 ± 8.3 years, 2 Males). Anamnestic data, neurological examination (Scale for the Assessment and Rating of Ataxia (SARA), Activities of Daily Living (ADL 0–36) and Instrumental Activities of Daily Living (IADL)), Nerve Conduction Study (NCS) and peripheral nerves high-resolution ultrasound (HRUS) were collected. For each patient, 26 nerve sites were evaluated both quantitatively (Cross Sectional Area (CSA) assessment) and qualitatively. CSA values were compared with 20 healthy volunteers.

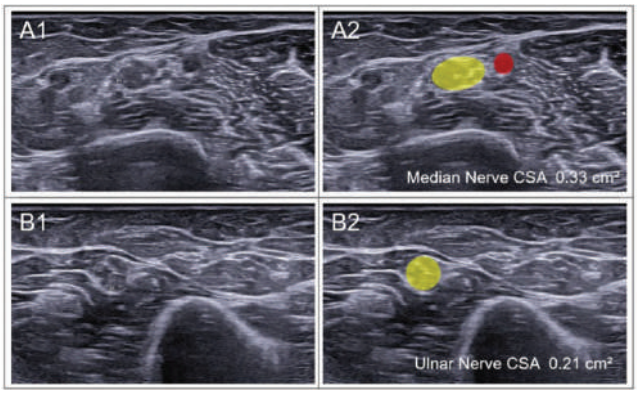
Results: In FRDA, HRUS showed a significant nerve enlargement of the Median and Ulnar nerves at the axilla and at the arm ($p < 0.001$). The cumulative count of affected nerve sites was directly associated with clinical disability, as assessed by SARA, ADL 0–36, and INCAT score, while displaying an inverse correlation with IADL.



Cross Sectional Area of Median and Ulnar nerves as assessed with high resolution nerve ultrasound examination in patients with Friedreich's ataxia (orange) and control participants (blue).



Cross Sectional Area of Tibial, Peroneal and Sural nerves as assessed with high resolution nerve ultrasound examination in patients with Friedreich's ataxia (orange) and control participants (blue).



High resolution nerve ultrasound examination showing an enlarged Median (A) and Ulnar (B) nerves at the arm in Friedreich's ataxia. Yellow circles indicate the nerves and red circles indicate the arteries.

Conclusion: Nerve ultrasound can detect alterations along the nerves in Friedreich's Ataxia. While NCS do not correlate with disease severity, HRUS shows a strong correlation with disease severity scores. Nerve ultrasound is a valuable tool in the assessment of Friedreich's Ataxia.

Disclosure: Nothing to disclose.

OPR-108 | Choroid plexus volume as a novel candidate neuroimaging marker of the Alzheimer's continuum: A prospective cohort study

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Background and aims: The clinical role and potential mechanisms of the choroid plexus (ChP) in Alzheimer's disease (AD) remains unclear.

Methods: This prospective cohort study enrolled 607 participants (110 HCs, 269 MCI, and 228 AD dementia). Relationship between ChP volume and CSF hallmarks (Aβ42, Aβ40, Aβ42/40, tTau, and pTau), neuropsychological tests (MMSE, MoCA, NPI, and ADL scores), and multimodal neuroimaging measures were analyzed. The mediating effects of ChP volume were examined on the relationship between CSF hallmarks and neuropsychological tests. The ChP volume performance to differentiate the presence/absence of cerebral Aβ42 deposition was determined using ROC analysis.

Results: The participants' mean age was 65.99 ± 8.79 years. Patients with AD dementia exhibited a larger baseline ChP volume than the other participants. ChP volume enlargement correlated with decreased Aβ42 and Aβ40 levels; lower MMSE and MoCA and higher NPI and ADL scores; lower volume, cortical thickness, and corrected cerebral blood flow in other cognition-related regions. ChP volume alone mediated and ChP–hippocampal volume combined chain mediated the association of CSF Aβ42 and Aβ40 levels with the MMSE scores (16.91%, 37.15%, 14.25%, and 27.82%, respectively). ChP volume better identified the presence/absence of cerebral Aβ42 deposition than hippocampal volume (AUC: 0.762 vs. 0.724). Generalized linear mixed-effects models discerned that baseline ChP volume was associated with subsequent decline and faster worsening in the MMSE, MoCA, and ADL scores with 10.03 ± 4.45 months' follow-up.

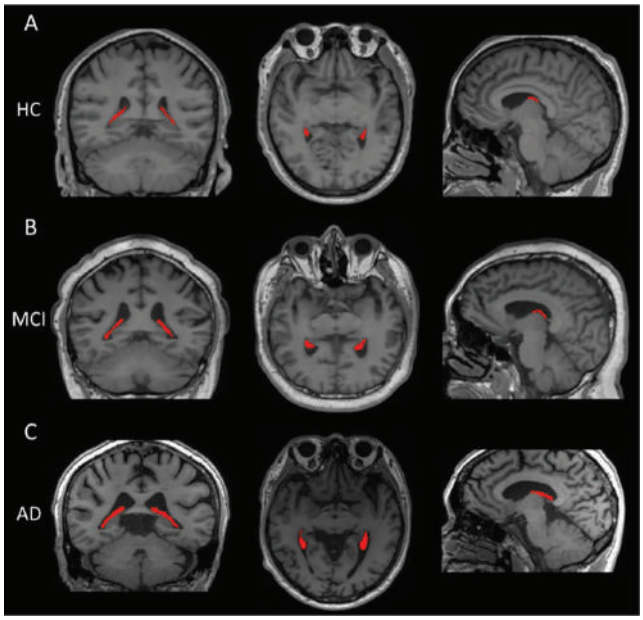

FIGURE 1 Comparisons among three representative 3D-T1 weighted images of the ChP volume in the three groups.

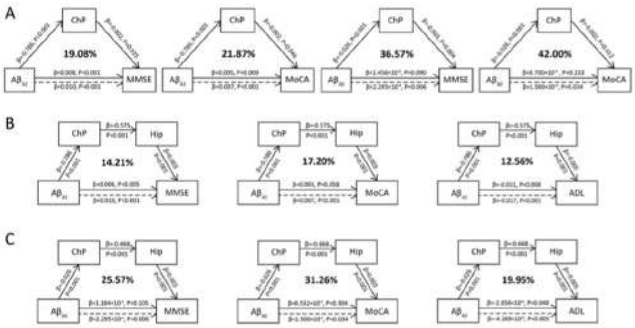

FIGURE 2 Simple and chain-mediating effects of ChP volume on the association of CSF hallmarks and neuropsychological tests.

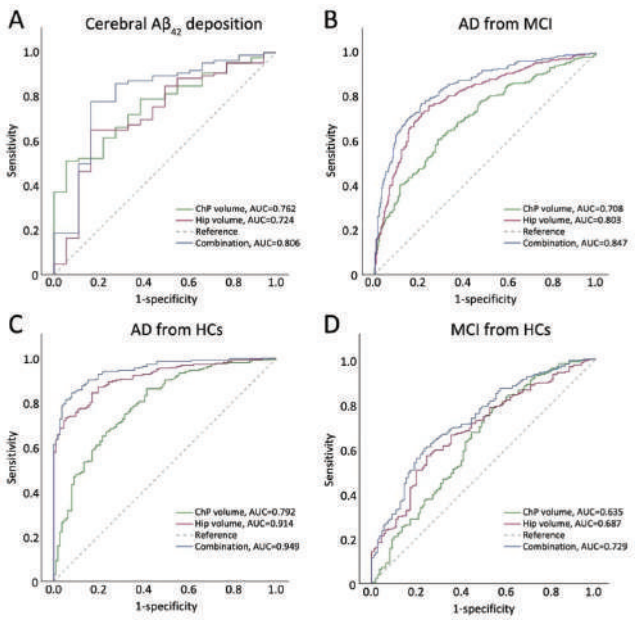

FIGURE 3 Receiver operating characteristic curves for choroid plexus and hippocampal volume for discriminating the absence/presence of cerebral pathological deposition, and distinguishing different disease stages.

Conclusion: ChP volume is a novel, candidate, non-invasive neuroimaging marker associated with neurodegenerative changes in Alzheimer's continuum. It can detect early cerebral Aβ42 deposition and predict prognosis in clinical practice.

Disclosure: Nothing to disclose.

OPR-109 | A data-driven and dynamic network connectivity approach differentiates atypical patterns in Alzheimer's disease

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Background and aims: From a macro-scale perspective, Alzheimer's disease (AD) can be conceptualized as a network-based syndrome, characterized by polysynaptic communication abnormalities assessed through functional magnetic resonance imaging (fMRI). The molecular hallmark of AD encompasses abnormalities involving amyloid-beta (A), tau (T) protein accumulation, and medial temporal lobe neurodegeneration (N).

Methods: In this study, we hypothesized that distinct ATN patterns would demonstrate specific spatiotemporal synchronization patterns measured using resting-state fMRI (rs-fMRI). We included individuals from the ADNI project. Dynamic functional connectivity (dFC) outcomes were measured using co-activation

patterns derived from the posterior cingulate cortex in 152 controls (74 ± 9 yrs) and projected to 334 patients (74 ± 10 yrs). ATN patterns were identified through a low-dimensional approach in conjunction with a K-means algorithm. Univariate, and multivariate approaches were applied to assess biological, behavioral, and dFC differences. Finally, we applied linear and non-linear classifiers to investigate whether dFC could predict ATN classifications.

Results: We identified three main ATN clusters. The first group displayed mild pathological alterations. The second cluster exhibited typical behavioral impairment alongside AD pathology. The third cluster demonstrated similar behavioral impairment but a divergent T (low) and N (high) pattern, suggestive of non-AD pathology. Univariate and multivariate analyses revealed two dFC patterns encompassing the default mode network and the occipito-temporal cortex linked, respectively, with typical and atypical ATN patterns. DFC exhibited an accuracy of approximately 90% in predicting ATN groups.

Conclusion: These results support the key association between macro-scale and molecular AD alterations. Notably, dFC markers can assist in identifying patients with AD-like clinical profiles but with different underlying pathologies.

Disclosure: Nothing to disclose.

OPR-110 | Is it time to utilise nerve ultrasonography in the journey of amyotrophic lateral sclerosis (ALS) diagnosis?

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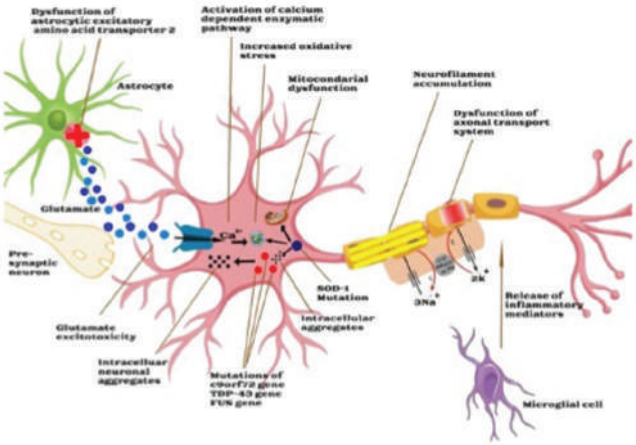
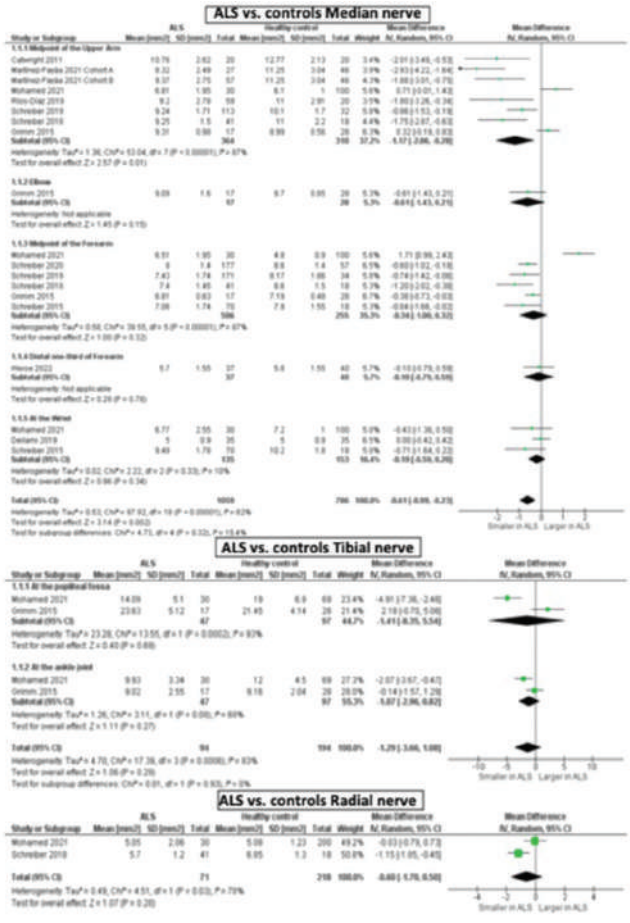
Background and aims: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease affecting upper and lower motor neurons, causing progressive atrophy of muscles, hypertonia, and paralysis. This study aimed to assess the difference in CSA of several peripheral nerves, vagus and cervical roots measured via US between ALS patients and healthy controls to identify the main nerves that have atrophy during ALS.



Dysfunction of the molecular pathway in ALS. (Figure created by BioRender).

Methods: A systematic search was conducted on Cochrane, Clarivate Web of Science, PubMed, Scopus, and Embase for the mesh terms nerve, ultrasonography, and amyotrophic lateral sclerosis. A quality assessment and a double-arm meta-analysis were performed.

Results: 17 studies with a total of 935 ALS patients and 604 controls were included in this review. The overall mean difference showed that individuals with ALS had a significantly smaller CSA in comparison to healthy controls for median, ulnar, C6 root, and phrenic nerves. However, no significant difference in the CSA was found in radial, vagal, sural and tibial nerves.



Mean difference of bilateral median, tibial and radial nerves CSAs between ALS patients and healthy controls.

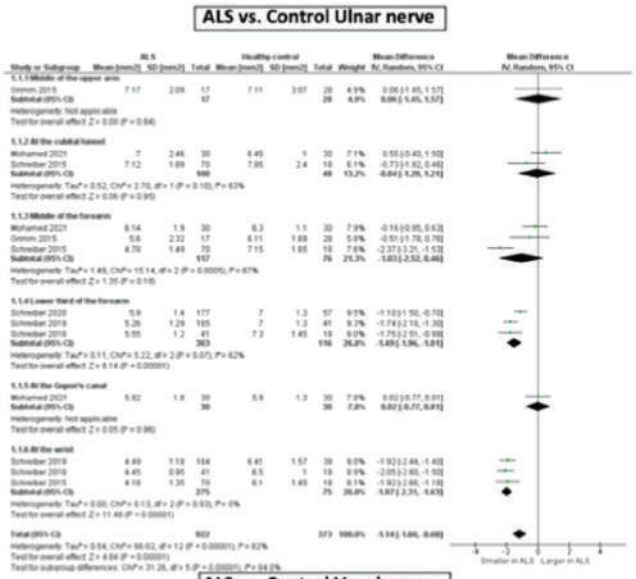


Table 3. Mean difference of CSA values for nerves reported by single studies.

Study	Nerve measured	Controls Mean (mm^2)	Controls SD	Controls Number	ALS Mean (mm^2)	ALS SD	ALS Number	MD (mm^2)	P
Noderu2014	C6 root	7.6	1.6	37	5.34	1.6	35	2.26	<0.001
Suratov2021	Phrenic (Rt)	1.62	0.45	28	1.08	0.39	38	0.54	<0.00001
	Phrenic (Lt)	1.39	0.31	28	1.02	0.34	38	0.37	<0.00001

Mean difference of bilateral ulnar, vagal, C6 root and phrenic nerves CSAs between ALS patients and healthy controls.

Conclusion: Our results confirmed anatomic sites to potentially differentiate individuals with ALS from healthy controls such as the median nerve at the mid-arm and the ulnar nerve at the wrist and the lower third of the forearm.

Disclosure: Nothing to disclose.

Headache & pain 2

OPR-111 | **Evaluating the impact of lacosamide, pregabalin, and tapentadol on spinal biomarkers in human subjects**

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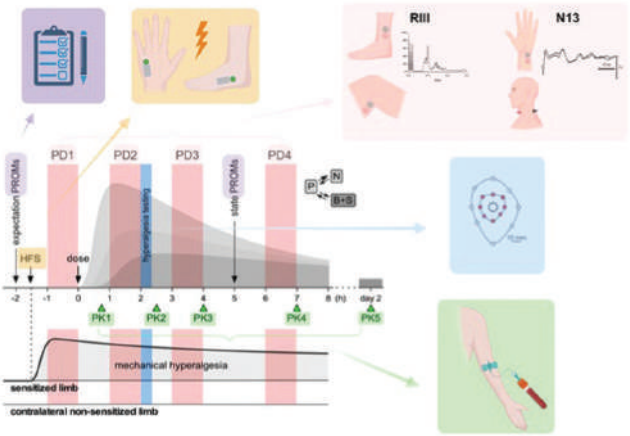
Background and aims: The BioPain subtopic of IMI-PainCare project aimed to test the effectiveness of selected biomarkers for evaluating drug effects and target interactions in new analgesic development. Within this framework, the BioPain-RCT2 assessed the efficacy of lacosamide, pregabalin, and tapentadol against placebo on neurophysiological spinal biomarkers, specifically the RIII flexion reflex and the cervical N13 component of somatosensory evoked potentials, under normal and hyperalgesic conditions induced by high-frequency electrical skin stimulation (HFS).

Methods: A multi-center, double-blind, placebo-controlled 4-period, 4-way crossover pharmacodynamic and pharmacokinetic study in healthy subjects. Spinal biomarkers were measured before and at three time points after administering the three medications and placebo. The study evaluated drug effects on neurophysiological responses in induced hyperalgesia and normal states. It included blood samples for PK analysis. The primary statistical analysis focused on changes in RIII area and N13 amplitudes under tapentadol, with secondary analyses on other treatments' impacts.



Experimental design.

Results: Three different centres enrolled 24 subjects. The blinded analysis showed an effect of tapentadol on the R3 area and a trend towards the significance of pregabalin at the sensitized side, not reaching the set significance level (0.025). No significant effect of drugs on the N13 was observed. Exploratory analysis showed drug effects on the RIII threshold compared to placebo, with tapentadol and PGB also affecting pain ratings.

Conclusion: Tapentadol, and to a lesser extent Pregabalin, prevent the spinal excitability changes induced by secondary hyperalgesia models as assessed with the RIII reflex. This experimental design failed to identify a significant effect of tapentadol on the sensitized N13.

Disclosure: This project has received funding from the Innovative Medicines Initiative 2 Joint undertaking under grant agreement No 777500. This Joint Undertaking receives support from the European

Union's Horizon 2020 research and innovation program and EFPIA. Disclaimer: The statements and opinions presented here reflect the author's view and neither IMI nor the European Union, EFPIA, or any Associated Partners are responsible for any use that may be made of the information contained therein.

OPR-112 | Brain connectivity changes induced by monoclonal antibodies targeting the CGRP pathway in migraine patients

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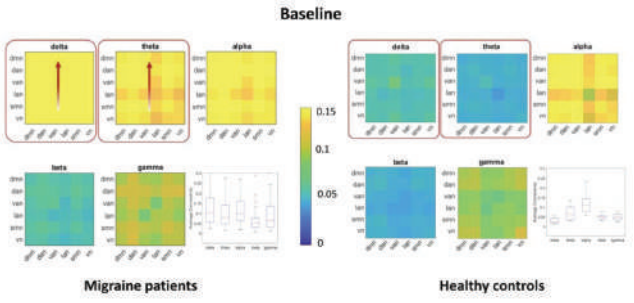
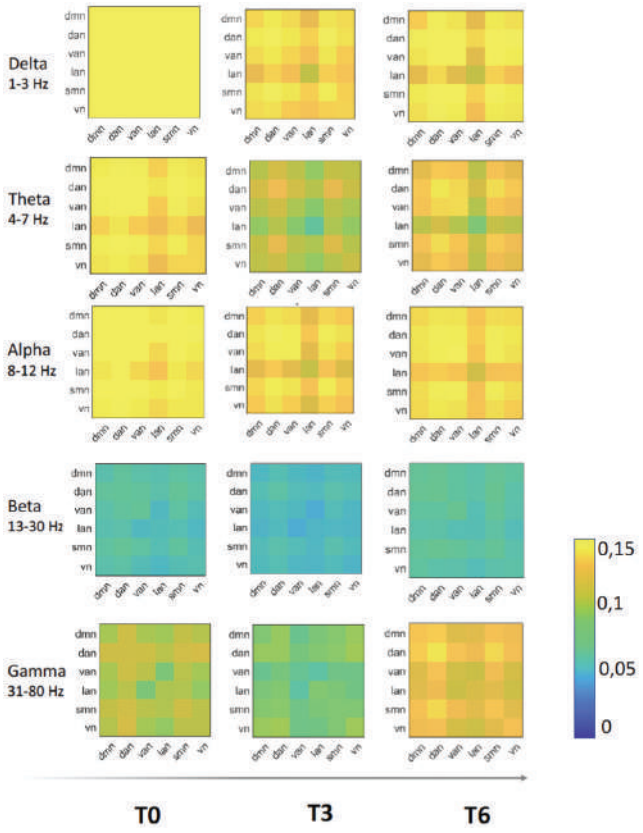
Background and aims: Previous studies demonstrated central and peripheral changes related to monoclonal antibodies directed against the CGRP pathway (mAbs) administration, without reaching a consensus on their mechanism of action. Our study aims to evaluate differences in resting state networks (RSNs) connectivity in migraine patients (MiG) undergoing mAbs treatment.

Methods: This is a prospective, real-life, open label study based on three HD-EEG recordings, namely T0 at baseline, T3 and T6 after 3 and 6 months of mAbs treatment. We assessed connectivity for separate frequency bands (alpha, beta, gamma, theta and delta) for six RSNs: default mode network (DMN), dorsal and ventral attention networks (DAN-VAN), language network (LAN), somatomotor network (SMN) and visual network (VN). We also performed a single HD-EEG assessment in healthy controls (HCs).

Results: We evaluated 62 migraine patients (age 45.4 ± 12.0 years, 54 females, 56.4% with chronic migraine) and 32 HCs (age 38.0 ± 14.0, 16 females). At T6, 62.9% of patients qualified as Responders (reduction in MMDs ≥50% when compared to baseline). At baseline, migraine patients presented an enhanced connectivity in delta and theta frequency bands compared to HCs for all analysed RSNs. At T6, connectivity in the delta and theta bands became comparable between Responders and HCs, while Non-responders maintained higher connectivity in the delta and theta bands compared to both HCs and Responders.

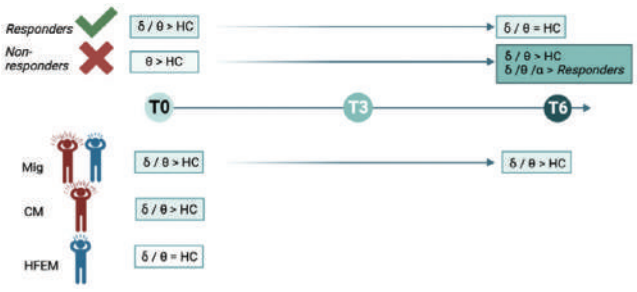


Comparison of inter-network connectivity between migraine patients and healthy controls at baseline. Average RSN connectivity is reported in the box and whiskers plot with median connectivity values for each band and related interquartile ranges.



Longitudinal inter-network seed-based connectivity analysis. Comparison between migraine patients in different treatment timepoints (T0: baseline, T3: 3 months of mAbs treatment, T6: 6 months of mAbs treatment). Coding is color-based ranging from blue, re.

Conclusion: Our study demonstrated an enhanced slow frequencies whole-brain connectivity in migraine patients. Treatment with anti-CGRP monoclonal antibodies induced a positive modulation of functional connectivity in the delta and theta bands in Responder patients.



Summary of study findings. Mig: migraine patients, CM: chronic migraine, HFEM: high frequency episodic migraine patients.

Disclosure: Nothing to disclose.

OPR-113 | Role of specific microRNAs in cluster headache: correlation with disease phenotype and neuropeptide levels

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Background and aims: The role of specific microRNAs was studied in episodic and chronic migraine, but their possible involvement in cluster headache is yet to be elucidated. Our objective is to evaluate the role of specific microRNAs in episodic cluster headache in active phase (AeCH), remission phase (ReCH), chronic cluster headache (cCH), and healthy controls (HCs).

Methods: In this cross-sectional study, we assessed gene expression of miR-382-5p, miR-34a-5p, and miR-155 in peripheral blood mononuclear cells (Relative Quantification). AeCH and cCH patients were assessed outside of an acute cluster headache attack.

Results: We enrolled 18 AeCH (45.7 ± 12.8 years, 14 males, 16.3 ± 9.6 attacks/week), 7 ReCH (48.6 ± 19.8 years, 5 males), 10 cCH (50.1 ± 16.2 years, 9 males, 21.4 ± 18.8 attacks/week), and 14 HCs (45.4 ± 15.2 years, 2 males). miR-382-5p expression was higher in AeCH (1.7 ± 0.8) when compared to ReCH (0.8 ± 0.2) and HCs (0.3 ± 0.1) ($p < 0.005$ for all comparisons). miR-34a expression was higher in AeCH (1.7 ± 0.4) when compared with ReCH (1.0 ± 0.3), cCH (1.2 ± 0.3) and HCs (0.5 ± 0.2) ($p < 0.001$ for all comparisons). miR-155 expression was lower in HCs (0.4 ± 0.1) compared to all CH subgroups ($p = 0.001$ for all comparisons), with no difference among AeCH (1.7 ± 0.5), ReCH (1.3 ± 0.3) and cCH (1.3 ± 0.5).

Conclusion: miR-382-5p, miR-34a-5p and miR-155 expression is increased in cluster headache when compared to HCs. MiR-382-5p and miR-34a-5p were associated with disease activity, being higher in AeCH patients when compared to ReCH. MicroRNAs expression of cCH was in-between active and remission phases of episodic cluster headache patients. Our data supports the role of specific microRNAs in the pathophysiology of different primary headaches.

Disclosure: Cristina Tassorelli has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva; lectured at symposia and is a principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva; received research grants from the European Commission, the Italian Ministry of Health, the Italian Multiple Sclerosis Foundation, and the Migraine Research Foundation; and serves as an associate editor for Cephalalgia and The Journal of Headache and Pain. Roberto Di Icco received speaker honoraria for scientific presentations from Eli-Lilly, and Teva, and has participated as advisory board for Pfizer. Gloria Vaghi reports consultant fees from Lundbeck.

OPR-114 | Evaluation of perivascular and extracellular space properties in migraine: A potential index for glymphatic clearance

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Background and aims: The glymphatic system is a network of perivascular spaces (PVS) that facilitates fluid exchange and peptide clearance in the brain. We aim to investigate if glymphatic dysfunction contributes to migraine pathophysiology, and examine its variations between patients studied during the interictal phase and those studied while experiencing headache.

Methods: One hundred twenty migraine patients (95 interictal, 25 with headache) and 53 controls underwent diffusion tensor (DTI) and susceptibility weighted (SWI) magnetic resonance imaging. Using DTI and SWI, we computed the Diffusion Along Perivascular Space (DTI-ALPS) index, reflecting diffusivity in the PVS near the left lateral ventricle. This index serves as a proxy for regional glymphatic function. Based on previous evidence showing an association between glymphatic function and changes within intra/extracellular compartments, we employed neurite orientation dispersion and density imaging to evaluate voxel-wise maps of white matter extracellular (EVF) and intracellular (IVF) volume fraction. Thus, providing a comprehensive insights into the glymphatic system functioning. Age- and sex-adjusted between-group comparisons were run using R and FSL software.

Results: Compared to controls, migraine patients were older (mean age: patients 39 (12), controls 41 (14), $p = 0.02$) and had a higher proportion of female subjects (female: patients 82, controls 24, $p = 0.006$). We found no significant differences between patients and controls, neither concerning the DTI-ALPS index nor regarding EVF and IVF. No differences were even observed between subgroups of patients.

Conclusion: These results suggest the absence of abnormalities in the PVS and white matter extracellular compartment, indicating normal functioning of the glymphatic system in migraine.

Disclosure: Nothing to disclose in relation to this work.

OPR-115 | Defining mechanisms and new treatments for headache in raised intracranial pressure

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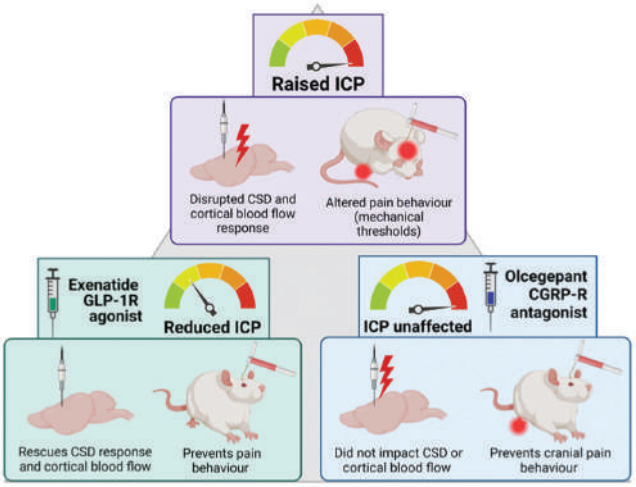
Background and aims: Elevated intracranial pressure (ICP) is associated with migraine-like headaches, but the mechanisms are unclear. Glucagon-like peptide-1 (GLP-1) receptor agonism can reduce ICP, while migraines are associated with increased calcitonin gene-related peptide (CGRP), and therapeutic benefits are observed with CGRP blockade. We investigated migraine mechanisms in a raised ICP rat model, investigating the effects of GLP-1 receptor agonism and CGRP inhibition on ICP and nociception.

Methods: A validated rat model with intracisternal kaolin injection hindering CSF drainage was used. Mechanical hyperalgesia via von Frey filament testing, steady-state potential and cortical blood flow responses to cortical spreading depression (CSD) were assessed. Responses were investigated following treatment with GLP-1 receptor agonist exenatide or CGRP receptor antagonist olcegepant.

Results: Kaolin increased ICP [median(range) 15.96 mmHg (8.97) $n=8$] controls [6.02 mmHg (1.79) $n=6$ $p=0.0007$]. Mechanical thresholds were reduced in raised ICP (mean(SD) hind paw baseline: 5.78 g (2.81), day 7 3.34 g (2.22) $p<0.001$, periorbital baseline: 6.13 g (2.07), day 7 2.35 g (1.91) $n=12$ $p<0.001$). Raised ICP drastically altered CSD responses [depolarisation duration raised ICP: 108.81 s (222.12) $n=11$, controls 37.54 s (108.38) $n=9$ $p=0.038$, repolarisation duration raised ICP: 1824.26 s (3499.54) $n=12$, controls 86.96 s (140.05) $n=9$ $p<0.0001$]. CBF change was also reduced (85.55% (30.84) $n=9$) versus controls (217.64% (37.70) $n=8$ $p<0.0001$).

Conclusion: These data suggest that elevated ICP results in mechanical hyperalgesia, a sign of cutaneous allodynia. GLP-1 receptor agonism reduced ICP, prevented changes in mechanical thresholds and restored responses to CSD. CGRP receptor antagonism prevented periorbital pain behaviour, indicating a potential role for CGRP in driving pain responses associated with elevated ICP.



Increased ICP resulted in mechanical hyperalgesia and altered CSD responses. Reducing ICP via GLP-1 receptor agonism restored mechanical thresholds and CSD responses, while CGRP receptor antagonism prevented periorbital pain behaviour.

Disclosure: OG reports scientific consultancy fees from Invex Therapeutics 2020 which were outside the work in this article. AJS reports personal fees from Invex therapeutics in her role as Director with stock holdings, during the conduct of the study (since 28.06.2019); other for advisory boards from Allergan, Novartis, Cheisi and Amgen outside the submitted work. All other authors declare no competing interests.

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ABSTRACT

ePresentations

Saturday, June 29 2024

Ageing and dementia 1

EPR-001 | Five-year hospital readmission rates of older patients with or without use of central nervous system depressant medications

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Background and Aims: Older patients are particularly sensitive to inhibitory CNS effects of prescription drugs, and are more often afflicted by multimorbidity and polypharmacy, which may augment these issues. We have shown associations between use of CNS depressant drugs (CNSDs) and cognitive function, quality of life, multimorbidity and mortality. In this prospective longitudinal follow-up study, we examined hospital readmissions among older patients in relation to their use of CNSDs (opioids, sedatives and hypnotics).
Methods: Consecutively recruited patients aged 65–90 among inpatient admissions to medical departments of a large university hospital. Written informed consent was a pre-requisite. Medication information and sociodemographics were collected and patients were tested using validated cognitive instruments, quality of life scales and pain assessments. Follow-up was over 5 years from index admission, surviving patients were reassessed in person, mortality data and readmissions data were accessed through electronic patient records.
Results: 246 patients were included (56% females). 100 were CNSD users, 146 non-users. Age at inclusion was 75 (95% CI 74–76) for non-users and 79 (CI 77–80) for users ($p < 0.001$). At 5-year follow-up, 52% had died with significantly higher mortality among CNSD users. Females were more commonly CNSD users ($p < 0.001$). There was no difference in readmissions (number of readmissions or total number of readmission days) between users and non-users whether or not analysis was performed on all included patients or only on those that were alive after 5 years.
Conclusion: CNSDs use was associated with mortality but not readmissions.
Disclosure: Research funding by Lundbeck Pharma and various lecture honoraria are acknowledged.

EPR-002 | Safety and efficacy of transcranial pulse stimulation in Alzheimer's disease

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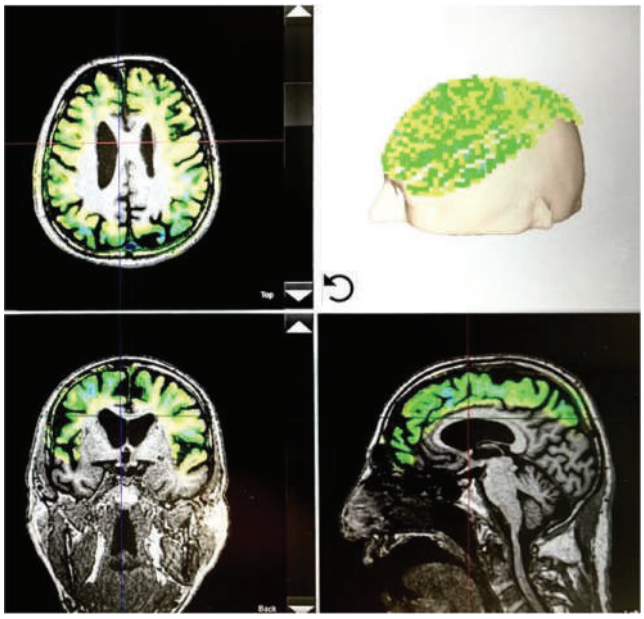
Department of Brain Stimulation, Alexius/Josef Hospital, Neuss, Germany

Background and Aims: Alzheimer's disease (AD) is the most common form of dementia worldwide. Recently, transcranial pulse stimulation (TPS) has opened up the possibility of non-invasive brain stimulation using focussed ultrasound pulses. Since 2022, we have been one of the first centers worldwide using TPS and present the data collected so far.
Methods: Dementia screening was carried out on the basis of the currently valid German guideline. Each of our patients received six therapy sessions within two weeks with an energy amount of 0.2 mJ/mm^2 per individual pulse and a total number of 6000 pulses/session. Thanks to 3D navigation based on MRI images, pulses were applied individually bilaterally to the frontal, parietal and temporal cortex. We have treated a total of 86 patients with AD to date. The Color–Word Interference Test (Stroop Test) with the following pre/post design was used in 52 patients for close monitoring of executive function and working memory: t0 pre-stimulation, t1 after 6 treatments.
Results: The mean age was 75.8 years (54% female) with an average Mini Mental State Examination score of 21.8 points. 82% patients were able to maintain or improve their speed in the Stroop Test. No long-term side effects were observed in any patient.
Conclusion: We conclude that with the help of TPS, an improvement in cognitive deficits in patients with AD is possible. The present study is the largest data collection on this topic to date. Sham-controlled trials with larger samples are needed to prove the effectiveness of the treatment in patients with AD.



3D neuronavigation of TPS.

Disclosure: A. R. Günes: Storz Medical Co. (Speaker) M. Beglau: Nothing to disclose. M. Köhne: Nothing to disclose. U. Sprick: Janssen Co. (Member of Advisory Boards), Storz Medical Co.(Speaker), Get on Institute (Speaker).

EPR-003 | Plasma p-tau217 as a useful biomarker to track AD progression in non-demented persons

A. Mendes[1]; F. Ribaldi[1]; A. Lathuiliere[1]; N. Ashton[2]; S. Janelidze[3]; H. Zetterberg[2]; M. Scheffler[4]; F. Assal[5]; V. Garibotto[6]; K. Blennow[2]; O. Hansson[3]; G. Frisoni[1]

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Background and Aims: Plasma biomarkers have been investigated to assess their efficacy in the early identification of Alzheimer's disease (AD). This is especially significant during the pre-dementia stages to enable a prompt intervention. Thus, the goal of this study was to test differences in plasma biomarkers between the cognitively unimpaired (CU) and mild cognitive impairment (MCI) groups and evaluate how they correlated with the traditional biomarkers in a Geneva Memory Center non-demented cohort.

Methods: The sample consisted of 100 subjects (CU = 33; MCI = 67). Plasma (p-tau217, p-tau231, p-tau181, GFAP, and NfL), amyloid-PET centiloid, tau-PET SUVr, and MRI (hippocampal volume) from these people were used in the study. The differences between CU and MCI in plasma biomarkers were addressed using Mann–Whitney tests. Additionally, we calculated the association between plasma and traditional biomarkers using Pearson correlation.

Results: All plasma biomarkers, except p-tau231, demonstrated statistically significant differences between CU and MCI ($p < 0.05$). However, p-tau217 revealed a higher effect size ($\delta = 0.95$) between clinical stages in comparison with other biomarkers (δrange = 0.25–0.41). Likewise, p-tau217 showed the highest correlation coefficient with centiloid ($r = 0.63$) and tau-SUVr ($r = 0.79$). For the hippocampal volume, p-tau181 revealed the highest correlation ($r = -0.42$).

Conclusion: Plasma p-tau217 showed higher disparities between CU and MCI individuals, as well as higher correlations with centiloid and tau-SUVr. This implies that p-tau217 could serve as a valuable indicator for monitoring the AD progression, as it exhibits a stronger association with conventional measures.

Disclosure: Nothing to disclose.

EPR-004 | Cognitive decline associated to baseline plasma NfL, p-tau217 and tau-PET SUVr in mild cognitive impairment subjects

A. Mendes[1]; F. Ribaldi[1]; A. Lathuiliere[1]; N. Ashton[2]; S. Janelidze[3]; H. Zetterberg[2]; M. Scheffler[4]; F. Assal[5]; V. Garibotto[6]; K. Blennow[2]; O. Hansson[3]; G. Frisoni[1]

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Background and Aims: Plasma biomarkers are being extensively researched in relation to Alzheimer's disease (AD) due to their potential to facilitate widespread screening. One possible application of the plasma biomarkers is the prediction of cognitive decline in non-demented individuals, such as the mild cognitive impairment (MCI) population. However, the comparison of the predictive levels of cognitive deterioration between plasma and traditional biomarkers is still not clear. Therefore, we compared how plasma (i.e., p-tau181, p-tau231, p-tau217, GFAP, NfL, and Aβ42/40) and neuroimaging biomarkers (i.e., amyloid-PET centiloid, tau-PET global-suvr, and hippocampal volume) predict cognitive decline in the Geneva Memory Center cohort.

Methods: A total of 67 MCI subjects were included in this study. Linear mixed-effect regression models were performed to assess the association between baseline levels of each biomarker and cognitive decline. Lastly, we calculated sample sizes for future AD preventive clinical trials, considering the inclusion of plasma biomarker positivity.

Results: Cognitive decline was significantly predicted by baseline plasma NfL ($\beta = -0.53$) and p-tau217 ($\beta = -0.59$), and tau-SUVR ($\beta = -0.91$) ($p < 0.05$). Finally, we showed that if NfL is added to the criteria for future AD clinical trials, the number of people in the samples could drop by as much as two-thirds if they have positive amyloid-PET and tau-PET scans.

Conclusion: Plasma biomarkers NfL and p-tau217 significantly predict cognitive decline as tau-SUVR during MCI. Moreover, identifying at-risk amyloid-positive subjects using plasma NfL can reduce sample sizes for future clinical trials.

Disclosure: Nothing to disclose.

EPR-005 | ATN system and disease-modifying treatment eligibility in a hospital-based cohort

E. Canu[1]; G. Rugarli[2]; F. Coraglia[3]; S. Basaia[1]; G. Cecchetti[4]; S. Calloni[5]; P. Vezzulli[5]; E. Spinelli[2]; R. Santangelo[6]; F. Caso[7]; A. Falini[8]; G. Magnani[7]; M. Filippi[9]; F. Agosta[2]

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Background and Aims: To apply the AT(N) classification to a cohort of patients with Alzheimer's disease (AD) and related disorders, and to investigate how many cases would be eligible for the disease-modifying treatments.

Methods: We conducted a retrospective evaluation of 429 patients referred to the Memory Center of IRCCS San Raffaele Hospital in Milan. Patients underwent clinical/neuropsychological assessments, lumbar puncture, structural brain imaging, and positron emission tomography (FDG-PET). Patients were stratified according to AT(N) classification, group comparisons were performed and the number of eligible cases for anti-β amyloid monoclonal antibodies was calculated.

Results: Sociodemographic and clinical features were similar across groups. Although the clinical presentation was similar, the A+T+N+ group showed more severe cognitive impairment in memory, language, attention, executive, and visuospatial functions compared to other AT(N) groups. Notably, T+ patients demonstrated greater memory complaints compared to T- cases. FDG-PET outperformed MRI and CT in distinguishing A+ from A- patients. Although the 60.8% of the observed cases were A+, only the 17.2% were eligible for amyloid-targeting treatments.

Conclusion: The AT(N) classification is applicable in a real-world clinical setting. The classification system provided insights into clinical management and treatment strategies. Low cognitive performance and specific regional FDG-PET hypometabolism at diagnosis are highly suggestive for A+T+ or A-T+ profiles. This work provides also a realistic picture of the proportion of AD patients eligible for disease-modifying treatments emphasizing the need for early detection. Funding. Foundation Research on Alzheimer Disease. Cofunding from Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

Disclosure: E Canu receives research supports from the Italian Ministry of Health; G Rugarli, F Coraglia, SF Calloni, PQ Vezzulli, R Santangelo, EG Spinelli, F Caso, A Falini, G Magnani have nothing to disclose; S. Basaia receives research support from the Italian Ministry of Health; G. Cecchetti received speaker honoraria from Neopharmed Gentili; M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. F. Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, ARiSLA, the ERC, the EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease (France).

EPR-006 | Association between genetic and fluid biomarkers of glymphatic pathology and clinical phenotypes in Parkinson's disease

E. de Natale[1]; A. Terry[1]; H. Wilson[1]; H. Wright[1]; J. Wollaston Moss[2]; L. Knowles[2]; F. Niccolini[3]; S. Albayati[4]; M. Politis[1]
[1]*Neurodegeneration Imaging Group, University of Exeter Medical School, London, UK;* [2]*Royal Devon University Healthcare NHS Foundation Trust, Exeter, UK;* [3]*Frimley Health NHS Foundation Trust & St George's University Hospitals, UK;* [4]*East Kent Hospitals University NHS Foundation Trust, Ashford, UK*

Background and Aims: Dysfunction of the glymphatic system is implicated in Parkinson's disease (PD) pathophysiology, but the precise mechanisms remain elusive. We present preliminary findings from an ongoing cross-sectional cohort study examining the role of single nucleotide polymorphisms (SNPs) in the Aquaporin-4 (AQP4) gene, as well as blood levels of AQP4 and S100β, as markers of glymphatic and astrocytic pathology, in relation to disease grading, staging, and sleep outcomes in PD.
Methods: A total of 176 PD patients underwent assessments of motor and non-motor symptoms, with particular emphasis on sleep parameters using the Parkinson's disease Sleep Scale (PDSS), Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), and cognitive performance through the Montreal Cognitive Assessment (MoCA) and Cambridge Neuropsychological Test Automated Battery (CANTAB). Venous blood samples were analysed for variants in SNPs of the AQP4 gene, as well as plasma levels of AQP4, S100β and total α-synuclein.
Results: In the entire cohort, lower plasma S100β levels correlated with higher MDS-UPDRS part 3 (rho = -0.245, $p=0.001$), higher total MDS-UPDRS (rho = -0.276, $p<0.001$), higher Hoehn & Yahr (rho = -0.196, $p=0.012$) scores, and lower PDSS scores (rho=0.237, $p=0.007$). Higher total plasma α-synuclein levels correlated with lower AQP4 levels (rho = -0.194, $p=0.011$). Carriers of the AQP4 rs162007 SNP demonstrated higher ESS scores ($p=0.01$) and lower blood α-syunclein ($p=0.045$). Carriers of the rs162009 SNP exhibited elevated ESS scores ($p=0.02$) and a trend towards higher AQP4 plasma levels ($p=0.06$).
Conclusion: These findings suggest a role of genetic and peripheral markers of glymphatic pathology in determining PD phenotypes associated with altered sleep and cognition.
Disclosure: Nothing to disclose.

EPR-007 | Copper and ceruloplasmin: Relationship with CSF biomarkers in Alzheimer's disease

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Background and Aims: Despite the prevailing amyloid cascade hypothesis in Alzheimer's disease (AD) pathophysiology, numerous alternative pathways, including neuroinflammation, oxidative stress and lysosomal dysfunction, have been implicated in the disease. Emerging studies propose a potential involvement of copper and ceruloplasmin in AD pathophysiology, given the binding sites for copper on both amyloid precursor protein and beta-amyloid (Aβ), along with the observed association between cerebrospinal fluid ceruloplasmin and disease progression. This study aimed to determine the relationship between copper and ceruloplasmin levels and the cerebrospinal fluid biomarker profile in AD.
Methods: Serum copper and ceruloplasmin levels were assessed in AD-diagnosed patients supported by biomarkers. Univariate analyses, including Spearman correlations and t-student tests, were conducted. Linear regressions, adjusting for relevant variables, were performed to investigate the association between copper, ceruloplasmin and cerebrospinal fluid biomarkers.
Results: A total of 132 patients were included (60.6% female). The mean age was 68.8 ±7.7, with a mean onset age of 65.4 ±7.7. In linear regression, Aβ42 was associated with Aβ40 ($\beta=0.040$, 95 % CI = [0.033, 0.047], $p<0.001$) and copper ($\beta=175.11$, 95 % CI = [18.39, 331.82], $p=0.029$). Tau was associated with ceruloplasmin ($\beta=3184.50$, 95 % CI = [246.33, 6122.68], $p=0.034$) and ptau ($\beta=6.61$, 95 % CI = [5.38, 7.83], $p<0.001$). Ptau was associated with tau ($\beta=0.091$, 95%CI = [0.074, 0.108], $p<0.001$), and Aβ40 ($\beta=0.008$, 95 % CI = [0.005, 0.012], $p<0.001$).
Conclusion: These findings contribute valuable in vivo evidence, emphasizing the association of serum copper and ceruloplasmin with AD biomarkers, underscoring the potential significance of copper and ceruloplasmin in metal metabolism regulation and modulation of oxidative stress and inflammation in AD.
Disclosure: Nothing to disclose.

EPR-008 | Risk of dysphagia in primary progressive aphasia: demographic, clinical, behavioural and neuroanatomical features

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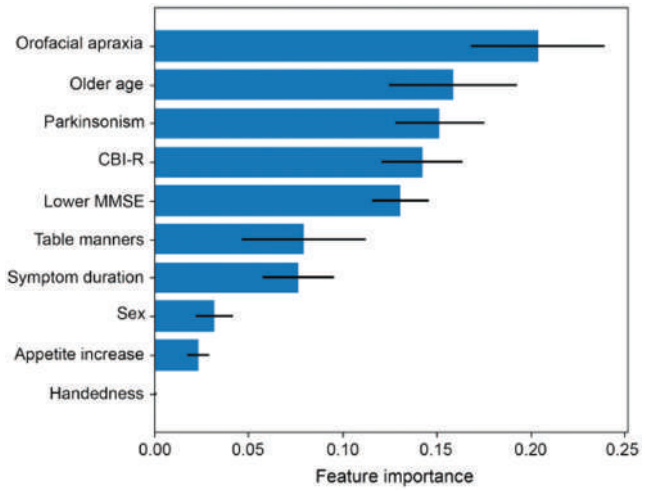
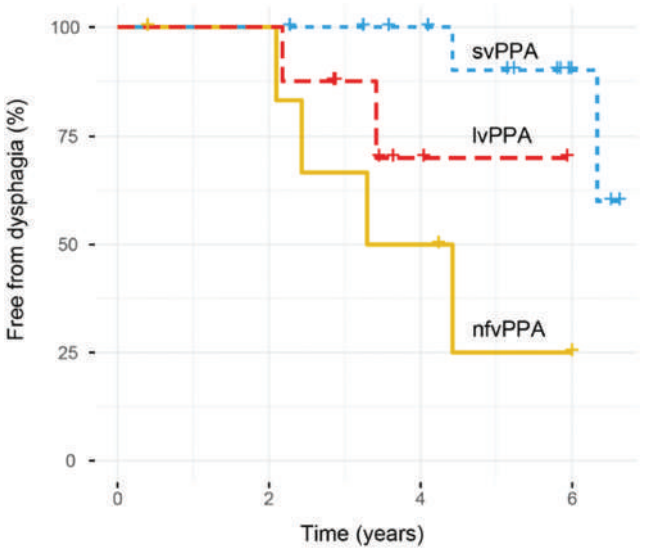
Background and Aims: We aim to investigate clinical, neuropsychological, and neuroanatomical features associated with dysphagia in patients with primary progressive aphasia (PPA).
Methods: 56 PPA patients were enrolled in this study (21 nonfluent/agrammatic variant PPA (nfvPPA), 22 semantic variant PPA (svPPA), 13 logopenic variant PPA (lvPPA)). The presence of dysphagia at baseline or development of dysphagia during follow-up was recorded. Demographic, clinical, and behavioural data were used as candidate input features to train a random forest machine learning

model. Brain MRI scans were processed using voxel-based morphometry (VBM) to assess neuroanatomical associations.

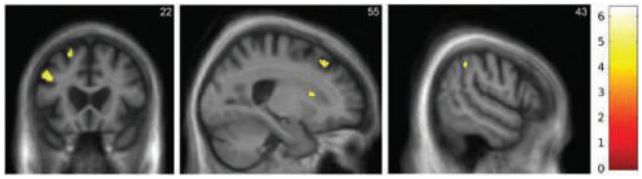
Results: Dysphagia at baseline was more prevalent in nfvPPA (43%) compared to svPPA (5%) and lvPPA (0%). The machine learning model revealed a hierarchy of features that accurately predicted dysphagia in the nfvPPA group, with the most important being orofacial apraxia, followed by age, presence of parkinsonism, Cambridge Behavioural Inventory Revised (CBI-R), Mini Mental State Examination (MMSE) score, decline in table manners, and symptom duration (Figure 1). During follow-up, dysphagia developed in eight (17%) of initially non-dysphagic PPA patients, with nfvPPA showing a significantly higher proportion. Cox's regression analysis revealed lower MMSE, presence of orofacial apraxia, and higher CBI-R scores as predictors of dysphagia (Figure 2). Neuroanatomically, dysphagia in nfvPPA was associated with regional grey matter atrophy in the left middle frontal gyrus, right superior frontal gyrus, right supramarginal gyrus, and right caudate (Figure 3).



Bar chart showing the relative importance (with 95% confidence intervals) of clinical features associated with dysphagia (at baseline) in patients with nonfluent/agrammatic variant primary progressive aphasia.



Kaplan-Meier survival analysis for proportions of patients developing dysphagia during follow-up in each primary progressive aphasia syndromic group. nfvPPA ($n=12$), svPPA ($n=21$) and lvPPA ($n=13$).



Statistical parametric maps showing regional grey matter differences between subgroups of patients with nfvPPA who did and did not report dysphagia, based on a voxel-based morphometric analysis of their brain MR images

Conclusion: This is the first study that identified demographic, clinical, behavioural, and neuroanatomical features associated with dysphagia in nfvPPA, providing valuable insights into identifying PPA patients at risk of dysphagia.

Disclosure: Nothing to disclose.

EPR-009 | Diagnostic Reliability of PET and CSF Biomarkers in Diagnosis of Alzheimer's Disease in a Real-World Setting

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Background and Aims: Amyloid-PET and cerebrospinal fluid (CSF) biomarker analysis are the gold standard diagnostic tools for Alzheimer's disease (AD). High concordance rates are described for diagnostic sensitivity and specificity between PET and CSF, however, in the individual patient setting, proof of amyloid positivity can be ambiguous. We aim here to study patients with AD in comparing the sensitivity of Amyloid-PET and CSF analysis for diagnostic accuracy.

Methods: Patient data from 2017 to 2022 was retrieved and statistically analyzed. Patients with a diagnosis of AD or MCI due to AD (per NIA-AA definition) with amyloid-PET and CSF analysis were included. Amyloid-PET results were visually assessed for cerebral amyloidopathy. Analysis of CSF biomarkers amyloid-beta-42 and Innotest Amyloid Tau Index (IATI; calculated amyloid-beta-42/240+[1.18xt-Tau]) were conducted via INNOTEST, and we define CSF biomarker positivity as amyloid-beta-42 <500 pg/mL and/or IATI <1.

Results: We included 63 patients. Median age of onset was 60.5 (SD10.9). Median duration to amyloid-PET was 3.1 years (SD2.5) and to CSF analysis 2.6 years (SD2.5). 71% of patients had positive amyloid-PET and CSF biomarkers. In patients with positive amyloid-PET (84%), 0% were CSF biomarker negative. In patients with

negative amyloid-PET (16%), 100% were CSF biomarker-positive. In patients with positive CSF biomarkers (100%; 87% amyloid-beta-42; 97% IATI), 16% were amyloid–PET-negative.

Conclusion: We find no complete concordance between PET and CSF analysis. CSF biomarkers show high positivity rates when considering both amyloid-beta-42 and IATI. In cases of strong suspicion of AD pathology, both PET and CSF analysis should be performed to avoid false-negative results.

Disclosure: Nothing to disclose.

Autonomic nervous system diseases

EPR-010 | Autonomic dysfunction in minimal change multiple system atrophy

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Background and Aims: Minimal change multiple system atrophy (MSA) has been reported as an early pathologic form in which glial cytoplasmic inclusions are found in the striatonigral or olivopontocerebellar systems but without neuronal loss. Autonomic nervous system involvement, a defining feature of MSA, has not been specifically investigated in minimal change MSA, which is presumed to be preclinical. We sought to characterize autonomic dysfunction in minimal change MSA.

Methods: Clinical histories, neurologic examinations, and autonomic test results were reviewed in 6 cases of pathologically confirmed minimal change MSA.

Results: All 6 cases were men, their average age 61. All had signs of parkinsonism, and 5 had a history of dream-enactment behavior. Symptoms of autonomic dysfunction included lightheadedness in 5, constipation in 6, urinary dysfunction in 6, urinary overflow incontinence in 5, erectile failure in 3, exercise intolerance in 1, anhidrosis in 1, and orthostatic syncope in 1. Orthostatic hypotension was present in 5, 4 of whom required pharmacologic treatment. Three were dependent on catheterization to empty their bladders. Three had undergone autonomic testing, which showed normal postganglionic sudomotor function and mildly reduced cardiovagal function. Cardiovascular adrenergic function was moderately impaired in one and normal in another. Average composite autonomic severity score was 3.5.

Conclusion: We found evidence of clinical autonomic dysfunction in all cases of minimal change MSA. Our findings support the conclusion that autonomic involvement is an early feature of MSA and that impaired central nervous system autonomic function precedes neuronal loss.

Disclosure: Nothing to disclose.

EPR-011 | Autonomic functions and dopaminergic correlates in Dementia with Lewy Body: A preliminary study

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Background and Aims: Both autonomic failure and nigrostriatal denervation are well-known features of dementia with Lewy body (DLB). However, the relationship between the two has been poorly investigated. We aimed to assess cardiovascular and sudomotor autonomic function tests (AFTs) in DLB and to evaluate the relationship between AFTs and 123I-ioflupane dopamine transporter uptake at single photo-emission computed tomography (DAT-SPECT).

Methods: 15 DLB patients and 20 healthy controls (HC) underwent head-up tilt-test (HUTT), Valsalva Maneuver, deep-breathing, cold-face, hand-grip test (HG), electrochemical skin conductance (ESC). DLB patients also underwent DAT-SPECT, we used the DaTQUANT software for semi-quantitative analysis.

Results: DLB patients showed lower delta heart rate at third minute of HUTT ($p=0.016$), Valsalva Ratio ($p<0.001$) and Overshoot ($p=0.004$), lower delta systolic (ΔSBP, $p=0.002$) and diastolic blood pressure (ΔDBP, $p<0.001$) at HG, lower inspiration-espiration difference at deep-breathing ($p=0.004$), and lower hands-feet ESC than HC (both $p=0.003$). Of all the AFTs, only HG responses correlated with striatal DaTQUANT measures: HG ΔDBP strongly inversely correlated with bilateral uptake of 123I-FP in the anterior (Right: rho -0.691, p 0.004; Left: rho -0.676, p 0.006) and posterior putamen (Right: rho -0.769, $p<0.001$; Left: rho -0.663, p 0.007).

Conclusion: Despite the absence of overt orthostatic hypotension, DLB patients showed covert dysautonomia encompassing adrenergic and parasympathetic dysfunction. Moreover, the functioning of sympathetic peripheral efferent pathways to vessels, reflected by HG ΔDBP, was inversely associated with nigrostriatal denervation. This could suggest the presence of different profiles of peripheral-predominant versus central-predominant impairment in DLB patients.

Disclosure: Nothing to disclose.

EPR-012 | EAN/EFAS survey on autonomic training and clinical autonomic skills of European residents and neurologists

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Background and Aims: Autonomic Nervous System (ANS) disorders have a high prevalence both in the general population and in several neurological conditions, but information on clinical autonomic training opportunities across Europe is currently limited. Here we evaluated the current state of autonomic education, clinical skills and post-graduate educational preferences among European neurology residents and neurologists.

Methods: A 23-item questionnaire was distributed online among European neurologists and neurology residents. The questions covered demographic characteristics, clinical autonomic training received and preferred post-graduate educational format. Clinical autonomic knowledge was self-assessed with five basic multiple-choice questions.

Results: Two-hundred eighty-five individuals answered the survey (60% female, mostly 25–34 years-old). Most respondents trained in East/South/Greater Europe (75%), were practicing neurology for

Table 1 – Survey demographics, training and learning preferences in ANS disorders and response to multiple-choice questions.

Total number of responders	285
Gender	Female – 170 (60%)
Age	
- 18 - 24	2 (1%)
- 25 - 34	131 (46%)
- 35 - 44	68 (24%)
- 45 - 54	33 (12%)
- 55 - 64	34 (12%)
- 65+	17 (6%)
Training country region	
- East/South/Greater Europe	215 (75%)
- West/North Europe	70 (25%)
Working country region	
- East/South/Greater Europe	210 (74%)
- West/North Europe	75 (26%)
For how many years have you been practicing in Neurology?	
- Resident	77 (27%)
- Less than 5 years	53 (19%)
- 5 – 10 years	35 (12%)
- More than 10 years	104 (36%)
- Past practice	16 (6%)
Setting of current practice	
- Public hospital	99 (35%)
- University hospital	192 (67%)
- Private practice	30 (11%)
- Private clinic	31 (11%)
- Other	4 (1%)
- Not applicable	5 (2%)
Formal training received in ANS	
- Compulsory rotation during the residency	13 (5%)
- Compulsory educational course during the residency	21 (7%)
- Facultative rotation during the residency	17 (6%)
- Facultative educational course in the residency context	26 (9%)
- Part of another educational course (e.g., post-graduate courses, congresses)	75 (26%)
- Autonomic topics were discussed within other rotations (i.e. movement disorders, clinical neurophysiology, etc)	134 (47%)
- No training at all	91 (32%)
Autonomic field of training during residency	
- Syncope and other cardiovascular disorders	180 (63%)
- Bladder dysfunction	96 (34%)
- Bowel dysfunction	51 (18%)
- Sexual dysfunction	35 (12%)
- Thermoregulatory disorders	47 (17%)
- Ophthalmological disorders	36 (13%)

EAN/EFAS survey on autonomic training and clinical autonomic skills of European residents and neurologists.

>10 years (42%) and worked in university hospitals (67%). Eighty percent of respondents reported that ANS disorders were covered in the neurology curriculum during their medical studies. During their neurology residency, people mostly received ANS training within rotations in other neurological sub-specialities (47%). The most frequently trained ANS complaint was syncope (63%), followed by bladder, bowel, thermoregulatory, ophthalmological, or sexual disorders. Self-confidence in assessing and managing autonomic domains followed the same order. All responders stated that clinical autonomic skills are important for a good clinical neurological practice, 92% would like to increase their ANS knowledge. The self-assessment questions highlighted knowledge gaps in the management of neurogenic bladder disturbances.

Conclusion: To date, clinical autonomic training has mostly focused on the cardiovascular autonomic domain and European neurologists and residents feel the need to increase their clinical autonomic knowledge.

Disclosure: Nothing to disclose.

EPR-013 | A predominant sympathetic drive may underlie sleep, thermoregulatory and cardiovascular abnormalities in PSP

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Background and Aims: Sleep-wake cycle and the autonomic nervous system (ANS) can be impaired in neurodegenerative diseases. We aimed to explore the possible interaction between ANS and sleep-wake cycle abnormalities in Progressive Supranuclear Palsy (PSP).

Methods: We prospectively recorded 48-h video-polysomnography, body core temperature (BcT) and blood pressure (BP) (Portapres® Model-2, Finapres Medical Systems, The Netherlands) in 15 PSP patients (disease duration 5.7 ±2.6 years) under controlled environmental conditions. We analysed sleep parameters (Table 1) and state-dependent modulation for BcT, BP and heart rate (HR) from the last 24 hours of recording.

Sleep-wake cycle parameters of PSP patients

Dark period	
TST (min)	286.8 ± 118.3§
Sleep efficiency (%)	52.9 ± 20.1§
WASO (min)	231.9 ± 137.2*
Awakenings (n)	37.7 ± 15.5
N1 (%)	24.2 ± 13.7*
N2 (%)	45.1 ± 9.1§
N3 (%)	24.2 ± 14.7*
REM (%)	9.9 ± 8.7§
PLMI	56.0 ± 44.2
AHI	8.1 ± 5.3
Light period	
TST (min)	51 ± 46.9
N1 (%)	54.2 ± 25.3
N2 (%)	33.6 ± 20.9
N3 (%)	11.9 ± 16.2
REM (%)	0.3 ± 1.1
Dark + Light (24 h)	
TST (min)	337.8 ± 131.9
N1 (%)	26.3 ± 12.0
N2 (%)	41.6 ± 14.9
N3 (%)	23.6 ± 13.6
REM (%)	8.5 ± 7.2

TST = total sleep time; WASO = wake after sleep onset; PLMI = periodic limb movement index; AHI = apnoea hypopnea index; * increased compared to normative values for this age group; § decreased compared to normative values for this age group.

Results: Patients slept less than 5 h/night with frequent awakenings, however daytime naps were shorter than 60 min and mainly represented by light sleep resulting in a 24-h total sleep time lower than the recommended 7 hours of sleep. Compared to younger controls, PSP slept less during both day and night but only 2 patients reported excessive daytime sleepiness. There were no significant differences in sleep parameters in patients according to the presence of sleep disorders. Compared to controls patients showed significantly higher BcT values and a higher MESOR. Twelve patients presented a reduced/non/reverse-dipping BP pattern.

Conclusion: PSP patients showed a significant reduction of sleep during night-time not associated with a compensatory increase of sleep during daytime leading to a profound sleep deprivation. This hyperarousal state may be related to reduced homeostatic sleep drive. Increased BcT values and abnormal BP profile may also reflect a primary ANS involvement.

Disclosure: Nothing to disclose.

EPR-014 | The dynamic sweat test in patients with pure autonomic failure: A pilot study

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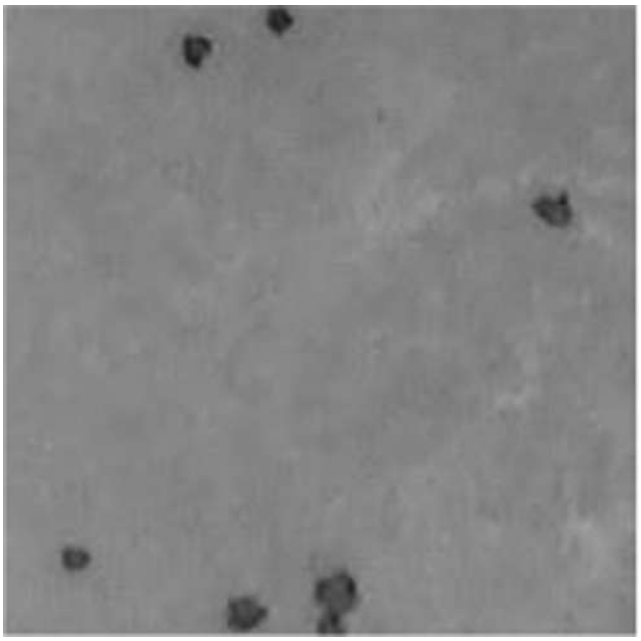
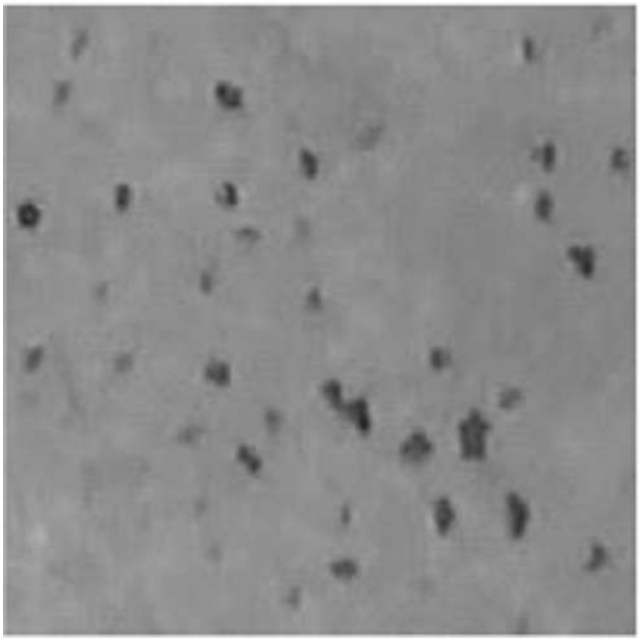
Background and Aims: The dynamic sweat test (DST) is an established tool for the evaluation of sudomotor function. We aimed to characterize the sudomotor pattern of patients affected by pure autonomic failure (PAF) with the DST, and to evaluate its usefulness in distinguishing patients with phenoconversion to overt parkinsonism.
Methods: As part of an ongoing longitudinal study on alpha-synucleinopathies (QSA-PRODROMAL), consecutive patients with an initial diagnosis of PAF and available DST data were included. Patients were followed up in clinic and diagnoses were revised at follow-up. Number of activated sweat glands, mean gland sweat production, and total sweat of a 1 cm^2 area of upper and lower limbs were investigated (Figures 1 and 2). Data were analysed using non-parametric tests, presented as median and interquartile ranges.



Left leg DST results at the time of sweat glands confluence in a PAF patient, area 1 cm2, drops count 7, sweat output per gland 2.24 nL/min, total area sweat output 15.70 nL/cm^2/min.



Right leg DST results at the time of sweat glands confluence in an MSA-P patient, area 1 cm^2, drops count 35, sweat output per gland 1.96 nL/min, total area sweat output 68.63 nL/cm^2/min.

Results: 34 patients (11F, age 62 [57–71] years) with an initial diagnosis of PAF were included. 7 patients phenoconverted (4MSA-P, 2DLB, and 1PD), while 27 retained a PAF phenotype. There was a trend, although not statistically significant, in reduction of total sweat production, both for upper (PAF 213.99 [99.07–406.57], non-PAF 415.92 [120.72–552.53] nL/cm^2/min, $p = 0.641$) and lower (PAF 47.63 [23.39–140.43], non-PAF 116.16 [60.35–181.58] nL/cm^2/min, $p = 0.066$) limbs.
Conclusion: Total sweat production measured with a quantitative postganglionic sudomotor test might be lower in patients with predominantly peripheral autonomic involvement (PAF phenotype) compared to the ones with widespread alpha-synucleinopathies. DST may possibly aid in distinguishing different phenotypes, but future studies and wider samples are needed to confirm the role of such technique.
Disclosure: Sander L holds a grant from the University of Basel, Switzerland, the other authors have nothing to disclose; Iodice V is supported by the National Institute for Health Research, University College London Hospitals Biomedical Research Centre; the remaining authors have nothing to disclose.

EPR-015 | Autonomic assessment in patients with hereditary transthyretin amyloidosis and asymptomatic carriers – A follow-up study

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Background and Aims: Hereditary transthyretin amyloidosis (ATTRv) is a progressive disease with early, disabling autonomic manifestations in 40%–80% of patients. With effective targeted disease-modifying treatments (DMT) markers of disease progression are needed. This study describes progression of autonomic failure (AuF) in ATTRv patients and asymptomatic carriers using autonomic function testing (AFT) and ambulatory blood pressure (BP) monitoring (ABPM).

Methods: 53 patients and 6 TTR mutation carriers (31%F, mean age 54 [range 28–78]y; one individual became symptomatic during follow-up [FU]) had AFT at baseline (BL) and at FU (median interval 23 [range 7–133] months) using Finapres NOVA. 45 subjects (6 carriers) had ABPM with FU. Three AuF stages were defined: normal AFT (0), mild parasympathetic and/or sympathetic impairment (I), severe AuF with neurogenic orthostatic hypotension (II). BP dipping profile was defined according to the consensus criteria.

Results: All six subjects (2 carriers) with initial stage 0 developed stage I within 4 years. Progression from stage I to II was detected in 4/27 patients within 2 years, one patient on DMT improved to stage 0. Eight out of 24 patients improved from stage II to stage I within 2 years (one started DMT). No carrier had stage II AuF. ABPM showed normal dipping profile in 15 subjects (one carrier) at BL, 7/15 developed pathologic dipping profile at FU.

Conclusion: Cardiovascular autonomic failure and impaired circadian BP profile are frequent, early features in ATTRv, with progression over time. Carriers showed subclinical, mainly parasympathetic dysfunction. Improvement in AuF can occur with DMT but further studies are warranted to assess treatment effects in detail.

Disclosure: LS holds a grant from the University of Basel, Switzerland. GC, SJ, AT, GTI, CA, CJW, MMR, CJM: nothing to disclose. JDG provides consultancy for Alnylam, AstraZeneca, Bridgebio, Ionis, Intellia and ATTRalus. VI is supported by the National Institute for Health Research, University College London Hospitals Biomedical Research Centre.

EPR-016 | Octreotide improves PPH and orthostatic tolerance in patients in patients with alpha-synucleinopathies

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Background and Aims: Postprandial hypotension (PPH) is common in patients with autonomic failure although the pathophysiology remains unclear. The effect of octreotide on PPH and orthostatic hypotension (OH) has not been fully evaluated in patients with alpha synucleinopathies, particularly with improving orthostatic tolerance levels.

Methods: We retrospectively evaluated patients with established diagnoses of cardiovascular autonomic failure due to alpha-synucleinopathy with postprandial hypotension who were assessed at our autonomic centre between 2013 and 2021 and underwent cardiovascular autonomic assessment, liquid meal challenge test pre and post-octreotide. Autonomic function testing included tilt table, standing, pressor tests, heart rate responses to Valsalva manoeuvre and deep breathing using Finapres NOVA.

Results: Sixty-seven patients were included (8 patients with Parkinson's disease, 19 with Multiple System Atrophy, and 40 with Pure autonomic failure) with a mean age of 64.4 years and a median disease duration of 6 years. Octreotide improved both OH and PPH. It delayed the onset of orthostatic hypotension ($p = 0.006$), time to maximal BP drop ($p < 0.001$), decreased the magnitude of BP drop in pre-meal tilt by 22.9 mmHg systolic and 12.8 mmHg diastolic ($p < 0.001$), delayed the onset of PPH ($p = 0.006$), decreased the magnitude of maximal PPH (20 mmHg systolic and 12mmHg diastolic) and resolved PPH in 28 patients (42% of the patients) ($p < 0.001$).

Conclusion: Octreotide significantly improved both OH and PPH and the associated orthostatic tolerance in individuals with alpha-synucleinopathy.

Disclosure: The authors have no information to disclose.

EPR-017 | Nocturnal supine blood pressure during head-up tilt sleeping in Parkinson's disease and parkinsonism

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Background and Aims: The co-occurrence of supine hypertension and orthostatic hypotension due to autonomic failure is common in

people with Parkinson's disease (PD) or parkinsonism such as multiple system atrophy (MSA). Head-up tilt sleeping is an intervention that potentially tackles both. So far, the effect of tilted sleeping on the supine blood pressure (BP) has not been investigated.

Methods: This is an interim analysis of the Heads-Up trial (NCT05551377), on the first 12 participants (PD: 10, MSA: 2). Participants slept horizontal for one baseline week, and then gradually increased the sleeping angle to either 1°, 6° and 12° or to 6°, 12° and 18°, for two weeks each. In this interim analysis, the baseline and the 12° angle were used according to the intention-to-treat principle, irrespective of adherence. Data from the night-time ambulatory BP measurement were extracted. Nocturnal BP was recorded twice per hour, and the change score was calculated to examine the mean and 95% confidence interval (CI) of the difference in nocturnal supine BP.

Results: A reduction in the nocturnal systolic BP (mean = -5 mmHg; CI [-14, 5]) and diastolic BP (mean = -9 mmHg; CI [-20, 3]) was found, showing a tendency towards a lower nocturnal BP while sleeping in a 12° full body tilt compared to horizontal sleeping. We noted substantial interindividual differences in effect size.

Conclusion: We found a trend towards a positive effect of head-up tilt sleeping on nocturnal supine BP. Further analysis of the complete Heads-Up cohort allows us to examine the reasons behind substantial interindividual differences.

Disclosure: This project was supported by MJFF grant MJFF-020200.

EPR-018 | Multimodal autonomic biomarkers differentiate pure autonomic failure from other alpha-synucleinopathies

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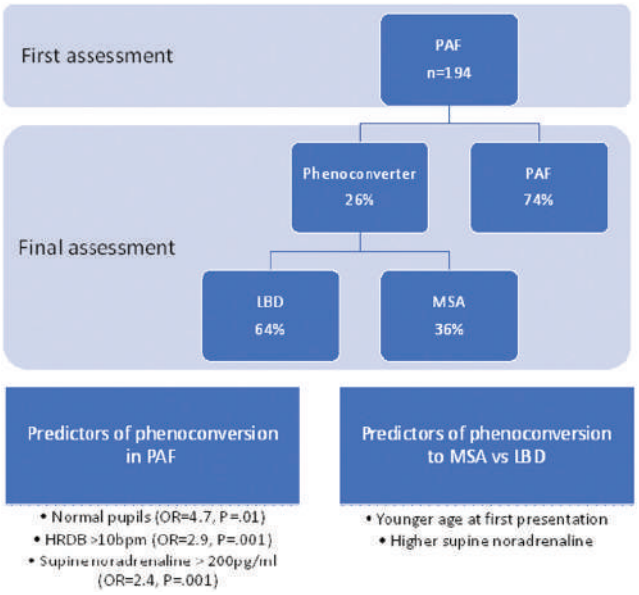
Background and Aims: Pure autonomic failure (PAF) presents with progressive autonomic failure without other neurological features. A third later develop central neurological features, fulfilling criteria for multiple system atrophy (MSA) and Lewy body diseases (LBD), including Parkinson's disease and Dementia with Lewy bodies. We hypothesized that multimodal autonomic biomarkers could distinguish between PAF, MSA and LBD, and predict phenoconversion in patients presenting with PAF.

Methods: 391 patients were studied with cardiovascular autonomic testing (Finapres systems), plasma catecholamines, pupillometry, and COMPASS-31 autonomic symptom and SF-36 quality of life questionnaires. Patients presenting with PAF were followed up to monitor for the emergence of central neurological features. Autonomic biomarkers at initial assessment were used in a logistic regression model to identify predictors for final diagnosis.

Results: Patients with a final diagnosis of PAF ($n = 146$) had significantly greater orthostatic hypotension on tilt, lower supine noradrenaline, and sympathetic pupillary deficits at initial assessment compared to both MSA ($n = 157$) and LBD ($n = 88$). 26% presenting with PAF phenoconverted to MSA/LBD after median follow-up of 13 years (IQR 7–18 years), with normal pupils (OR 4.7; $p = .01$) and supine noradrenaline >200 pg/mL (OR 2.4; $p < .001$) at first assessment predicting future phenoconversion. Patients with PAF reported more severe orthostatic intolerance with similarly diminished quality of life compared to MSA.



Multimodal biomarkers at initial assessment predicting phenoconversion from PAF to MSA or LBD by final assessment HRDB: heart rate variability with deep breathing.

Conclusion: We found greater orthostatic hypotension, lower supine noradrenaline and more frequent sympathetic pupillary deficits in PAF compared to other alpha-synucleinopathies, suggestive of greater post-ganglionic adrenergic denervation. Severe symptomatic orthostatic hypotension is associated with marked physical disability in PAF, even in the absence of other neurological features.

Disclosure: SK was supported by the Guarantors of Brain Entry Fellowship. MPL and VI are supported by NIHR UCL Biomedical Research Centre.

Cerebrovascular diseases

EPR-019 | Cerebral amyloid angiopathy in Alzheimer's disease: A comparison between different versions of the Boston criteria

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Background and Aims: Cerebral amyloid angiopathy (CAA) is a common small vessel disease and the main driver of iatrogenic amyloid-related imaging abnormalities in Alzheimer's disease (AD). We investigated the prevalence of CAA imaging features, and compared different versions of the Boston Criteria for CAA diagnosis in AD subjects.

Methods: Single center retrospective analysis of patients with mild cognitive impairment (MCI) or early stage dementia due to AD. Hemorrhagic (cerebral microbleeds, CMB; cortical superficial siderosis, cSS) and non-hemorrhagic (severe enlarged perivascular spaces in the centrum semiovale, EPVS; subcortical multispot white matter changes) were evaluated on magnetic resonance images. CAA was rated as absent, possible or probable based on the original (V1.0), modified (V1.5), and last updated (V2.0) Boston Criteria.

Results: A total of 75 subjects were included (mean age 71.6+8.1 years, 46.7% males, mean disease duration 2.6+2.0 years) of whom 68 (90.7%) had MCI-AD. EPVS and subcortical multispot white matter changes were highly prevalent (54.7% and 36.0% respectively) whereas lobar CMB and cSS had a lower frequency (1 lobar CMB 16.0%, > 2 lobar CMB 12.0%; focal cSS 1.3%, disseminated cSS 6.7%). EPVS presence was associated with a higher lobar CMB burden. CAA frequency increased from V1 (14.7% possible and 9.3% probable) to V1.5 (13.3% possible and 13.3% probable) and V2.0 (42.7% possible and 26.7% probable).

Conclusion: Non-hemorrhagic CAA features are more common than hemorrhagic markers in AD and more than one in four patients has probable CAA according to the V 2.0 Boston criteria. These findings might inform future trials.

Disclosure: Dr. Morotti declares consulting and advisory board activity for EMC-REG International and AstraZeneca.

EPR-020 | Investigating the impact of anemia on survival after acute ischemic stroke: A nationwide registry-based cohort study

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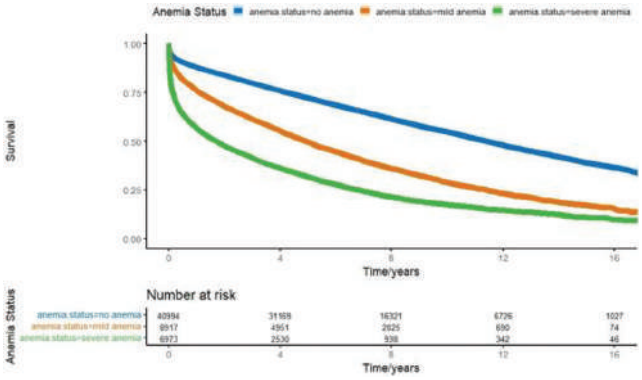
Background and Aims: Anemia at presentation of acute ischemic stroke (AIS) is associated with significant morbidity and mortality. The comparative impact of anemia severity on long-term survival after AIS has not been well studied.

Methods: All patients with first onset AIS from 2005 to 2019 in the Singapore Stroke Registry were included. They were stratified according to anemia status, as no anemia, mild anemia (Hb 11 to <13g/dL) and severe anemia (Hb <11g/dL). The primary outcome was longitudinal mortality. Patients without an event were censored at the end of the registry period (2019). The Cox proportional hazards regression was used to assess the association between post-AIS mortality and anemia. The Kaplan-Meier method was used to compare survival probabilities between groups.

Results: A total of 56,884 patients were analyzed, of which 40,994 (72.1%) had no anemia, 8917 (15.7%) had mild anemia, and 6973 (12.2%) had severe anemia. Patients with mild/severe anemia were older than patients without anemia ($p < 0.001$). Patients with mild anemia (HR 1.35, 95% CI 1.31 to 1.39, $p < 0.001$) and severe anemia (HR 1.90, 95% CI 1.84 to 1.96, $p < 0.001$) were at significant greater risk for mortality than patients without anemia, after adjustment for gender, ethnicity, age, history of transient ischemic attack, ischemic heart disease, smoking, diabetes, hyperlipidemia, hypertension, atrial fibrillation, and treatment with thrombolytics and antiplatelets. The long-term survival of patients with anemia is markedly worse than those without anemia ($p < 0.001$).



Kaplan Meier Curve.

	Unadjusted model		Multivariable-adjusted model^	
Anemia Status	HR (95% CI)	P	HR (95% CI)	P
Overall (30,079 events out of 56,884)				
No anemia	-		-	
Mild anemia	2.03 (95% CI 1.98 to 2.09)	<0.001	1.35 (95% CI 1.31 to 1.39)	<0.001
Severe anemia	3.26 (95% CI 3.16 to 3.36)	<0.001	1.90 (95% CI 1.84 to 1.96)	<0.001

^ Adjusted for age, gender, ethnicity, age, history of transient ischemic attack, history of ischemic heart disease, history of atrial fibrillation, smoking, diabetes, hypertension, treatment with thrombolytics and antiplatelets

Cox regression analyses for longitudinal mortality by anemia groups.

Conclusion: An increasing severity of anemia is associated with poorer survival outcomes in AIS patients.

Disclosure: Nothing to disclose.

EPR-021 | Impact of SMuRF and atrial fibrillation on mortality after Ischemic Stroke: A Nationwide Registry-based cohort study

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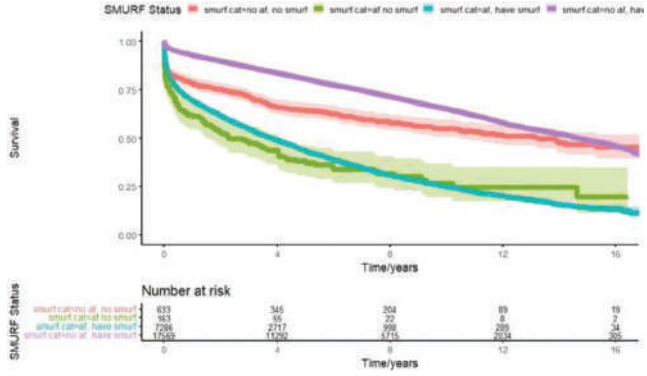
Background and Aims: Existing literature suggests an inverse relationship between standard modifiable risk factors (SMuRF) – comprising smoking, hypertension, diabetes, hyperlipidemia, and mortality in patients with myocardial infarction. The occurrence of this paradox in patients with acute ischemic stroke (AIS) has not been investigated.
Methods: Patients with first onset AIS between 2005 and 2019 and with complete information regarding SMuRF components and history of atrial fibrillation (AF) in the Singapore Stroke Registry were included. They were classified as (i) no AF and no SMuRF (633, 2.5%); (ii) history of AF but no SMuRF (163, 0.6%); (iii) history of AF with SMuRF (7286, 28.4%); (iv) no AF with SMuRF (17569, 68.5%). The primary endpoint was longitudinal mortality. Patients without the event were censored at the end of the registry period (2019). The Cox proportional hazards regression was used to assess the association between mortality, SMuRF and AF. The Kaplan-Meier method was used to evaluate survival between groups.
Results: AF+ and SMuRF- patients with first onset AIS had significantly higher incidence of mortality (HR 1.32, 95% CI 1.05 to 1.65, $p=0.017$) than AF- and SMuRF- patients, after adjustment for age, gender, ethnicity, anemia, history of transient ischemic attack, ischemic heart disease, and treatment with thrombolytics and antiplatelets. AF- and SMuRF+ patients were associated with the lowest mortality rate (HR 0.62, 95% CI 0.55 to 0.71, $p<0.001$) in the multivariate model.



Kaplan-Meier Survival Curves.

	Unadjusted model		Multivariable-adjusted model^	
Anemia Status	HR (95% CI)	P	HR (95% CI)	P
Overall (9979 events out of 25,651)				
AF- and SMuRF-	-		-	
AF- and SMuRF+	0.62 (95% CI 0.55 to 0.71)	<0.001	0.62 (95% CI 0.55 to 0.71)	<0.001
AF+ and SMuRF-	2.44 (95% CI 1.95 to 3.06)	<0.001	1.32 (95% CI 1.05 to 1.65)	0.017
AF+ and SMuRF+	2.22 (95% CI 1.96 to 2.51)	<0.001	0.96 (95% CI 0.84 to 1.09)	0.5

^ Adjusted for age, gender, ethnicity, age, anemia, history of transient ischemic attack, history of ischemic heart disease, treatment with thrombolytics and antiplatelets

Cox regression analyses of mortality by SMuRF and AF groups.

Conclusion: Patients with AF have an increased risk of mortality after AIS. The impact of SMuRF on mortality is paradoxical in stroke patients without AF.
Disclosure: Nothing to disclose.

EPR-022 | Predictors of stroke mimics in emergency department: An easy-to-use mimics prediction score

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Background and Aims: Early differential diagnosis between stroke and stroke mimics is a challenge in the management of acute patients in the Emergency Department (ED). The primary aim of this study is to identify diagnostic predictors of stroke mimics based on demographic, clinical parameters and vital signs acquired in the ED during the triage phase of patients with suspected stroke. Secondly, we aimed to develop a diagnostic score predictive of stroke mimics.
Methods: In this retrospective, observational study, we enrolled patients admitted to the ED of a comprehensive stroke center for suspected stroke. Univariate comparisons were performed using Mann–Whitney U-test, Kruskal–Wallis and chi-squared test, as appropriate. Logistic regression was used to perform the adjusted analyses. We then computed a predictive score based on each variable's β coefficient.
Results: 2768 patients with a suspected diagnosis of stroke were included in the study of whom 1189 (43%) with stroke mimics. After multivariate logistic regression we observed that age, systolic blood pressure, speech and motor disorders, previous stroke, hemiplegia and congestive heart failure were independent predictors of stroke, while sensory disorders, headache, seizure, disorientation, syncope, dementia and renal disease were predictors of stroke mimics. Based on machine learning prediction model, we developed an easy-to-use score based exclusively on triage data that can accurately discriminate strokes from stroke mimics.

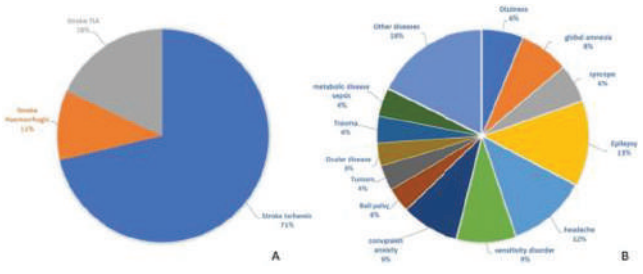

FIGURE 1. Graphics illustrating the prevalence of each stroke subtype (panel A) and of different types of stroke mimics diagnosis (panel B) in our patient population.

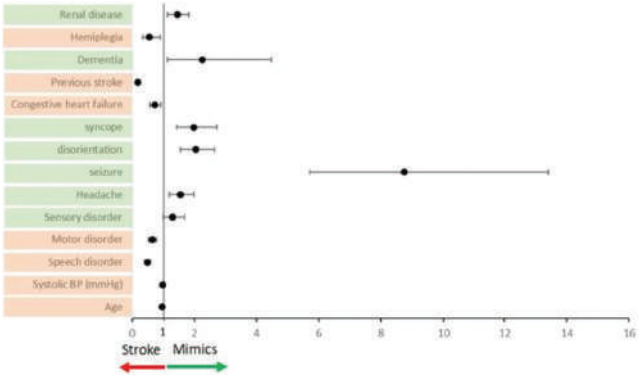

FIGURE 2. The forest plot of the multivariate logistic regression analysis for the discrimination between stroke and stroke mimics.

TABLE 1. The predictive score for the discrimination between stroke and stroke mimics. Negative values are suggestive for stroke mimics, while positive values for stroke. An overall score ≥4 is associated with a 87.8% probability of stroke diagnosis.

RISK FACTOR	CATEGORIES	REFERENCE VALUE (Wa)	βi (Wa − Wxxx)	Points
Age	<30	**24.5** [1° percentile: 20]	0	0
βi = -0.0286	30-39	34.5	-0.286	-1
	40-49	44.5	-0.572	-2
	50-59	54.5	-0.858	-3
	60-69	64.5	-1.144	-4
	70-79	74.5	-1.430	-5
	>79	85.5 [99° percentile: 91]	-1.745	-7
Systolic BP	<120	105 [1° percentile: 90]	0.2625	1
βi = -0.0105	120-139	**130**	0	0
	140-159	150	-0.210	-1
	160-179	170	-0.420	-2
	180-199	190	-0.630	-2
	>200	210 [99° percentile: 220]	-0.840	-3
Speech disorder	No	**0**	0	0
βi = -0.7183	Yes	1	-0.7183	-3
Motor disorder	No	**0**	0	0
βi = -0.4435	Yes	1	-0.4435	-2
Sensory disorder	No	0	0	0
βi = 0.2667	Yes	1	0.2667	1
Headache	No	**0**	0	0
βi = 0.4341	Yes	1	0.4341	2
Seizure	No	**0**	0	0
βi = 2.1686	Yes	1	2.1686	8
disorientation	No	**0**	0	0
βi = 0.7108	Yes	1	0.7108	3
syncope	No	**0**	0	0
βi = 0.6842	Yes	1	0.6842	3
Congestive heart failure	No	**0**	0	0
βi = -0.3198	Yes	1	-0.3198	-1
Previous stroke	No	**0**	0	0
βi = -1.6949	Yes	1	-1.6949	-6
Dementia	No	**0**	0	0
βi = 0.8125	Yes	1	0.8125	3
Hemiplegia	No	**0**	0	0
βi = -0.5999	Yes	1	-0.5999	-2
Renal disease	No	**0**	0	0
βi = 0.3706	Yes	1	0.3706	1

Conclusion: The identification of independent predictors of stroke mimics and the new mimics score could be useful tools for emergency physicians to stratify patients with suspected stroke and direct them towards a more appropriate diagnostic and therapeutic pathway.

Disclosure: Nothing to disclose.

EPR-023 | Acute imbalance syndrome (AIS) versus acute vestibular syndrome (AVS): differentiation matters

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Background and Aims: Stroke is a major differential diagnosis in patients with acute vertigo/dizziness/imbalance. Diagnostic tests like HINTS are optimized for presentations with spontaneous nystagmus (SPN), called acute vestibular syndrome (AVS). However, in recent studies a relevant proportion of patients with stroke-related vertigo/dizziness had no SPN, but postural imbalance. For this phenotype, the term acute imbalance syndrome (AIS) was coined. We outlined the pathoanatomical differences of AIS/AVS and its clinical implications.

Methods: Seventy-five patients (66.7 ±12.6 y) with acute vertigo/dizziness/imbalance due to MRI-proven stroke were included and classified as AIS/AVS documenting vestibular/ocular motor/postural signs. Stroke lesion distribution was depicted in MNI space and supplemented by structural disconnectome mapping. Multivariate lesion symptom mapping based on support-vector regression and disconnectome mapping were applied.

Results: AIS was diagnosed in 58%, AVS in 39%, central positional vertigo in 3% of patients. In AIS, lesions were located in the anterior cerebellar lobe/deep cerebellar nuclei (SCA/PICA territory) connecting to the bilateral pontomesencephalic tegmentum. AVS stroke lesions were mostly located in the posterior cerebellar/

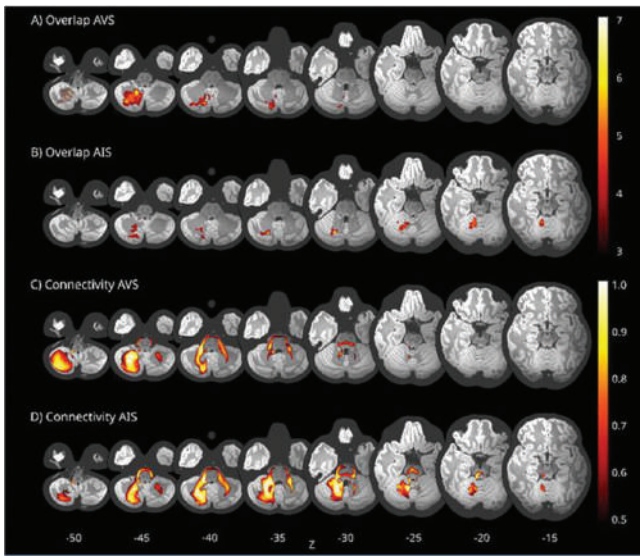

FIGURE 1. Lesion distribution and structural connectivity in the AVS and AIS subgroups. Warmer colors represent more lesion overlap or a higher degree of probability of connections.

flocculonodular lobe (PICA/AICA territory) and connected to the ipsilesional vestibular nucleus (VN)/bilateral medial longitudinal fascicle (MLF). SPN intensity correlated with voxels in the cerebellar lobules VI-IX connecting to VN/MLF.

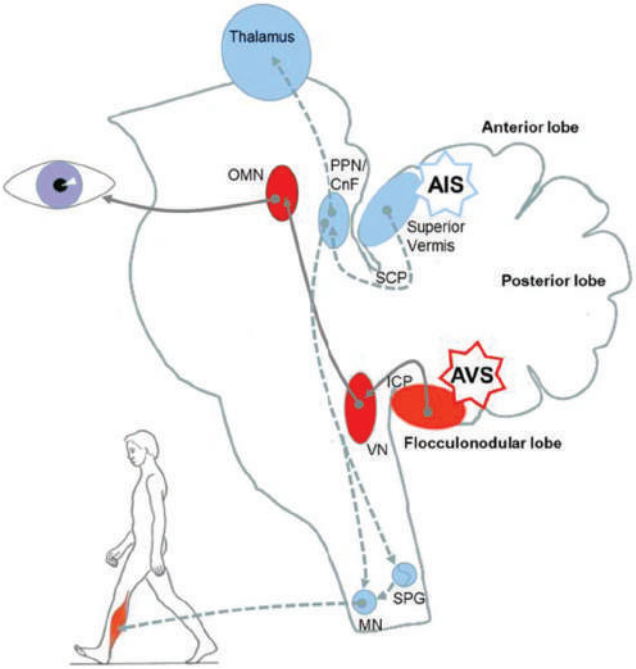

FIGURE 2. Pathophysiology of AIS and AVS.

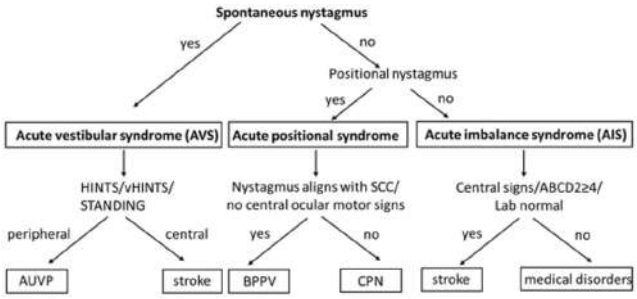

FIGURE 3. Clinical pathways for differentiation of AVS, AIS and acute positional syndrome.

Conclusion: AIS accounts for more than half of patients with stroke-related vertigo/dizziness/imbalance. AIS lesions were located in the anterior cerebellar lobe disturbing cerebellar-pontomesencephalic networks for posture/gait control. AVS lesions affected the posterior cerebellar/flocculonodular lobe and associated vestibulo-ocular reflex networks. Recognition of both clinical phenotypes is essential to identify all strokes among patients with vertigo/dizziness in the ER.

Disclosure: Nothing to disclose.

EPR-024 | Abstract withdrawn

EPR-025 | Cerebral atrophy patterns identify patients at risk of delirium following thrombectomy of large vessel occlusion stroke

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Background and Aims: Post-stroke-delirium has been linked to worse outcome in patients with acute cerebrovascular disease; identification of individuals at risk may prevent delirium and thereby improve outcome. We investigate the role of cerebral atrophy and white matter lesions (WML) as predictive factors for the development of post-stroke-delirium in patients with large vessel occlusion (LVO) ischemic stroke treated by mechanical thrombectomy (MT).

Methods: 747 patients (53.4% female) prospectively enrolled in the Gutenberg-Stroke-Study (May 2018–November 2022) were analyzed with regard to diagnosis of delirium during hospital stay. Native computed tomography (CT)-imaging based parameters of cerebral atrophy (global cortical atrophy [GCA] score, posterior atrophy score [Koedam], medial temporal lobe atrophy [MTA] score) and WML (Fazekas score) were compared on univariate level. Multiple logistic regression analysis (adjusted for age, sex and variables with differences on univariate level) was conducted to identify an independent predictive value of cerebral atrophy and WML for development of delirium.

Results: We report 8.2% of patients (61/747) developing delirium following MT of LVO. Pathological age-adjusted cerebral atrophy scores were more frequent in patients with delirium (GCA: 54.1% versus 38.5%, $p=0.015$; Koedam:31.1% versus 16.1%, $p=0.004$; MTA:24.6% versus 11.7%, $p=0.004$), whereas premorbid clinical diagnosis of dementia (6.6% versus 4.1%, $p=0.360$) and burden of WML were similar. In multiple logistic regression analysis, pathological MTA score resulted as an independent predictor of delirium (aOR [95%CI]: 2.126 [1.065–4.244], $p=0.033$).

Conclusion: Besides conventional risk factors, pathological MTA scores may be an easy-to-apply criterium to identify individuals at risk of developing delirium following MT of LVO, allowing for targeted preventive measures.

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EPR-026 | Non-contrast CT markers as a predictor for underlying cerebral amyloid angiopathy

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Background and Aims: Non-contrast CT (NCCT) markers of intracerebral haemorrhage (ICH) are associated with haematoma expansion and poor clinical outcome. However, their prevalence in different ICH aetiologies, such as sporadic cerebral amyloid angiopathy (sCAA), Dutch-type hereditary CAA (D-CAA), and deep perforator arteriopathy (DPA), remains unclear. We assessed the prevalence of NCCT markers in ICH-patients and established if they can predict CAA as underlying aetiology.
Methods: We assessed CT scans of initial and recurrent ICHs of consecutive patients with sCAA, D-CAA, and DPA, for the presence of 9 NCCT markers: black hole sign, blend sign, island sign, satellite sign, swirl sign, irregular shape, fluid level, hypodensity, and heterogeneous density. We compared their prevalence between the three aetiologies and used binomial regression models to identify NCCT markers predictive for underlying CAA (sCAA and D-CAA) compared to DPA.
Results: We assessed 316 NCCT scans from 231 ICH-patients (mean age 69, 52% female): 64 with sCAA, 67 with D-CAA, and 100 with DPA. In 40% of NCCTs no markers were present. The blend, island, and satellite sign were seen more often in both sCAA and D-CAA patients, while hypodensity was found more often in patients with DPA (all $p < 0.01$). In regression analyses, the island (OR = 7.0, 95%CI:1.4–34.4), blend (OR = 4.8, 95%CI:1.4–16.7), and satellite signs (OR = 4.0, 95%CI:1.8–8.9) were associated with underlying CAA, while CAA was less often present in case of hypodensity (OR = 0.4, 95%CI:0.2–0.7).
Conclusion: The blend, island, and satellite sign are associated with underlying CAA, while hypodensity is associated with DPA. These markers may help identify the underlying cause of ICH.
Disclosure: Nothing to disclose.

Spinal cord and root disorders

EPR-027 | Longitudinally extensive myelopathy: When do you biopsy the spinal cord?

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Background and Aims: A neuroinflammatory demyelinating disorder is the likely diagnosis in adolescents and young adults presenting with a subacutely progressive paraplegia with longitudinally extensive intrinsic signal change within the spinal cord. However, failure to respond to immunotherapy should alert the clinician to consider alternative diagnosis.
Methods: Two young Asian patients (F = 17 y; M = 21 y) were diagnosed with treatment-refractory double seronegative NMOSD based on their clinical evaluation and MRI changes. Symptom onset in the female patient followed COVID-19 vaccination; the male patient had a preceding febrile illness. P100 latencies in VEP were prolonged in the female patient. MRI signal abnormalities and lesion enhancement were in keeping with the changes reported in longitudinally extensive transverse myelitis.
Results: There was minimal response to high dose corticosteroids, anti-CD20 monoclonal antibody (rituximab) and human IVIg in the female patient. No treatment response was seen after high dose steroids and antiviral (aciclovir) in the male patient. Due to the relentless progression of myelopathy, biopsy of enhancing spinal cord lesion was undertaken in both patients that confirmed the diagnosis of high-grade spinal cord astrocytoma. Despite radiotherapy, both patients succumbed to death within 6 months of the confirmed tissue diagnosis.
Conclusion: Failure of clinical response to steroids, rituximab, IVig and/or plasma exchange should alert clinicians to seek a tissue diagnosis of seronegative patients with longitudinally extensive signal abnormalities within spinal cord. The possibility of high-grade astrocytoma must be considered in treatment-refractory monophasic double-seronegative NMOSD presenting with a progressive myelopathy.
Disclosure: There is no competing interest.

EPR-028 | Autonomic dysreflexia and dysfunction—A case series and literature review

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Background and Aims: One potential complication to spinal cord injury (SCI), autonomic dysfunction can be triggered by a multitude of stimuli. In cases where the injury is sustained above Th6, potentially life-threatening attacks of spiking blood pressure may occur termed autonomic dysreflexia (AD). Here, we present a series of four individuals experiencing AD from our specialized rehabilitation center and expand upon this through a systematic review of the literature on autonomic dysfunction
Methods: A prospective enrollment of four persons with SCI and concomitant AD was performed. Case histories and charts are reported. A review according to PRISMA guidelines was performed. Keywords were autonomic dysfunction or dysautonomia and SCI across PubMed, EMBASE and Cochrane Library of Clinical Trials (CENTRAL).
Results: The case series presented here displays the large degree of heterogeneity in the incipient stimuli and the time to development

of AD. A particularly important point, AD adversely affected rehabilitation and quality of life of all four patients. Literature search returned 247 studies on different aspects of autonomic dysfunction secondary to SCI. Autonomic dysfunction occurs at very high frequency and may in some cases life-threatening complications. This is especially prevalent in cases cardiovascular dysregulation. Gastrointestinal and urological complications were also prevalent with a clinically significant impact on quality of life.

Conclusion: Autonomic dysreflexia and dysfunction present a complex aspect of SCI whose impact and treatment is incompletely understood. Restorative treatments are in general not available. Causes, natural history and progression remain issues in need of clarification in order to improve potential restorative therapies.

Disclosure: The authors declare there is nothing to disclose.

EPR-029 | Serum Glial fibrillary acidic protein is associated with motor function in adult Spinal muscular atrophy

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Background and Aims: In adult spinal muscular atrophy (SMA), there is an unmet need for biomarkers to monitor the disease progression and treatment response. 5q-SMA mouse models have provided evidence of astrocyte activation and increased levels of Glial fibrillary acidic protein (GFAP). Aims of this study were to assess serum GFAP (sGFAP) levels in patients with 5q-SMA and age- and sex matched healthy controls (HCs), as well as associations with clinical disability in SMA, namely Motor Function Measure (MFM) and 6-Minute-walk-test (6-MWT).

Methods: We prospectively examined twenty patients with 5q-SMA, types 2 and 3 (mean age/SD 41.3/11.6y, 9 women) and twenty age- and sex-matched HCs (mean age/SD 41.7/11.4y, 9 women). sGFAP concentrations were measured using the ultrasensitive single molecule array (Simoa) technology. Associations between sGFAP concentrations and MFM and 6-MWT were analyzed using Spearman Rank correlations and linear regression analyses.

Results: In patients with SMA, sGFAP concentrations were significantly elevated by 52% ($p=0.021$) compared to age- and sex-matched HCs. Significant associations were found between sGFAP concentrations and MFM (rho: −0.61, $p=0.006$) and 6-MWT (rho: −0.69, $p=0.019$). In linear regression analyses, sGFAP concentrations accounted for 43% of MFM variance and 35% of 6-MWT variance, respectively.

Conclusion: sGFAP concentration, a marker of astrocyte dysfunction, is elevated in adult patients with SMA and inversely correlates with metrics of motor function and endurance in ambulatory patients. Further longitudinal studies are necessary to evaluate the potential of this novel biomarker as a marker for disease progression and therapeutic response in SMA.

Disclosure: The study was funded by Biogen. The funder did not play any role in the concept and design of the study and acquisition, analysis, and interpretation of the data.

EPR-030 | A spatiotemporal atlas of acute spinal cord injury

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Background and Aims: Spinal cord injury (SCI) triggers a cascade of intricate molecular and cellular changes that determine its outcome.

Methods: Spatial transcriptomics (ST) is a recent emerging technology that enables high-throughput measurement of gene expression while retaining the anatomic information. In this study, we have developed a bioinformatic toolset to resolve the spatiotemporal organization of the injured spinal cord and quantitatively assess in situ cell-cell communication following SCI.

Results: By analyzing existing single-cell RNA-sequencing datasets alongside our spatial data, we delineate a unique subpopulation of astrocytes, termed Astro-GMii, that migrate from white matter to grey matter and become reactive and neuro-supportive during the acute phase of SCI. Further, we identify Igfbp2 as a molecular marker and driver of Astro-GMii, as its overexpression promotes astrocyte migration, proliferation and reactivity. Moreover, we demonstrate that the conditioned medium derived from Igfbp2-overexpressing astrocytes, as well as the secreted IGFBP2 protein alone, foster neurite outgrowth. Finally, by administering IGFBP2 in vivo, we observe a significant reduction in neuronal loss and remarkable improvements in functional recovery in mice with SCI.

Conclusion: Together, this study not only provides a comprehensive molecular atlas of SCI but also exemplifies how the rich resource can be applied to endow cells and genes, such as Astro-GMii and Igfbp2, with new functional insight and therapeutic potential.

Disclosure: Nothing to disclose.

EPR-031 | Spinal dural arteriovenous fistulas – A single center experience

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Background and Aims: Spinal dural arteriovenous fistulas (SDAVF) are a rare subtype of vascular malformation, which leads to venous congestion and subsequent progressive myelopathy, leading to considerable morbidity in affected patients. We aim to describe clinical and imaging features of patients with SDAVF.

Methods: We conducted an observational retrospective study including all patients diagnosed with SDAVF at our hospital over the last 15 years, confirmed by digital subtraction angiography (DSA), using keyword search through spinal cord DSA reports.

Results: We included 13 patients in our study, whose detailed characteristics are presented in Table 1. The median age at diagnosis was 59 years and 7 patients were female. The median time from symptom onset to SDAVF diagnosis was 9 months, and most patients presented with more than one symptom at the time of diagnosis. Five patients had a misdiagnosis before confirmation of SDAVF, and 4 underwent targeted treatment for those suspected conditions. Most patients underwent surgical treatment (62%) and one patient was treated with a combined endovascular and surgical approach. There was no statistically significant difference between modified Aminoff and Logue's Scale (mALS) scores assessed before treatment and at 24-months follow-up after treatment (Table 2).

TABLE 1. Characteristics of patients with SDAVFs.

Characteristic	
Age (years)	55 (36-74)
Men, n (%)	6 (46)
Symptom onset, n (%)	
Progressive	12 (92)
Abrupt	1 (8)
Primary symptom, n (%)	
Lower extremity weakness	3 (23)
Sensory abnormality	3 (23)
Complex symptoms	7 (54)
Misdiagnosis, n (%)	5 (38)
Inflammatory	3 (23)
Neoplastic	1 (8)
Infectious	1 (8)
Time from symptom onset to SDAVF diagnosis (months), median (Q25%-Q75%)	9 (1-17)
Imaging findings on spinal cord MRI	
SDAVF location, n (%)	
Above T7	2 (15)
T7-T12	6 (46)
Below T12	5 (39)
Presence of flow-voids, n(%)	12 (92)
Length of spinal cord edema, median (Q25%-Q75%)	6 (0-12)
Time from symptom onset to SDAVF treatment (months), median (Q25%-Q75%)	10 (2-18)
Treatment modality, n (%)	
Endovascular embolism	1 (8)
Neurosurgery	8 (62)
Combined treatment	1 (8)
None	3 (23)
Recurrence, n (%)	2 (15)
Reintervention, n(%)	2 (15)

TABLE 2. Comparison between modified Aminoff and Logue's Scale (mALS) before and after treatment

mALS, median (Q25%-Q75%)	Before treatment	24-months follow-up after treatment	Delta-mALS, median (Q25%-Q75%)
Gait	3 (2-4)	4 (2-4)	0 (-0,5 – 1,5)
Urination	1 (0-2)	2 (0-2)	0 (-0,5 – 2)
Defecation	0 (0-1)	0 (0-2)	0 (-0,5 – 2)

Conclusion: Despite adequate treatment, our patients did not exhibit substantial improvement, which could possibly be related to delayed diagnosis and intervention. SDAVF remains a source of considerable morbidity in affected individuals, exerting a significant impact on their quality of life even following proper diagnosis and treatment.

Disclosure: Nothing to disclose.

EPR-032 | Gender-based analysis of perioperative and early postoperative complications in tubular microdiscectomy

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Background and Aims: After spine surgery, many factors, including variations in anthropomorphic parameters and co-morbidities, may contribute to the difference in complication rates between both genders. Previous literature suggests that gender may affect the incidence of specific spinal disorders, such as lumbar degenerative disc disease, lumbar disc radiculopathy, and cauda equina syndrome.

Methods: This retrospective multicenter study, conducted in two specialized spine centers in Baghdad, Iraq, involved 302 patients with lumbar disc herniation (174 males and 128 females) from January 2016 to January 2022. Data collection included comprehensive assessments of clinical and surgical outcomes, utilizing the Core Outcome Measures Index (COMI) score at two, six, and twelve weeks.

Results: 134 males (77%) and 104 females (81%) were below 40 years old, while 40 males (23% of males) and 24 females (18.8% of females) were 40 or older. There was a significant difference in mean operative times ($p < 0.001$). The most common specific complication was spondylodiscitis with 6 males (3.4% of males) and 3 females (2.3% of females), while the most common general complication was post-op back spasm with 6 males (3.4% of males) and 4 females (3.1% of females).

Conclusion: Gender has a minimal impact on most perioperative and early postoperative complications. Longer operative times in females raise questions about gender-specific differences across spine surgeries and specialties, necessitating further research.

Disclosure: Nothing to disclose.

EPR-033 | Local fibrinolysis in a patient with spinal cord ischaemia secondary to abdominal aortic surgery

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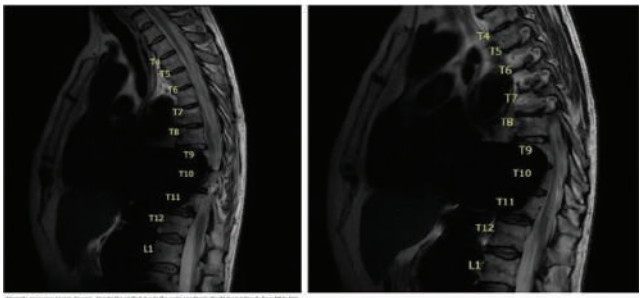
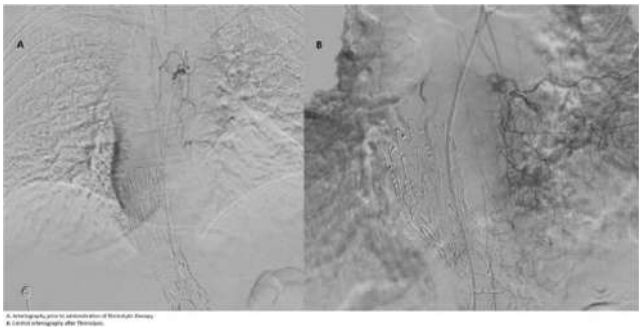
Background and Aims: Acute spinal cord ischemia (AMI) is an uncommon yet severe condition that results in substantial functional impairment for the patients. Diagnosis can be challenging at times, and there is a lack of robust evidence supporting the local fibrinolytic therapy.

Methods: We present the clinical case of a 63-year-old female patient with a history of smoking, hypertension, hypercholesterolemia and recent surgery to exclude abdominal aortic aneurysm by endoprosthesis, who presented with a progressive episode of less than 1 week duration of disabling low back pain and lower limb allodynia with sudden worsening in the Emergency Department. Examination revealed an almost complete spinal cord syndrome with moderate-severe paraparesis, hyperreflexia, inexhaustible clonus, tactoalgesic hypoesthesia at D8-D10 and urinary retention. Magnetic resonance imaging showed a signal abnormality in the posterior half of the spinal cord of recent onset extending from D8 to D11, consistent with spinal cord ischaemia (Image 1). Angiography showed an anterior spinal artery occlusion at the level of D6 (Image 2A).



Magnetic resonance images showing, despite the artefact due to aortic prosthesis, the T2 hyperintensity from D8 to D11.

Results: 7 mg of intra-arterial tissue plasminogen activator were administered into the left D6 radicular branch of the anterior spinal artery. Angiographic control was performed 10 minutes later and showed increased flow in the vessel (Image 2B). The patient experienced significant neurological improvement, which was observed immediately and maintained during 6 months of clinical follow-up at a regional rehabilitation hospital and neurology outpatient clinics (Table 1).



A. Arteriography prior to administration of fibrinolytic therapy. B. Control arteriography after fibrinolysis.

	AT THE BEGGINING OF HOSPITALISATION		AT THE END OF HOSPITALISATION	
	RIGHT LEG	LEFT LEG	RIGHT LEG	LEFT LEG
Hip flexion*	3-	3-	4-	4-
Hip extension*	4-	4	4-	4+
Hip abduction*	5	4+	4+	4+
Hip adduction*	2	2	5	5
Knee flexion*	2	4-	4	4+
Knee extension*	3-	4-	4-	4-
Plantar flexion*	4-	5	4	4
Dorsal flexion*	1	5	3	4-
Foot inversión*	3-	5	4-	4-
Foot eversión*	1	5	1	4-
Cutaneous-plantar reflex (Babinski sign)	Extensor (positive)	Extensor (positive)	Extensor (positive)	Flexor (negative)
Clonus (Achilles tendon reflex)	2 jerks	3 jerks	10 jerks	3 jerks
Sensory spinal cord level	D11	D8	D12	D10
Vibrational sensitivity (Rydel-Seiffer)	Hallux: 0/8 Tibial tuberosity: 2/8	Hallux: 2/8 Tibial tuberosity : 2/8	Hallux: 8/8 Tibial tuberosity: 8/8	Hallux: 8/8 Tibial tuberosity: 8/8

** Muscle balance based on MRC strenath scale*

Clinical examination before and after the fibrinolytic therapy.

Conclusion: Local fibrinolytic therapy may emerge as a potentially useful intervention, with standardized use offering benefits for a subset of patients.

Disclosure: Nothing to disclose.

EPR-034 | Clinico-radiologic characteristics of spontaneous spinal cord infarction in Korean patients: A single-center study

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Background and Aims: Spinal cord infarction (SCI) is a rare condition, accounting for less than 1% of all strokes, which has resulted in limited research on the subject. Therefore, our aim was to determine the clinical features associated with spontaneous SCI in Korean patients.

Methods: In this retrospective analysis, we reviewed the medical records of individuals diagnosed with spontaneous SCI at Keimyung University Dongsan Hospital between 2017 and 2023.

Results: We identified 23 patients (13 male, 10 female) with a mean age of 65.6±11.0 years. The median time from onset to hospital arrival was 20.4 (6.4–60.7) hours. Notable presentations included complete cord syndrome (34.8%) and hemicord syndrome (30.4%). The etiology of SCI remained undetermined in a significant proportion of patients (60.9%), although laboratory test results suggested a high risk of atherosclerosis, hypercoagulability, or inflammation. The initial MRI was negative in 52.2% of cases, but subsequent scans revealed lesions in two-thirds of patients, predominantly in the cervical cord (20.0%), thoracic cord (45.0%), and conus (20.0%). On admission, the mean modified Rankin Scale (mRS) was 3.9 ±1.4, and 52.2% of patients were confined to a wheelchair. Common symptoms included dysuria (69.6%) and adjacent pain (47.8%). Treatment included antiplatelet agents and statins. At discharge, the mean mRS was 3.6 ±1.6 and 47.8% of patients remained wheelchair bound. At a mean of 5 (2.0–12.0) months after discharge, the mRS improved to 2.6 ±1.4, with only 13.6% requiring a wheelchair.

Conclusion: This study provides insight into the clinical and radiological characteristics of spontaneous SCI in the Korean population.

Disclosure: Nothing to disclose.

Neuroimmunology 1

EPR-035 | Long-term potentiation plasticity is impaired in AQP4-NMOSD patients

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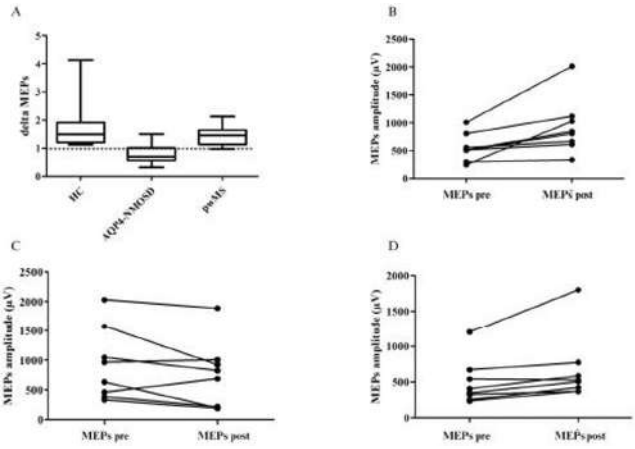
Background and Aims: Aquaporin-4-positive neuromyelitis optica spectrum disorder (AQP4-NMOSD) is usually characterized by a poor recovery from the attacks and the appearance of few asymptomatic interictal MRI lesions. The impairment of cortical plasticity might be the mechanism underlying these observations. This study aimed to explore neuroplasticity in AQP4-NMOSD patients by examining intermittent theta burst stimulation (iTBS) long-term potentiation (LTP), in AQP4-NMOSD and multiple sclerosis (MS) patients.

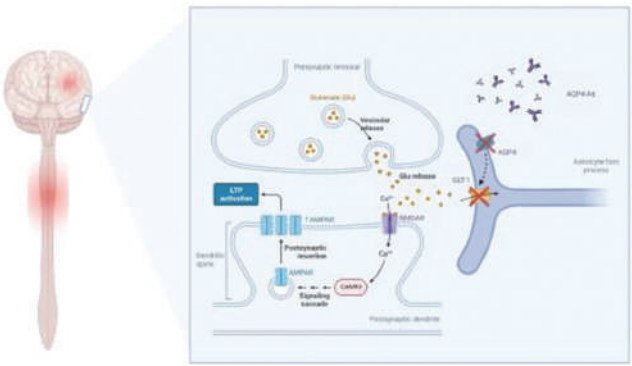
Methods: We enrolled 8 right-handed AQP4-NMOSD, 8 relapsing-remitting MS (RRMS) and 8 healthy control (HC). For each group we evaluated motor evoked potentials (MEPs) before an intermittent theta-burst (iTBS) stimulation. Five minutes after iTBS we reassess MEPs.

Results: A significant difference in post iTBS MEPs modification (delta MEPs) was observed among the three groups (*p*: 0.006). Post-hoc comparison revealed that patients with AQP4-NMOSD significantly differed from both HC and patients with MS (*p*: 0.012 and 0.022 respectively). No baseline differences in MEPs amplitude were identified.



Panel A: Distribution of delta MEPs values of the three populations. There is statistically significance differences between AQP4-NMOSD patients and HC and between AQP4-NMOSD patients ad pwMS. Changes in MEPSs amplitude after iTBS in HC (Panel B), AQP4-NM.

Conclusion: Our pilot study demonstrates for the first time in vivo, a LTP impairment in patients with AQP4-NMOSD. This deficit in plasticity mechanisms could elucidate crucial clinical features of AQP4-NMOSD and aligns with animal model studies proposing AQP4 as a pivotal channel in glutamatergic transmission Furthermore, the concept of an impaired LTP in AQP4-NMOSD patients could pave the way to future rehabilitation approaches.



Schematic representation of glutamatergic excitotoxicity induced by AQP4 antibodies. The AQP4 trafficking dysregulation caused by the AQP4-Ab presents in NMOSD patients caused an impaired function in the GLT-1 leading to an accumulation of glutamate in th.

Disclosure: Nothing to disclose.

EPR-036 | Clinical presentation and disease course in a series of eight patients with neurosarcoidosis

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Background and aims: Sarcoidosis is an immune-mediated multisystem disorder characterized by granulomatous inflammation of affected organs. Neurosarcoidosis is a form of sarcoidosis affecting the central or the peripheral nervous system and is usually associated with other peripheral organ involvement, but it may occur in isolation.
Methods: Retrospective analysis of patients who were diagnosed with neurosarcoidosis with or without other organ involvement at the Cyprus Institute of Neurology and Genetics.
Results: Eight patients were included, of which 3 were female. The mean age at onset disease was 56.5 ± 14.0 (range: 30–73) years old. The mean duration of follow-up was 3 + 1.9 years. Two out of 8 cases presented with isolated neurosarcoidosis. Cranial nerve involvement was present in 5 out of 8 cases, of which the facial nerve was the most commonly affected; 4 patients presented Bell's palsy. One patient presented with normal pressure hydrocephalus, a rare presentation of neurosarcoidosis. Five out of six patients had increased cerebrospinal fluid (CSF) angiotensin converting enzyme (ACE) level with a mean value of 2.31 + 0.9 umol/min/L (normal range: <1.2 umol/min/L). Two of five patients presented elevated CD4+/CD8+ levels, while oligoclonal band pattern showed a great variability. In regards to treatment, all patients received oral corticosteroids and 4 patients also received azathioprine, with good overall response.
Conclusion: Neurosarcoidosis is a relatively uncommon and challenging diagnosis, especially in the absence of systemic manifestations. This case series highlights both common and rare complications of neurosarcoidosis with the goal to facilitate better recognition and timely management of the disease.
Disclosure: Nothing to disclose.

EPR-037 | Role of pregnancy in MOG antibody-associated disease activity and pregnancy outcomes

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Background and Aims: The relation between MOGAD and pregnancy is not fully understood, despite recent studies showing a higher attack rate in the puerperium. We aim to determine the pregnancy role in MOGAD disease activity, and characterize MOGAD effect on pregnancy outcomes.
Methods: This observational retrospective study included all women with any pregnancy and MOGAD diagnosis registered at NMO highly specialized service, Oxford, until December 2023. Baseline variables and pregnancy details were collected. Pregnancy outcomes and pregnancy-related disease attacks were analysed. We defined as pregnancy-related attacks those that occurred in the year previous to estimated date of conception, during pregnancy and in the first year postpartum. A sub analysis assessed if disease activity was influenced by pregnancy through logistic binary regression. The annualized relapse rate (ARR) and its association with pregnancy was also calculated.
Results: We identified ninety-one women with a total of 205 pregnancies. Preeclampsia (2.2%) and miscarriage (11.2%) rate were within expected range. There was an increase in ARR in the nine months postpartum, higher in the first three months, reaching 2.125 in patients with pregnancy-related presenting attack, and 0.973 in those with NMOSD previously diagnosed. We analysed other factors related to a higher relapse risk and did not find any significant association.
Conclusion: Our results showed clear high MOGAD activity in the postpartum period, particularly at the disease presentation, suggesting that pregnancy & puerperium may be a "disease trigger". There was no clear association between MOGAD and pregnancy outcomes.
Disclosure: Nothing to disclose.

EPR-038 | Development Of Multiplexed Electroanalytical Biosensing Platforms For The Clinical Diagnosis Of Alzheimer's Disease

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Background and Aims: Novel biomarkers for the early diagnosis of Alzheimer's disease (AD) are needed. Among the new approaches

developed in the last years, circulating autoantibodies (AAbs) and their target proteins (autoantigens) are promising candidate biomarkers to aid in AD early diagnosis. We aimed here to validate the potential of electrochemical biosensors for AD-diagnosis based on the amperometric measurement of AD-specific plasma autoantibodies.

Methods: An immunoplatform based on the use of Halo-MBs (magnetic beads) modified with previously validated AD autoantigens was developed. Autoantigens were cloned and expressed as HaloTag fusion peptides/proteins in mammalian cells. Their oriented covalent immobilization to MBs allowed for the efficient and selective capture of AAbs from plasma. Finally, signal was developed by amperometric transduction on disposable electrodes using the H_2O_2/HQ (hydroquinone) system.

Results: AAbs against two aberrant AD-associated peptides, four peptide autoantigens identified by Phage Microarrays, and three full-length AD autoantigens identified by multiomics analyses were differentially detected in AD patients from controls. Thus, we described here the first multiplexed bioplatform for AD diagnosis by targeting AD-specific plasma AAbs. The analytical operational characteristics of this biosensor demonstrated its significant clinical diagnostic potential in a single test and in less than 90 minutes.

Conclusion: These results acknowledge a reliably and minimally invasive method for AD diagnosis based on amperometric biosensing platforms detecting plasma autoantibodies against AD-specific autoantigens with a high sensitivity and specificity, and a high potential as point-of-care (POC) devices for the clinical diagnosis of AD by liquid biopsy and in less than 90 minutes.

Disclosure: Nothing to disclosure.

EPR-039 | Brain biopsies in unexplained neurological disorder have a high diagnostic and therapeutic yield, while being safe

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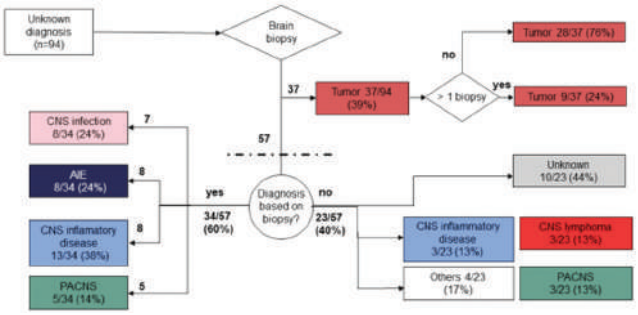
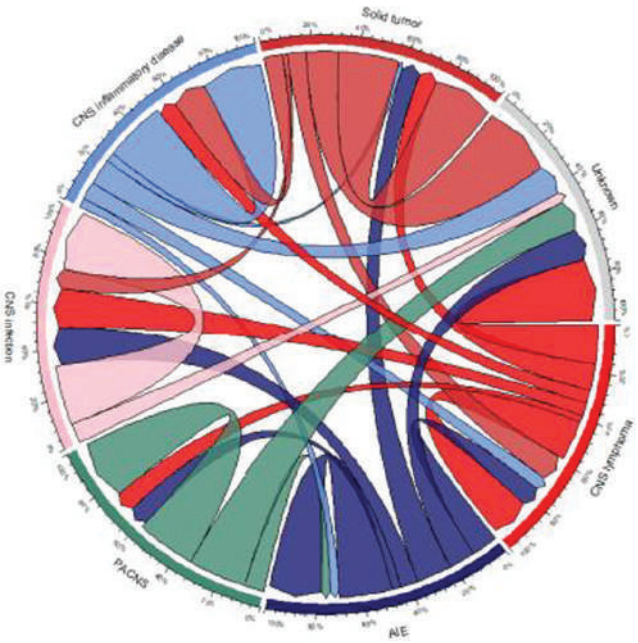
Background and Aims: Major progress has been made in the diagnosis of central nervous system (CNS) disorders, as various minimally invasive diagnostic techniques were introduced. Consequently, the role of brain biopsies in CNS disorders is unknown. We aimed to study the diagnostic yield, therapeutic implications and safety of brain biopsies in CNS disorders with unknown etiology.

Methods: In this retrospective cohort study, all adult patients who were referred for a diagnostic work-up to our academic center with neuroinflammatory, neuro-oncological and virological expertise and underwent brain biopsy between January 2010 and December 2023 were included. Typical cases of CNS neoplasms and infections were not analyzed. Brain biopsies were evaluated with respect to diagnostic and therapeutic impact and complication rate.

Results: A biopsy was performed in 636 patients, of whom 542 had a typical phenotype with matching pathological diagnosis. Ninety-four patients with CNS disorder of unknown cause, with 105 biopsies, were analyzed (44% female, median age 58 years, range 19-79). Final diagnoses included CNS neoplasms (37/94, 39%), CNS inflammatory disorders (13/94, 14%), CNS infections (8/94, 9%), autoimmune encephalitis (8/94, 9%), and primary angiitis of the CNS (5/94, 5%). The first biopsy had a diagnostic impact in 65%, increasing up to 75% after repeated biopsies. In 75% of the cases, brain biopsy changed the treatment strategy. Biopsy was complicated by symptomatic intracranial haemorrhage in 4/105 biopsies (4%).



Flowchart showing diagnostic categories based on brain biopsy.



Chord diagram showing shift of diagnoses: before versus after brain biopsy.

Conclusion: In a selected population of patients with unexplained CNS disorders, the diagnostic yield and therapeutic impact of brain biopsies are high, while being relatively safe.

Disclosure: P.A. Sillevis Smitt holds a patent for the detection of anti-DNER, he received research support from Euroimmun. M.J. Titulaer has filed a patent, on behalf of the Erasmus MC, for methods for typing neurologic disorders and cancer, and devices for use therein; has received research funds for serving on a scientific advisory board of Horizon Therapeutics, for consultation at Guidepoint Global LLC, for consultation at UCB, for teaching colleagues at Novartis; and has received an unrestricted research grant from Euroimmun AG and from CSL Behring.

EPR-040 | Optic neuropathies related to immune checkpoint inhibitors: a case series and systematic review of the literature

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Background and Aims: Optic neuritis related to immune checkpoint inhibitors (ICIs) have been rarely reported and poorly described. However, their knowledge is essential to promptly manage them since a persistent visual decline is reported in approximately half of the patients.

Methods: We report a retrospective series of patients with an ICI-related optic neuropathy referred to our departments between 2018 and 2022, and a systematic search of the literature with the aim to describe their features, outcome and tolerance of ICI reintroduction. Based on the evidence or not of optic nerve impairment at the MRI or visual evoked potentials, we distinguished cases of papillitis or optic neuritis.

Results: We identified three patients in our institution and 35 cases from the literature. The symptoms occurred after a median time of 10 weeks and three doses of ICIs. The most common pattern consisted of painless reduction of visual acuity and bilateral papilledema. Papillitis were commonly associated with uveitis (71%) whereas optic neuritis with other neurotoxicities (29%). In 66% of published cases, a visual deficit persisted despite the use of corticosteroids. Unlike other reports, all patients of our series experienced a complete recovery. Given such a quick improvement, we continued the ICIs in two patients, with good tolerance.

Conclusion: We found two main clinical patterns: (i) papillitis, usually associated with other intraocular inflammation, and (ii) optic neuritis, more often associated with other neurological toxicities and which lead to a worse outcome. Based on our experience, ICI treatment discontinuation is not mandatory in case of non-severe optical neuropathies.

Disclosure: No disclosure of interests to declare.

EPR-041 | MOG antibody titres in relapsing disease: Implications to clinical practice

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Background and Aims: Myelin oligodendrocyte glycoprotein IgG (MOG-IgG) of titres 200 or more are considered positive/diagnostic for MOG associated disease (MOGAD). Early reports suggest patients who become seronegative are less likely to relapse but some patients showed otherwise. To compare relapsing paediatric MOGAD patients who remain persistently seropositive versus those who are reported as seronegative on follow-up.

Methods: retrospective review of clinical and paraclinical data of patients with relapsing MOGAD who had ongoing long term follow-up, and at least two serum samples tested for MOG-IgG by live cell-based assay

Results: Among 41 patients with MOGAD, 15 (36.5%) had a relapsing course. Mean follow-up duration 78.5months with 11 being persistently seropositive over mean of 5.6 (range 0.92–14) years 7 females; mean 8.3 (range 4–11) years; Both seropersistent and seroconverting groups did not differ on presentation and subsequent demyelinating phenotypes, both clinically and radiologically. Seroconverting group had mean 5.7 $\pm$2.25 relapses with annualized relapse rate (ARR) of 0.63 $\pm$0.382. Seropersistent group had a mean of 2.9 $\pm$0.59 relapses with ARR of 0.85 $\pm$0.484. Mean time to seropersistent relapse was 43.6 months ($N=25$, range 2–120) versus seroconverting relapses 85.7 months ($N=7$; range 60–121). 57% of seronegative relapses had titres of 1:100. Disease-modifying therapies were commenced in 11/15 patients after the second clinical event. Overall, despite the seronegative status, follow-up extended disability status scale was worse.

Conclusion: Paediatric MOGAD patients can relapse after a seronegative test result, most of whom still have detectable serum MOG-IgG but below the diagnostic cut-off. It may be useful for titres to be included in MOG-Ab results to support clinical interpretation, particularly in relapsing disease.

Disclosure: Nothing to disclose.

EPR-042 | Activity and Manufacturing of KYV-101 Anti-CD19 CAR T Cells Derived from Patients With Neurological Autoimmune Diseases

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Background and Aims: B-cell targeting therapies demonstrate potential in neurological autoimmune diseases, but unmet needs remain, including treatment-free remission. KYV-101, a first-in-class, fully human autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, demonstrated promising clinical results in a myasthenia gravis (MG) patient (Haghikia et al. Lancet Neurology. 2023). KYV-101 holds promise to elicit deep, broad B-cell depletion and immune reset with a single infusion.

Methods: Autologous T cells were collected and enriched from patients with multiple sclerosis (MS) or MG. KYV-101 was generated by transducing T cells with a lentiviral vector encoding a fully human anti-CD19 CAR. Preclinical KYV-101 functional potency was assayed (cytokine release; cytotoxicity) in co-cultures with patient-derived CD19+ B cells, and CD19+ or CD19− control cells. Manufacturing expansion and functional potency from a clinical cohort of KYV-101 treated patients were also assessed.

Results: In preclinical assays, KYV-101 from MS patients induced greater dose-dependent cytotoxicity and IFN-gamma increases against CD19+ cells versus untransduced T cells and negligible responses following co-culture with CD19− cells. In the clinical cohort, KYV-101 manufactured from MS ($n=2$) and MG ($n=6$) patients displayed CD19-specific functional activity. Fold expansion ranges for KYV-101 from patients with MS ($n=2$) and MG ($n=6$) were 32.5–61x and 15.5–50x (Day 8; pre-harvest), respectively, which were similar to previously observed expansion from non-neurological autoimmune diseases.

Conclusion: KYV-101 from neurological autoimmune diseases shows activity specific for CD19+ cells. Manufacturing showed successful and consistent expansion across diseases. These data support further clinical investigation of KYV-101 as a novel therapy for neurological autoimmune diseases.

Disclosure: SP, SNS, JDB, HJK, JKC, RS, KW and TVB are employees of Kyverna Therapeutics during this work.

EPR-043 | Serological markers of clinical improvement in musk myasthenia gravis

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Background and Aims: In the last decade there has been a significant improvement in the clinical outcome of myasthenia gravis with antibodies against the muscle-specific tyrosine kinase (MuSK-MG), due to earlier recognition and effective treatments. However, biomarkers of disease severity and outcome are still lacking. In this study, we explored the role of (a) total MuSK-IgG levels; (b) MuSK-IgG subclasses; and (c) MuSK-IgG affinity as possible biomarkers of outcome in MuSK-MG patients.

Methods: Total MuSK-IgGs were quantified by flow cytometry and cell-based assay (CBA) serial dilutions. MuSK-IgG subclasses were analysed by flow cytometry. SAffCon assay was used for determining MuSK-IgG affinity.

Results: Forty-three sera were obtained at different time-points from 20 MuSK-MG patients, of whom 9/20 were treated with rituximab. In individual patients, MuSK-IgG levels decreased paralleling clinical improvement, either as measured by flow cytometry or by CBA end-point titration. In all samples, MuSK-IgG4 was the most frequent isotype, irrespective of disease outcome. We observed a significant reduction of MuSK-IgG4 and, to a lesser extent, of -IgG2 in patients with favourable clinical outcomes. Similar findings were confirmed in the subgroup of patients treated with rituximab. In a single patient, MuSK-IgG affinity increased after symptom exacerbation, while total MuSK-IgG and IgG4 levels remained stable, suggesting that affinity maturation can be a driver of clinical worsening.

Conclusion: Through a multimodal investigational approach, we showed that total MuSK-IgG levels, MuSK-IgG4 and -IgG2 levels and MuSK-IgG affinity can represent promising biomarkers of disease outcome in MuSK-MG and may be useful in guiding treatment choices.

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology

EPR-044 | Cognitive intra-individual variability as a modifier or outcome in speed of processing training in adults with HIV

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Background and Aims: Variability in cognitive performance within an individual, known as Cognitive Intra-Individual Variability (IIV), can arise from compromised cognitive control due to brain pathology. Individuals with HIV-Associated Neurocognitive Disorder (HAND) may experience increased cognitive IIV. We examined whether: 1) Speed of Processing (SOP) decreases cognitive IIV, and 2) cognitive IIV modifies the effects of SOP training in individuals with HAND or borderline HAND.

Methods: In this 3-group experimental design, 216 people living with HIV (PLWH) with HAND were randomized to either: 1) 10 hours

of SOP training ($n = 70$); 2) 20 hours of SOP training ($n = 73$), or 3) 10 hours of Internet Navigation Control Training ($n = 73$). Participants completed a seven-domain cognitive battery at baseline, posttest after training, and years 1 and 2 follow-up; from this, the coefficient of variation (CoV) served as the cognitive IIV dispersion score for each of the assessment points. Participants also completed a gold-standard measure of SOP (i.e., the Useful Field of View Test) at baseline, at posttest immediately after training, and at year 1 and year 2 follow-up assessments.

Results: Linear mixed-effect models did not reveal a clear pattern of SOP training effects on cognitive IIV. Yet, a three-way interaction tests between time, group, and baseline IIV CoV [$F(6, 453.96) = 1.74$, $p = 0.11$], and time, group, and baseline IIV CoV median split indicator [$F(6, 467.84) = 2.024$, $p = 0.061$] suggested potential moderation effects.

Conclusion: This study confirms that SOP training does not improve cognitive IIV; however, cognitive IIV may modify the effects of SOP training.

Disclosure: This work was supported by: NIH/National Institute of Mental Health R01-award (1R01MH106366-01A1; ClinicalTrials.gov; NCT02758093; PI: Vance) titled "An RCT of Speed of Processing Training in Middle-aged and Older Adults with HIV"; NIH/National Institute on Aging (NIA) R00-award (R00 AG048762; PI: Fazeli; ORWH NIH/NIA P30-award (Edward R. Roybal Center for Translational Research in Aging and Mobility; P30 AG022838; PI: Ball).

EPR-045 | Interoception, emotion, and social cognition in neurodegenerative diseases: a meta-analysis

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Background and Aims: Deficits in interoception, emotion, and social cognition are observed in various neurodegenerative diseases, and are likely due to degeneration within the allostatic-interoceptive network. Indeed, indirect evidence from individual imaging modality studies suggests a shared neurobiological basis underlying these impairments. Here, we employed a multimodal imaging meta-analytical approach to identify shared and disease-specific neural substrates in neurodegeneration for interoception, emotion, and social cognition deficits.

Methods: Using the Activated Likelihood Estimate (ALE) method, we conducted several meta-analyses, encompassing studies meeting inclusion criteria: metrics for interoception, emotion, or social cognition; neurodegenerative diseases (including dementias, parkinsonian and motor neuron disorders and multiple sclerosis); and neuroimaging (structural: MRI voxel-based morphometry; functional: fMRI and FDG-PET).

Results: From 20,593 studies, 149 met inclusion criteria (47 interoception, 58 emotion, 44 social cognition). Dysfunctions in interoception, emotion, and social cognition implicated a shared network involving the anterior cingulate cortex, insula, orbitofrontal cortex, amygdala, and thalamus across neurodegenerative diseases in both single and conjunction meta-analyses. Further, we replicated these results in behavioural-variant frontotemporal dementia (bvFTD) in subgroup analyses.

Conclusion: Our findings provide the meta-analytic evidence of common network dysfunction within the allostatic-interoceptive brain network, contributing to shared deficits in interoception, emotion, and social cognition across diverse neurodegenerative diseases and imaging modalities, as well as evidence supporting the unique role of this network in bvFTD. Future longitudinal research is needed to identify when deficits in interoception, emotion, and social cognition arise in neurodegenerative diseases. This will inform potential biomarkers of disease progression and will help to further refine our understanding of neurodegenerative processes.

Disclosure: The authors have received institutional and/or commercial support, unrelated to the present work. No conflicts of interest exist.

EPR-046 | Salience and executive control networks dynamism and cognition in neuromyelitis optica spectrum disorder

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Background and Aims: Salience (SN) and executive control networks (ECN) play a relevant role in cognitive functions. In neuromyelitis optica spectrum disorder (NMOSD), dynamic variations of brain connectivity within these networks have never been explored. We investigated static (S) and time-varying (TV) functional connectivity (FC) abnormalities of SN and ECN and their cognitive correlates in NMOSD patients.

Methods: Cognitive evaluation (Rao Battery) and 3.0T resting-state functional MRI were obtained from 34 right-handed anti-aquaporin-4 antibody-positive NMOSD patients and 39 sex- and age-matched healthy controls (HC). TVFC was estimated through sliding-window correlation analysis using the left and right dorsolateral prefrontal cortex (BA9) and the left insula as seeds. Mean connectivity indicated SFC.

Results: In NMOSD patients, the most frequently impaired domains were complex attention (44.8%), verbal memory (23.3%), fluency (12.9%) and visual memory (9.7%). Compared to HC, NMOSD patients showed significantly reduced SFC and TVFC of SN, mainly located in the bilateral temporal lobe ($p < 0.05$, corrected). NMOSD patients also exhibited reduced SFC in several regions of ECN ($p < 0.05$, corrected), including bilateral frontal and parietal lobes, right temporal lobe, left cerebellum and insula. Moreover, NMOSD patients presented increased SFC and TVFC of ECN versus HC in the right precuneus, cerebellum, and olfactory cortex and in left cuneus, precentral gyrus, and paracentral lobule. Reduced ECN SFC was associated with worse visual memory and fluency performances (r = range 0.36–0.45, $p <= 0.039$), while increased ECN TVFC was associated with better attention performances ($r = 0.54$, $p = 0.002$).

Conclusion: In NMOSD, abnormal SFC and TVFC of SN and ECN are associated with cognitive performances.

Disclosure: M. Gueye, N. Tedone, P. Valsasina have nothing to disclose. M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPR-047 | Decision-Reinvestment differences in heart-rate variability contradicted in footballers, while mental-health correlates

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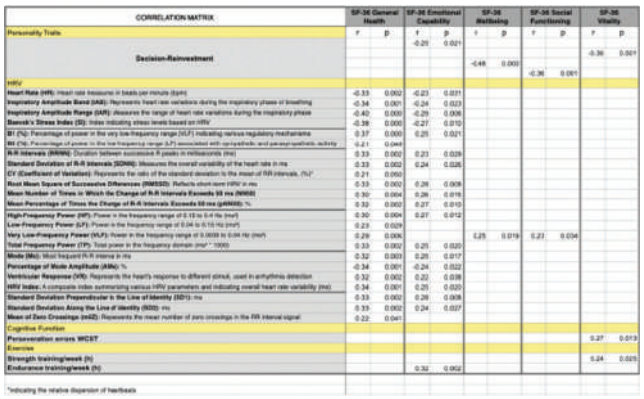
Background and Aims: Decision-reinvestment behaviour leads to significant decrease in both motor-control, cognitive performance, and cardiac vagal activity. Heart-rate variability (HRV) is as a physiological marker reflecting modulation of the autonomic nervous system, and therefore implicate chances in athletes' regeneration, health, and performance status. This cross-sectional study examined the relationship between HRV and cognitive function, perceived health, as well as reinvestment strategies. The hypothesis was that trait-related HRV differences do not occur in athletes, perceived pain will be greater in reinvester athletes and correlate with cognitive function.

Methods: HRV of 88 football player was recorded with an HRV-analyser for 5 min. Participants then self-reported their mental and physical health (SF-36), decision-reinvestment strategy, and performed a set of cognitive tests to examine memory function (Backwards Corsi), selective attention (STROOP), and cognitive flexibility (Wisconsin Card Sorting Test, WCST). Spearman correlations with corresponding tests were used to analyse correlations between continuous variables, and a Two-Sample Test was performed to evaluate HRV differences between groups.

Results: Significant correlation occur in perceived health with multiple parameters of HVR (Table 1), as well as decision-reinvestment, and preservation errors. A positive correlation exist in regard of mental health with both hours of endurance (p 0.002) and strength training (p 0.024). There were no group differences in HRV ($p > 0.05$).

TABLE 1. Correlation Matrix – Overview of Decision Reinvestment, HRV, cognitive function and exercise parameters that correlate with physical and mental health.



Conclusion: Exercise induced vagal activity may inhibit trait-related changes in HRV, and boost mental health. Athletes with lower mental health scores have increased preservation errors during WCST, and greater tendency to ruminate.

Disclosure: ECG based HRV analyser was provided by Nilas MV GmbH, Germany.

EPR-048 | Neurobiological and psychological markers of reaction to extreme stress: A three-generation study of Holocaust survivors and their offspring. War stress in Ukrainian refugees

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Background and Aims: Ukrainian war stress: Acute and ongoing war stress has a significant neurobiological impact on refugees from war-torn Ukraine. The psychological tests showed stress, depression, and anxiety. The influence of ongoing stress is present in the thalamus connected with parts of the limbic circuitry – insula, orbitofrontal cortex, and para-hippocampal gyrus. The structural and connectivity data in this study reveal the characteristics of acute and ongoing stress.

Methods: We explored three generations of Holocaust survivors (HS). The target was to identify lifelong impact of extreme stress (TSC-40, PCL-C, SOS-10) and post-traumatic growth (PTGI). HS 44, median age 81 years, controls 31; 2nd generation 86, controls 62; 3rd generation 88, controls 64.

Results: Psychological testing: stress-positive in three generations versus controls; PTGI-positive in HS. The second and third generation are also stressed. Neuroimaging – MRI. IN HS, the grey matter (GM) was reduced in insulas, anterior cingulate, temporal pole. In the 2nd and 3rd generation there is a clear difference in MRI connectivity compared to controls.

Conclusion: Life-long psychological and brain structure changes in people who survived holocaust were identified more than 70 years after World War II. Extreme prenatal, childhood and young adulthood stress has an irreversible lifelong impact on the brain. The consequences of holocaust-related trauma are transmitted to the 2nd and 3rd generation.

Disclosure: Nothing to disclose.

EPR-049 | Macroscale structural covariance network reveals the biological mechanisms of neuropsychiatric symptoms

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Background and Aims: The intricate and heterogeneous phenotypes associated with neuropsychiatric symptoms (NPSs) encumber exploration of their role in the neuropathology and underlying biological mechanisms of Alzheimer's disease (AD) continuum.

Methods: An individual-level Regional Radiomics Similarity Network (R2SN) for 487 patients with AD continuum (376 with NPSs vs. 111 without NPSs) were developed to refine the subtypes of NPS in the AD continuum. Distinct brain network dysfunction, multimodal neuroimaging burden, and clinical measures/progression of each NPS subtype were analyzed.

Results: Three NPS subtypes were identified based on 300 distinct key R2SN connections. Compared to those without NPS, the first NPS subtype (sNPS) and third NPS subtype (moNPS) exhibited significant opposite pattern of brain connectivity damage, while the second NPS subtype (miNPS) showed minimal differences (Figure 1). Both the sNPS and moNPS subtypes exhibited diminished baseline

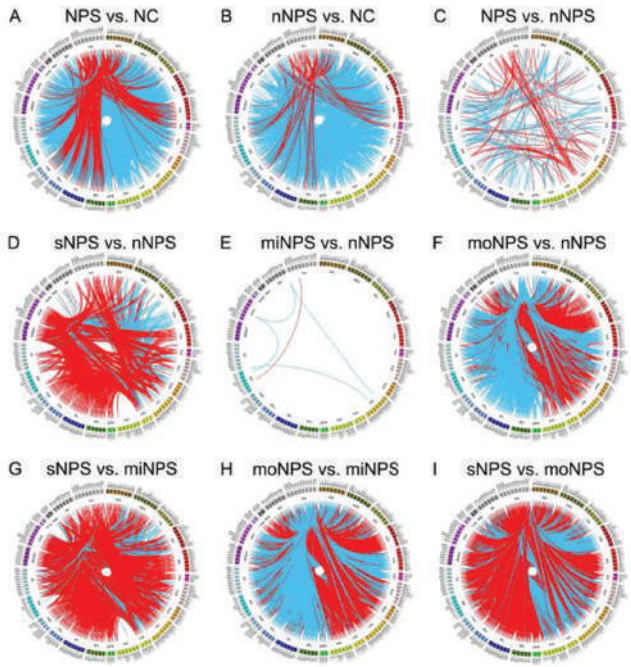

FIGURE 1. Characteristics of altered morphological connectivity in the R2SN profiles.

performance and rapid decline in the MMSE and MoCA scores, while no significant difference was discerned in miNPS. Both the sNPS and moNPS subtypes exhibited reduced regional grey matter volume, while miNPS subtype lacked significant structural brain changes but exhibited higher cerebral blood flow in some regions, suggesting early compensatory cerebral hyperperfusion (Figure 2). Gene set enrichment analysis (GSEA) elucidated each subtype's unique biological mechanisms associated with the contribution of NPS-related specific brain connectome dysfunctions to AD progression (Figure 3).

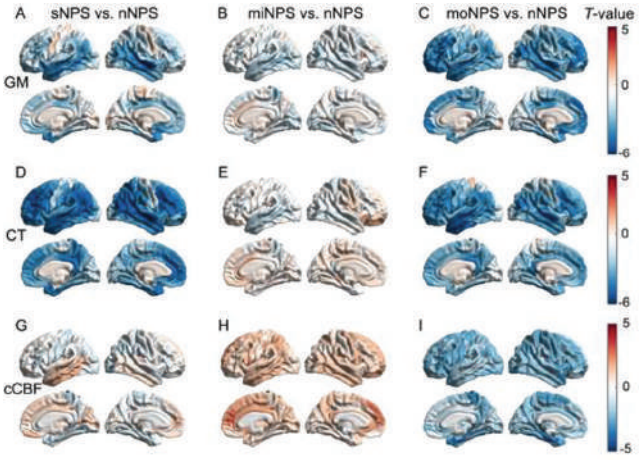

FIGURE 2. Differences in multimodal neuroimaging burden between three NPS subtypes in the AD continuum.

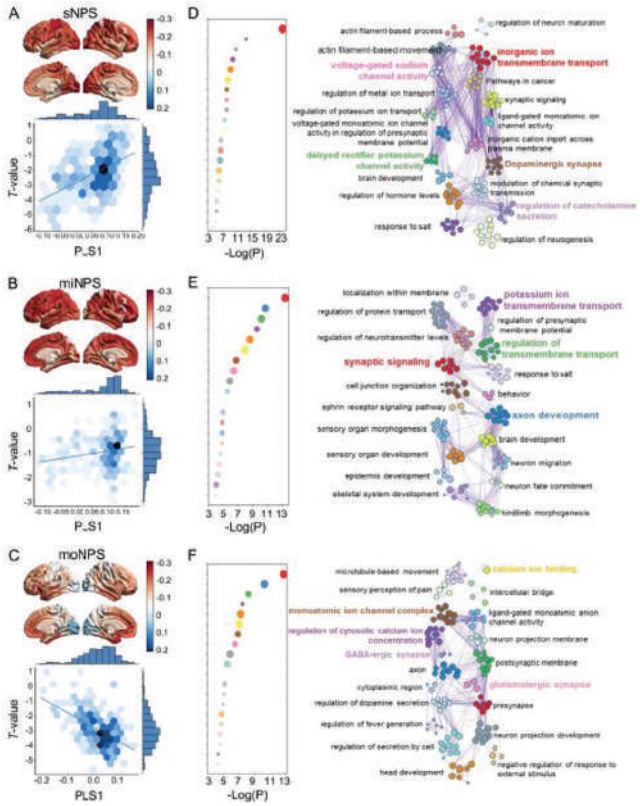

FIGURE 3. GSEA between three NPS subtypes and those without NPS in the AD continuum.

Conclusion: This is the first study to identify three distinct NPS subtypes on AD continuum through a data-driven approach, bridging the gap in the knowledge on the contributions of NPSs to AD continuum, and offering new insights into precise interventions for these patients.
Disclosure: Nothing to disclose.

EPR-050 | Decision-making, risk-taking, and divergent thinking differences between Italy and USA: Preliminary results

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Background and Aims: Today's society is characterized by complexity and uncertainty. Risk dominates individual and social consciousness, increasing the challenge of answering the question, "How do people make decisions?" (Nyhlen and Liden, 2014). Several variables are known to influence decision-making (DM) process and styles, including uncertainty avoidance and tolerance (Hofstede, 2007) as well as creativity (particularly Divergent Thinking, DT), although the data are controversial (Collins & Koeklin, 2012; Crepaldi et al., in press). However, few studies consider cultural differences. Based on these premises, the study presents the cultural differences between Italians and the US in risk-taking, DM and DT.
Methods: 55 Italians (39 females; mean age: 22.4; SD 2.7) and 57 Americans (32 females; mean age 20.0; SD 1.5) were involved. Questionnaires investigating risk (DOSPERT), DM style (GDMS), and creativity (AUT) were administered.
Results: No significant differences emerge in DM styles, but initial analyses show significant differences in ethical risk-taking (ITA>US, $t = 2.63$; $p < 0.05$) and substantial differences in the DT task in fluency (US >ITA, $t = -7{,}28$; $p < .001$) and originality (US>ITA, $t = -2{,}47$; $p < 0.05$).
Conclusion: Living successfully means acting efficiently; a better DM process should help people achieve better life outcomes. Findings suggest that there are differences in risk-taking and DT, two components of DM, although no differences in DM styles emerge. Knowing the role of these variables in different cultures can help support the DM process. Therefore, extending the research in the lifespan and increasing the number of samples for comparison is useful.
Disclosure: The author declared no conflict of interest.

EPR-051 | Deep brain stimulation of the posterior hypothalamus in aggression management – A case series analysis

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Background and Aims: Pathological aggression, common in neurodevelopmental disorders, includes intellectual disability and motor/verbal aggression. Affecting over 50% of autistic children and up to 45% with intellectual disability, it jeopardizes safety. Surgical interventions like posterior hypothalamus DBS reduce aggression by 91% with fewer adverse effects than direct lesioning.

Methods: A cohort study of 13 patients with refractory aggression who received bilateral posterior hypothalamus DBS treatment was conducted. They were evaluated pre- and postoperatively using the MOAS. Clinical and psychometric assessments were conducted by a multidisciplinary team, with statistical analysis comparing pre- and postoperative scores.

Results: The analysis included 13 cases, predominantly male, all with a history of intellectual disability (Table1 and 2). At the 6-month follow-up, a median improvement of 58% was observed in the post-DBS MOAS score compared to the pre-DBS MOAS baseline, which was statistically significant ($p=0.002$) (Figure1). Improvement ranged between 43% and 73%, except for one case, a 12-year-old patient, whose benefit was only 18%.

TABLE 1. Qualitative clinical characteristics of patients treated with DBS for aggression.

Variable	n=13	%
Man	10	76.9
Epilepsy	8	61.5
Adverse effects	2	15.4
Hyporexia	1	7.7
Gait worse	1	7.7

TABLE 2. Quantitative clinical characteristics of patients treated with DBS for aggression.

Variable	Median	P25	P75	Min	Max
Age (years)	26	24	32	12	38
MOAS preDBS	14	12	15	7	18
MOAS posDBS 6 months	5	4	5	4	14
Follow-up time (months)	36	18	66	6	76

MOAS: Modified Overt Aggression Scale, pre: preDBS, pos: posDBS 6 months.

FIGURE 1. Boxplot MOAS pre and pos DBS

Conclusion: In our case series, posterior hypothalamus DBS proves highly effective for refractory aggression, surpassing conventional therapies. This intervention poses a low risk, yielding significant improvements in patients.

Disclosure: Nothing to disclose.

EPR-052 | Prediction of language and verbal fluency in Parkinson's disease patients undergoing Deep Brain stimulation (DBS)

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Background and Aims: Deep brain stimulation (DBS) is a common treatment for motor deficits in Parkinson's disease (PD). We studied the effects on speech capacity (phonematic and semantic fluency) after DBS.

Methods: Findings related to speech and cognition in patients with PD who underwent DBS ($N=31$, F=12, M=19; mean age 63.5±10.06 years, disease duration 12.5±5.38 years, preoperative UPDRS 20±13.12, postoperative UPDRS 14±9.16, preoperative LEDD 1150± 536.29, postoperative LEDD 482±336.81). Phonematic and semantic fluency were assessed before and 6 to 8 months after DBS with a semantic fluency test (animals), a phonematic test (s-words), Digit Span forward and backward, Wisconsin Card Sorting Test, Mini Mental State Examination (MMSE) and Trail Making Test. We used GLM for the statistics. Potential confounders were age, MMSE, MoCA, Wisconsin Card Sorting Test and Digit Span.

Results: Phonemic fluency (preoperative 0.056 ±1.04; postoperative −0.306 ±0.83, $p=0.034$) and semantic fluency (preoperative −0.356 ±1.004; postoperative −0.90 ±0.73, $p=0.009$) decreased after DBS. None of the potential confounders had a significant effect. However, pre-, and postoperative phonemic fluency were

significantly correlated ($r=0.54$, $p<0.009$), as were pre- and postoperative semantic fluency ($r=0.62$, $p<0.001$). Interestingly, pre-, and postoperative MoCA scores were not significantly correlated.

Conclusion: 1. In PD patients, the best predictors of verbal fluency after DBS are preoperative phonemic and semantic fluency scores, while other predictors of low verbal fluency after DBS could not be confirmed. 2. Poor and borderline preoperative verbal fluency may be a relative contraindication for DBS in patients with Parkinson's disease.

Disclosure: Nothing to disclose.

Neurogenetics 1

EPR-053 | Leriglitazone halts disease progression in men with cerebral adrenoleukodystrophy

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Background and Aims: X-linked adrenoleukodystrophy (ALD) is an inherited disorder in which more than half of the male patients develop inflammatory demyelinating lesions with high lethality (cerebral ALD, CALD). Lesions typically involve corpus callosum, corticospinal tracts (CST) and cerebellum on brain MRI. Hematopoietic stem cell transplantation (HSCT) is the standard of care, but many patients are not eligible, particularly in case of CST lesions which have a poor prognosis. This study evaluates the efficacy of a new treatment, leriglitazone, in CALD.

Methods: We treated 13 men not eligible or awaiting HSCT. Patients were assessed every 3 months by clinical scoring, plasma biomarkers (including Neurofilament Light Chain or NfL, reflecting disease activity) and brain imaging comprising FLAIR, diffusion tensor imaging (DTI) and post-contrast 3D T1 sequences. Total lesion load and corticospinal tracts lesion load were measured longitudinally after lesion segmentation on FLAIR sequence. DTI markers were automatically calculated in 19 regions of deep white matter (BrainQuant platform of BrainTale Care). Gadolinium enhancements were assessed visually.

Results: Ten patients showed an excellent clinical response. Lesion load was significantly correlated with NfL and DTI metrics (FA, MD) in total white matter, which remained globally stable in these patients. All lesions involving the corticospinal tracts turned gadolinium-negative and downsized in most patients. Regional variations of MD were in line with the volumetric evolution of lesions.

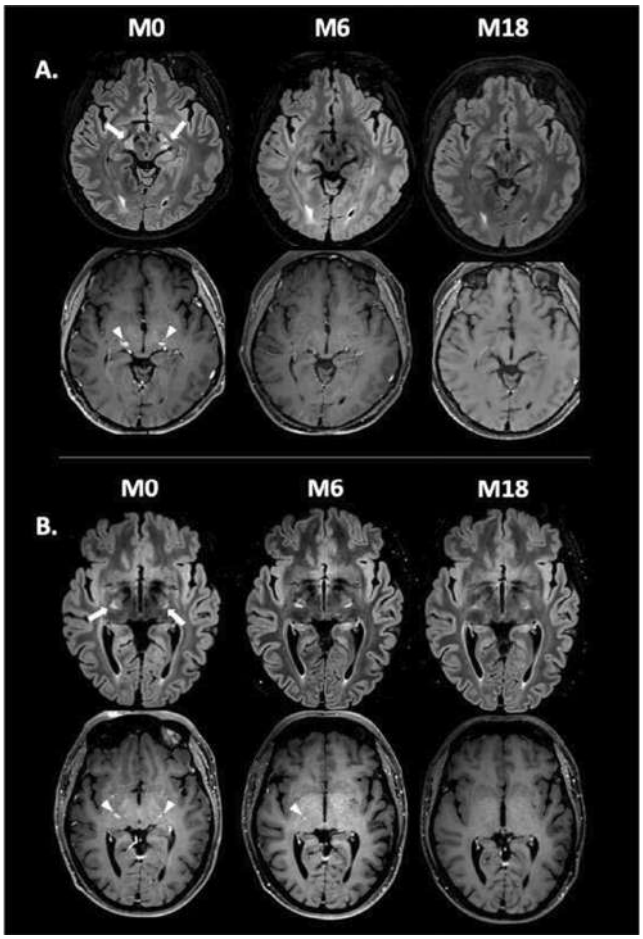

FIGURE 1. Evolution of CST lesion load on FLAIR (arrows) and gadolinium enhancements (arrowheads) in two CALD patients between baseline and M18.

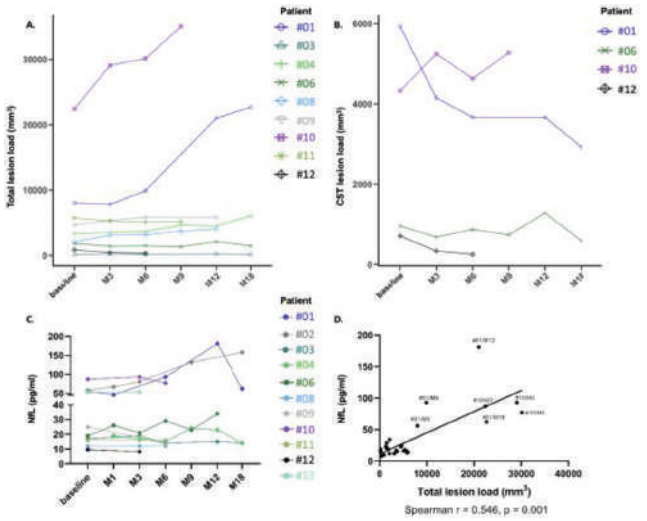

FIGURE 2. Evolution of total lesion load (A), CST lesion load (B) and NfL (C) over time, with correlation analysis between total lesion volume and NfL (D) showing a moderate significant correlation.

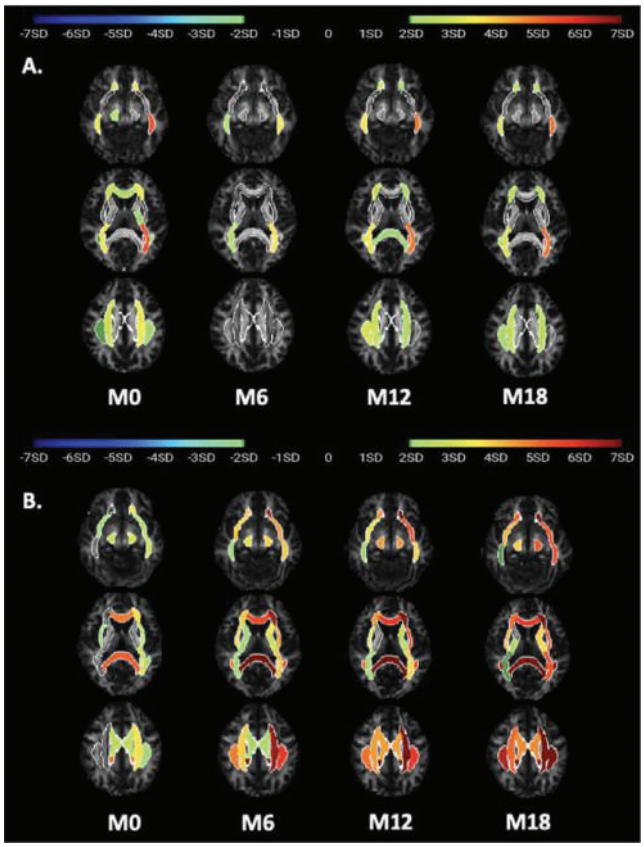

FIGURE 3. Evolution of the regional MD values (in standard deviations from healthy volunteers) in different regions of deep white-matter, in a patient with a positive evolution (A) and in a patient with deterioration (B).

Conclusion: These results show that leriglitazone can be an alternative treatment to HSCT in CALD, with a distinct action on the CST.

Disclosure: Nothing to disclose.

EPR-054 | ATP6V0C variants in epilepsy: Unraveling phenotypic patterns and genotype correlations

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Background and Aims: Variants in ATP6V0C have been associated with neurodevelopmental disorders and seizures. In the present study we aim to delineate the ATP6V0C epilepsy phenotypes.

Methods: We retrospectively analyzed 33 cases from 27 families with ATP6V0C variants. Cases were identified by an international network of epileptologists/geneticists. SPSS was used for statistical analysis.

Results: ATP6V0C variants were predominantly missense (88%), often de novo (73%), and exhibited an average seizure onset at 19 months, with febrile seizures in 77% of cases. Generalized tonic-clonic seizures were the predominant type (82%), with other types such as myoclonic, absences, tonic, and focal seizures occurring in approximately 25%–35% of patients. Unspecified developmental and epileptic encephalopathy ($n=11$) and genetic epilepsy with febrile seizure plus (GEFS+) ($n=9$) were commonly observed. Developmental delay affected 76% of patients (evenly distributed between severe, moderate, and mild categories), with half experiencing drug-resistant epilepsy (DRE). Valproate showed >50% seizure reduction in 10 of 15 patients but was ineffective in those with DRE. MRI abnormalities were noted in seven severe cases, showing delayed myelination and corpus callosum agenesis. Thirteen cases with TMR-4 variants displayed a more severe phenotype, including higher rates of developmental delay ($n=13$), DRE ($n=8$), and abnormal neurological examination ($n=8$) with hypotonia and dysmorphic facial features. Logistic regression analysis highlighted the significance of affected amino acid position in predicting moderate or severe developmental delay (OR 1.018, $p=0.034$).

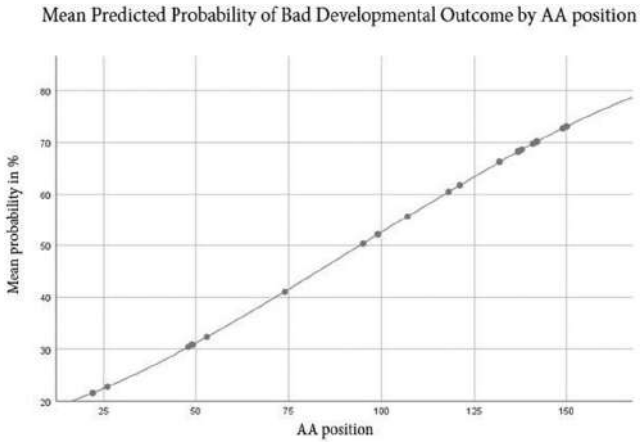

IMAGE 1. Logistic regression analysis.

Conclusion: ATP6V0C variants are linked to a spectrum of GEFS+ epilepsy phenotypes, underscoring a robust genotype-phenotype correlation.

Disclosure: Nothing to disclose.

EPR-055 | SORD and SORD2P inversion: long read sequencing identifies a novel genetic mechanism underlying inherited neuropathy

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Background and Aims: Despite the best efforts, over 50% of axonal CMT cases do not receive genetic confirmation. Notably, current short read technologies, including whole exome (WES) and whole genome sequencing (WGS), present major shortcomings in the study of structural variants and repeated regions, contributing to the missing heritability in CMT.

Methods: Here we leverage long read sequencing (LRS) and non-sequencing based optical genome mapping (OGM) to identify a large structural variant involving SORD and its pseudogene SORD2P, which disrupts SORD reading frame and causes SORD=CMT in multiple families.

Results: In three unrelated axonal CMT patients with high serum sorbitol and a heterozygous c.757delG SORD variant, LRS and OGM revealed a 200Kb inversion spanning two highly homologous SORD/SORD2P introns, undetectable by WES or WGS. Additionally, inverse PCR in 37 CMT cases with a heterozygous pathogenic SORD mutation identified this inversion in 4 (~10%) of them. This inversion occurred de novo in one family and was inherited from an asymptomatic parent in another. These cases resemble previously described SORD=CMT cases. Public data on 3D chromatin structure suggest SORD and SORD2P's proximity in the nucleus could facilitate such recombination events.

Conclusion: In conclusion, SORD/SORD2P inversion is key in axonal CMT cases with a single SORD mutation, especially when serum sorbitol is high. This study demonstrates LRS and OGM's effectiveness in identifying genetic causes in unresolved CMT cases, revealing a new mechanism by which structural variants in gene/pseudogene pairs (~3000 in the human genome) can cause genetic disease, often undetected by short-read sequencing technologies.

Disclosure: Nothing to disclose.

EPR-056 | A CCG expansion in ABCD3 causes oculopharyngodistal myopathy in individuals of European ancestry

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Background and Aims: Oculopharyngodistal myopathy (OPDM) is an inherited myopathy manifesting with a combination of ptosis, dysphagia, and distal weakness. Pathologically it is characterized by rimmed vacuoles and intranuclear inclusions on muscle biopsy. Recently, CGG/CCG repeat expansions in four different genes have been identified in OPDM patients of Asian ancestry. In this study we identified CCG expansions in ABCD3 in 35 OPDM cases from eight unrelated families and of European ancestry.

Methods: A combination of linkage studies, short-read whole genome sequencing and targeted long-read sequencing was employed for the gene discovery. Additional 68 patients with cranial myopathy or full OPDM were screened through repeat-primed PCR. ABCD3 expression on muscle and patients-derived fibroblast was quantified using RNA-sequencing, qPCR, and RNA FISH.

Results: CCG expansions in the 5'UTR of ABCD3 were independently identified in two large Australian OPDM families and through the 100,000 Genomics England Genome Project in three OPDM patients from two unrelated UK families. Targeted long-read sequencing confirmed the presence of mono-allelic CCG repeat expansions ranging from 118 to 694 repeats in all tested cases ($n=19$). Three additional ABCD3-positive patients were identified after PCR screening, for a total of 35 patients from eight unrelated families. ABCD3 transcript was upregulated in skeletal muscle and cells derived from affected OPDM individuals.

Conclusion: The study strengthens the association between the GCC/CCG repeat motif and a specific pattern of muscle weakness with prominent cranial involvement across different populations. The over-expression of ABCD3 transcript might play a role in the progressive skeletal muscle degeneration of this condition.

Disclosure: Nothing to disclose.

EPR-057 | Abstract withdrawn

EPR-058 | Evaluating outcome measures in ataxia in primary mitochondrial disease and spinocerebellar ataxia type 6

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Background and Aims: Progressive ataxia is a common neurological feature reported in primary mitochondrial disease (PMD). However, there were limited clinical studies systematically assessing the severity of ataxia in patients with PMD. This study aims to delineate the ataxic features of patients with PMD by comparing to patients with Spinocerebellar Ataxia type 6 (SCA6).

Methods: In this cross-sectional study, adults with genetically confirmed PMD, patients with SCA6, and healthy controls were recruited. The following assessments were performed: Clinician-reported measures: SARA (Scale for the Assessment and Rating of Ataxia), ICARS (International Cooperative Ataxia Rating Scale), INAS (Inventory of Non-Ataxia Signs), etc. Patient-reported measures: ABC (Activities-Specific Balance Confidence Scale), FES1 (Falls Efficacy Scale-International), FSS (Fatigue Severity Scale), etc. Instrumented balance and gait analysis

Results: Seventy participants (PMD, $n=37$; SCA6, $n=11$; healthy controls, $n=22$) completed this study. The mean age of SCA6 patients was significantly older than PMD patients (61 vs. 46, $p=0.018$). The severity of ataxia, measured by SARA (9 vs. 8.7) and ICARS (17.3 vs. 14.8), was similar between patients with PMD and SCA6 ($p>0.05$). Patients with PMD had more non-ataxia signs (INAS) than SCA6 (3 vs. 1, $p<0.001$). Significant correlations were identified between clinician- and patient-reported measures in both patient groups. Patients with PMD had larger displacement of centre of pressure compared to healthy controls (Figure).

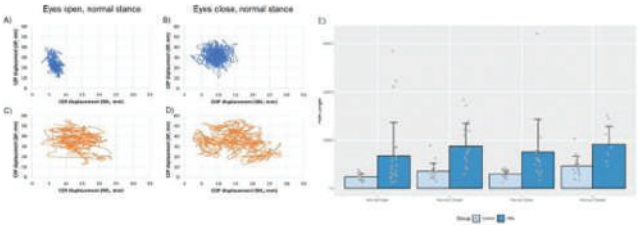

FIGURE. Force plate analysis. (A-B) age- & sex-matched healthy control and (C-D) a patient with a rare pathogenic mitochondrial DNA variant (m.7510T>C). (E) Comparisons of postural sway (path length) between age-matched controls and patients with PMD in D

Conclusion: Our findings show that the overall ataxic severity in PMD is comparable to SCA6. However, the impairment of balance and mobility in patients with PMD is also complicated by other additional neurological features.

Disclosure: The study was supported by Academy of Medical Sciences and Ataxia UK.

EPR-059 | Leber's hereditary optic neuropathy or Leigh syndrome—A digenic mechanism makes the difference

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Background and Aims: Leber's hereditary optic neuropathy (LHON) and Leigh syndrome (LS) represent in a way the opposite ends of the wide mitochondrial disease spectrum, with LHON being a relatively mild and tissue-specific disorder mostly in adolescents and young adults, and LS being a particularly severe and multi-systemic disorder mostly in children. Surprisingly, however, some cases of LS have been associated to genetic variants that in most instances cause LHON. We speculated that there must be an additional genetic cause leading to this huge phenotypic difference.
Methods: Five probands with LS harbouring the primary LHON variant m.11778G>A of the mitochondrial DNA (mtDNA) were investigated by whole exome sequencing.
Results: All five patients carried, in addition to the LHON-typical mtDNA variant, a heterozygous predicted loss of function or predicted deleterious missense variant in a nuclear-encoded Complex I subunit gene (NDUFS2 $n=3$, NDUFS7 $n=1$, NDUFS8 $n=1$).
Conclusion: Our findings provide an explanation for the longstanding enigma of severe LS being associated with primary LHON variants. While biallelic variants in nuclear-encoded Complex I subunit genes NDUFS2, NDUFS7 and NDUFS8 lead to recessive LS, a heterozygous variant in these genes (as for example in parents of recessive LS children) is not sufficient to cause disease. However, digenic inheritance of such a heterozygous nuclear variant in conjunction with a primary LHON variant leads to the extreme switch from LHON to LS phenotype.
Disclosure: Nothing to disclose.

EPR-060 | Preclinical development of a conjugate vaccine targeting poly-GA in C9orf72 ALS/FTD

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Background and Aims: A marked proportion of ALS and FTD patients carry a pathogenic (G4C2)n repeat expansion in C9orf72, which is translated into aggregating dipeptide repeat proteins, most abundantly poly-Glycine-Alanine. In mouse models, poly-GA aggregates promote neuroinflammation and secondary TDP-43 pathology, a key trigger of neuron loss, also in sporadic ALS/FTD. The GA-VAX consortium is developing a vaccine targeting poly-GA as a potential treatment for C9orf72 ALS/FTD by reducing poly-GA pathology and downstream toxicity through vaccine-induced antibodies.
Methods: Active immunization of mice; analysis of phenotype, biomarkers, and immunohistochemistry.
Results: Our initial studies demonstrated that active immunization with ovalbumin-conjugated (GA)10 significantly reduced poly-GA levels, neuroinflammation, and TDP-43 mislocalization in GA-CFP mice. Our latest data show that post-symptomatic immunization reduces serum neurofilament levels. To facilitate manufacturing of the vaccine, we optimized the formulation for solubility and immunogenicity. Our lead antigen (GA-VAX-01) shows high solubility, favourable immune response profiles, and improved motor function in GA-CFP mice. Next milestones are toxicology studies in rats and evaluation of additional efficacy parameters to support a clinical trial application.
Conclusion: The GA-VAX project represents a novel therapeutic approach for C9orf72-associated ALS and FTD. Recent developments, including promising pre-clinical results and ongoing studies, provide a strong basis for advancing our lead candidate GA-VAX-01 into clinical trials.
Disclosure: The GA-VAX consortium is funded by the EU Horizon Europe research and innovation programme, grant agreement No 101057649. HK and AS are employees at Intravacc BV. QZ and DE hold a patent application (PCT WO2020221937A1) describing anti-GA vaccination.

EPR-061 | Interim Results for Iluzanebart (VGL101) from IGNITE, the first interventional phase 2 study in patients with ALSP

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Background and Aims: There are no licensed therapies for adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), a rare, fatal, autosomal-dominant neurodegenerative microgliopathy characterized by rapidly progressive cognitive decline, neuropsychiatric symptoms, and motor dysfunction due to CSF1R gene mutations, indicating a critical unmet medical need. Iluzanebart (VGL101), a fully human IgG1 monoclonal antibody TREM2 receptor agonist, was well tolerated in a phase 1 healthy volunteer study and demonstrated durable target engagement and pharmacological activity following multiple dosing.
Methods: IGNITE (NCT05677659), the first interventional clinical trial in ALSP, is an ongoing, phase 2, multicentre, open-label study assessing iluzanebart safety/tolerability and proof-of-concept,

targeting up to 15 eligible adults with documented CSF1R mutation and clinical and MRI findings consistent with ALSP for enrolment. Participants will receive intravenous iluzanebart every 28 ±7 days for a total of 13 doses over 48 weeks. Primary endpoint is safety/tolerability assessed by adverse events (AEs); other endpoints include volumetric MRI measures, fluid biomarkers, and clinical measures.

Results: The interim analysis of the first 6 patients in IGNITE who have received iluzanebart 20 mg/kg for >=6 months showed favourable safety and tolerability, with no treatment-related severe or serious AEs or discontinuations due to AEs. Iluzanebart demonstrated CNS target engagement and downstream pharmacological activity. Changes in individual-level MRI measures and disease-related fluid biomarkers were generally supportive of an impact on ALSP disease pathophysiology (Table).

TABLE. IGNITE phase 2 summary of biomarker changes (6-month interim analysis).

ALSP patient segment at baseline[a]	Patient	Baseline NfL (pg/mL)	Baseline MoCA	Change in trajectory[b]				Iluzanebart impact based on biomarker changes
				MRI ventricular[c]	MRI grey matter[c]	sCSF1R[d]	NfL[e]	
Progressive disease	A	80	17					Slowing progression
	B	159	21					Slowing progression
	F	54	25					Slowing progression
Cognitively normal	D	10	28					Stabilization
	E	12	28					Stabilization
Potentially converting	C	42	30					Variable impact

[a]"Progressive disease" defined as NfL significantly higher than age-normal range, MoCA <26, and significant neurodegeneration and ALSP symptom of cognitive impairment; "cognitively normal" defined as NfL within age-normal range, MoCA ≥26, and other ALSP symptoms except cognitive; "potentially converting" defined as NfL higher than age-normal range, MoCA ≥26, and evidence of neurodegeneration and other ALSP symptoms except cognitive impairment.
[b]Meaningful (dark) or limited (light) changes in a direction consistent with treatment benefit are indicated in green; meaningful (dark) or limited (light) changes in a direction not consistent with treatment benefit are indicated in yellow.
[c]MRI trajectories assessed for 0-6 months in IGNITE vs pre-IGNITE run-in data (from ILLUMINATE Natural History study) for each patient.
[d]sCSF1R levels from cerebrospinal fluid assessed at 6 months in IGNITE vs 0 months (IGNITE baseline) for each patient.
[e]NfL levels from serum assessed for 0-6 months in IGNITE vs pre-IGNITE run-in data (for patients B, D, E, F) or for 6-9 months in IGNITE vs 0-6 months in IGNITE (for patients A, C).
ALSP, adult-onset leukoencephalopathy with axonal spheroids and pigmented glia; MoCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; NfL, neurofilament light chain; sCSF1R, soluble colony-stimulating factor 1 receptor.

Conclusion: These interim clinical trial results of iluzanebart support its continued development as a potential disease-modifying therapy for ALSP and TREM2 agonism as a potential therapeutic approach for this neurodegenerative disorder.

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Epilepsy 1

EPR-062 | Cenobamate in people with focal onset seizures: Insights from the Italian Expanded Access Program

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Background and Aims: This study assessed the effectiveness and tolerability of adjunctive cenobamate (CNB) for the treatment of focal seizures in the context of real-world clinical practice.

Methods: This was a retrospective, multicentre study including subjects prescribed CNB at 21 centres in Italy within the frame of the national Expanded Access Program. Study outcomes included the 3-, 6-, and 12-month rates of seizure response, seizure-freedom, and treatment discontinuation. The change in the number of concomitant ASMs and the incidence of adverse events (AEs) were evaluated.

Results: The study included 236 subjects with a median age of 38 years. The median number of prior and concomitant antiseizure medications (ASMs) was 7 and 3, respectively. The median baseline seizure frequency was 15 seizures/month. The 3-, 6-, and 12-month responder rates were 47.9%, 52.1%, and 57.0%; the corresponding rates of seizure freedom were 9.7%, 12.2%, and 14.0%. At 12 months, 29.1% and 6.1% of the subjects were sustained seizure responder and sustained seizure free. A reduction in the number of concomitant ASMs occurred in 48.2% of the subjects who were on CNB treatment at 12 months. Treatment discontinuation rates were 5.1%, 9.1% and 21.2% at 3, 6, and 12 months. Adverse events occurred in 58.3% of the participants and the most common were somnolence and dizziness; no serious AEs were reported.

Conclusion: Adjunctive CNB was associated with the reduction in seizure frequency and the load of concomitant ASMs in a cohort of subjects with highly refractory epilepsy. Adverse events were common and mostly mild-to-moderate in intensity.
Disclosure: Nothing to disclose.

EPR-063 | Prediction of epilepsy after ischaemic stroke: can we do higher? The modified SeLECT 2.0 score

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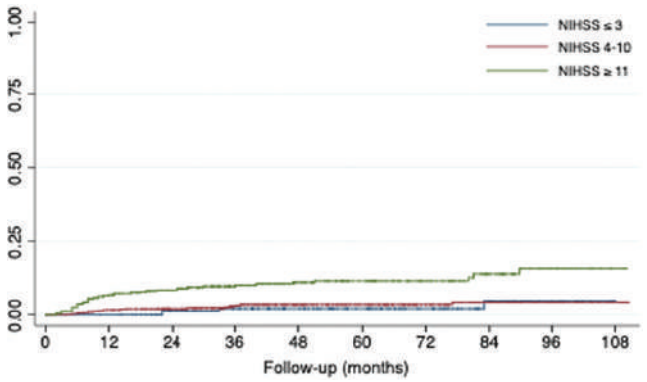
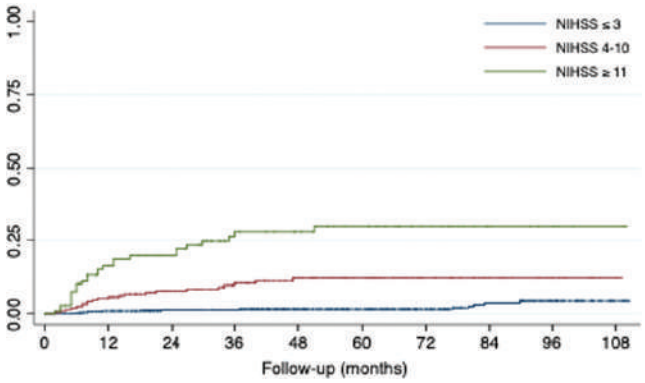
Background and Aims: The SeLECT 2.0 score is a prognostic model of unprovoked seizures after ischaemic stroke, but it does not consider the potential impact of revascularization. We aimed to explore whether replacing the severity of stroke at admission with the severity of stroke after treatment could improve the predictive accuracy of the score.
Methods: We retrospectively identified consecutive adults with acute first-ever ischaemic stroke who were admitted at the Stroke Unit of the Ospedale Civile Baggiovara and were treated with intravenous thrombolysis (IVT) and/or endovascular treatment (EVT). Study outcome was the occurrence of at least one unprovoked seizure presenting >7 days after stroke. The predictive power of the original and modified SeLECT 2.0 score was evaluated.
Results: Unprovoked seizures occurred in 65 (5.9%) out of 1094 subjects treated with IVT and/or EVT. The median values of the National Institutes of Health Stroke Scale at baseline and after treatment were 8 [5–14] and 1 [0–4]. The median values of the original and modified SeLECT2.0 scores were 3 [2–4] and 2 [1–3]. The modified SeLECT 2.0 score had higher values of Harrell's C and Somers' D parameters and lower values of Akaike's and Bayesian information criteria. The ROC curve for unprovoked seizures occurrence at 5 years was 0.663 and 0.851 for the original and modified scores.



Time to occurrence of unprovoked post-stroke seizures according to stroke severity at admission.



Time to occurrence of unprovoked post-stroke seizures according to post-treatment stroke severity.
Conclusion: Replacing baseline stroke severity with the stroke severity after treatment may improve the ability of the SeLECT 2.0 score to predict post-stroke epilepsy.
Disclosure: Nothing to disclose.

EPR-064 | Clinical and immunological studies in cryptogenic new-onset refractory status epilepticus

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Background and Aims: New-onset refractory status epilepticus (NORSE) can develop during infectious or autoimmune encephalitis, but many cases remain without identifiable causes despite extensive investigations (cryptogenic NORSE, c-NORSE). In these patients, underlying inflammatory or antibody-mediated mechanisms are often considered. The aim of our study was to assess the presence of neuronal antibodies in patients with c-NORSE using comprehensive

antibody testing that also included a novel human-based neuronal immunofluorescence assay.

Methods: We included patients diagnosed with c-NORSE whose serum and cerebrospinal fluid (CSF) were neuronal antibody-negative using conventional techniques (brain immunohistochemistry, cell-based assays). Clinical information was reviewed and samples were tested with live neurons derived from human induced pluripotent stem cells (iPSCs).

Results: Twenty-four patients were studied (63% female, median age 33 years). In 21/24 patients, status epilepticus (SE) was preceded by fever. All patients required intensive care unit admission and treatment with anaesthetics. Initial brain MRI was abnormal in 42% of cases, showing DWI or T2/FLAIR temporal (60%), extratemporal (10%) or combined (30%) abnormalities. Repeat MRI identified 8 additional patients with abnormalities during SE. CSF showed inflammatory changes in 83%, while oligoclonal bands were always absent. All patients received first line immunotherapy, with resolution of SE only in one. Eight patients received second line immunotherapy, with partial improvement in two. Two patients had antibodies against neuronal surface proteins (pending to characterize) visible only with human iPSCs-derived neurons.

Conclusion: Most patients (92%) with c-NORSE did not have novel unknown neuronal antibodies reacting with human iPSC-derived neurons, indicating that underlying mechanisms are probably not antibody-mediated.

Disclosure: Nothing to disclose.

EPR-065 | Autopsies Conducted on Epilepsy Cases: Most of them are SUDEP

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Background and Aims: Sudden unexpected death in epilepsy (SUDEP) is the most devastating complication of epilepsy. Recognizing clinical and autopsy findings pose challenges. This study aims to elucidate the pathogenesis and risk factors of SUDEP.

Methods: We analyzed epilepsy-related deaths between 2009 and 2019, evaluated by our Forensic Medicine Specialty Board, using demographic, autopsy data, and witness statements.

Results: For 108 cases (69% male), average age at death was 36.5±11.7 years, 94% had a diagnosed epilepsy, 66% were found deceased. Autopsies, conducted in 94% of cases, revealed the cause of death as SUDEP in 66%, non-SUDEP in 18%, possible SUDEP in 9%; SUDEP+ in 5%; and nearSUDEP in 2%. Among the 88 cases within the SUDEP spectrum, 80% had clues suggesting a pre-death seizure. Upon examining provoking factors, 38% of cases were found in the prone position, 13% had infections, 9% experienced sleep deprivation, 17% had medication nonadherence, and 3% had a history of alcohol&substance use. In 36% of cases, no antiepileptic drugs were detected in body fluids. Remarkably, 41% of SUDEP spectrum cases showed lividity on the body's front, contrasting with 7% in non-SUDEP cases, and 66.7% had residual urine in the bladder, contrasting with 25% ($p=0.011$, $p=0.047$ respectively).

Conclusion: The study shows most epilepsy-related deaths examined fall within the SUDEP spectrum, with findings like pre-death seizures, anterior lividity, and residual urine potentially serving as SUDEP indicators. Despite these correlations, no definitive autopsy features uniquely identify SUDEP, highlighting the need for further investigations.

Disclosure: This study has been presented in 59th Turkish National Neurology Congress.

EPR-066 | Prognostic factors in refractory and super-refractory status epilepticus: A retrospective review

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Background and Aims: Refractory Status Epilepticus (RSE) and super-refractory (SRSE) are challenging to treat, posing complex management issues for patients.

Methods: Retrospective study with analysis of potential prognostic factors in patients with RSE and SRSE hospitalized from 2019 to 2023 with the objective of identifying prognosis-influencing factors.

Results: 47 patients were included, 55.3% female. The mean age was 63.3 (±18.9) years, with a mean pre-admission mRankin of 2 (±1.6). The mean score on the Status Epilepticus Severity Score (STESS) at admission was 4.6 (±1.4). Cerebrovascular disease was the leading etiology (21.3%). Overall mortality was 68.1%. 51.1% of patients underwent at least one burst-suppression (BS) cycle. The STESS scale score showed a linear correlation with mRankin at 3 months ($r=0.64$). The major predictors of death were age ($p=0.05$) and the presence of non-convulsive SE ($p=0.042$). Patients who underwent BS had a lower mortality rate (45.8% vs. 91.3%, $p<0.001$), even when age-adjusted ($p=0.05$). In patients undergoing anesthetic treatment, 11 had RSE and 13 SRSE; no significant mortality differences (36.4% vs. 53.8%, $p=0.39$) or mRankin variations at 3 months (2.14 vs. 2.17, $p=0.97$) were observed between groups.

Conclusion: This study shows that patients with lower STESS scores have lower mortality and disability. It also highlights that the implementation of BS reduces mortality, regardless of age. In patients undergoing anesthetic treatment, there were no significant differences between RSE and SRSE regarding morbi-mortality. We believe that the underlying etiology, age, and physical robustness of the patients with SRSE may have contributed to this outcome.

Disclosure: Nothing to disclose.

EPR-067 | Abstract withdrawn

EPR-068 | Epilepsy Trends in Kazakhstan: A Retrospective Longitudinal Study of Data from UNEHS 2014–2020

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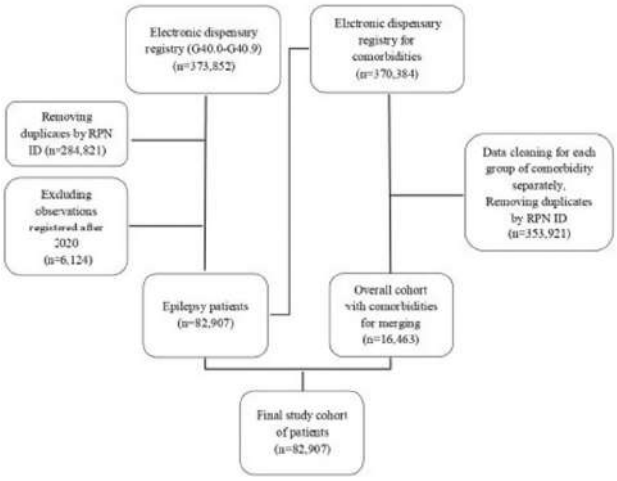
Background and Aims: There is limited epidemiological data for Central Asia. Kazakhstan is the largest country in this region. The purpose of this study was to fill the gaps in examining the incidence, prevalence, DALYs, and mortality-associated factors of epilepsy

Methods: Using the Unified National Electronic Health System of Kazakhstan over a seven-year span, we explored epidemiology, DALYs, and all-cause mortality. Regression models using Cox proportional hazards were used to analyze the sociodemographic, mental, behavioral, and neurological factors affecting survival

Flow chart of the cohort selection process from the Unified National Electronic Health System (UNEHS).



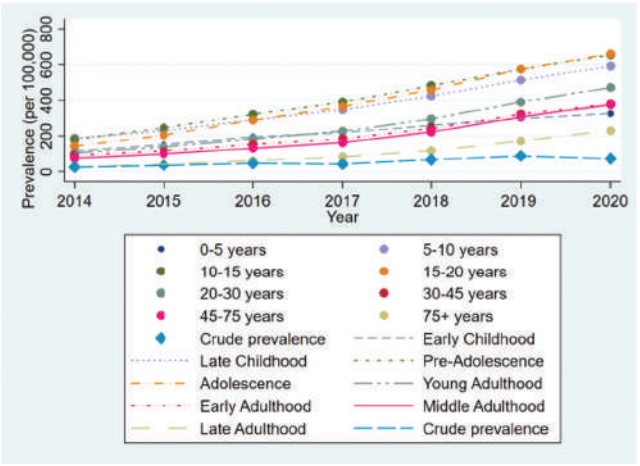
Flow chart.

Results: The total cohort comprised 82,907 patients, with a significant increase in the incidence of epilepsy from 26.15 in 2014 to 88.80 in 2020. Similar trends were observed in the prevalence rates, which tripled from 26.06 to 73.10. The oldest (≥75) and youngest (0–5 years) age groups had the highest statistics. While mortality rates fluctuated, the elderly and children had the greatest rates of 9.97 and 2.98 per 1000 PY respectively. DALYs revealed a substantial disease burden, with 153,532 DALYs being lost during the study period. A few comorbidities, such as cerebral palsy (aHR 2.23) and central nervous system atrophy (aHR, 27.79), markedly elevated all-cause mortality. Furthermore, extrapyramidal and movement disorders (aHR 2.16, $p=0.06$) and demyelinating diseases of the CNS (aHR 6.36, $p=0.06$) showed a trend toward increased mortality risk. Notably, none of the mental or behavioral comorbidities was associated with mortality.

Association of comorbidities with all-cause mortality in epilepsy patients

Variables	Crude HR	p-value	Model 1. Adjusted HR and 95% CI	p-value	Model 2. Adjusted HR and 95% CI	p-value
Organic, including symptomatic, mental disorders (F00-F09)	1.10 (0.79-1.54)	0.55	0.83 (0.59-1.17)	0.30	0.83 (0.59-1.16)	0.28
Mental and behavioural disorders due to psychoactive substance use (F10-F19)	2.47 (1.41-4.30)	0.001	1.53 (0.87-2.70)	0.14	1.56 (0.88-2.76)	0.12
Mental retardation (F70-F79)	0.47 (0.17-1.27)	0.14	0.68 (0.25-1.82)	0.44	0.58 (0.21-1.59)	0.29
Inflammatory diseases of the central nervous system (G00-G09)	1.13 (0.16-8.05)	0.90	1.85 (0.12-6.03)	0.87	0.84 (0.12-5.99)	0.86
Systemic atrophies primarily affecting the central nervous system (G10-G14)	25.41 (3.56-180.9)	0.001	28.36 (3.96-202.9)	0.001	27.79 (3.87-199.19)	0.001
Extrapyramidal and movement disorders (G20-G26)	5.67 (2.53-12.72)	<0.001	2.18 (0.96-4.92)	0.06	2.16 (0.96-4.90)	0.06
Demyelinating diseases of the central nervous system (G35-G37)	7.62 (1.07-54.25)	0.04	6.08 (0.85-43.47)	0.07	6.36 (0.89-45.53)	0.06
Episodic and paroxysmal disorders (G43-G47)	0.94 (0.23-3.77)	0.93	0.61 (0.15-2.45)	0.49	0.58 (0.15-2.37)	0.46
Diseases of myoneural junction and muscle (G70-G73)	7.58 (1.06-54.02)	0.04	6.48 (0.91-46.36)	0.06	5.57 (0.77-40.15)	0.08
Cerebral palsy and other paralytic syndromes (G80-G83)	1.23 (0.64-2.39)	0.53	2.10 (1.07-4.12)	0.03	2.23 (1.12-4.44)	0.02
Other disorders of the nervous system (G90-G99)	1.03 (0.51-2.08)	0.93	0.93 (0.46-1.87)	0.84	0.88 (0.43-1.79)	0.73

Association of comorbidities with all-cause mortality in epilepsy patients.



Prevalence 2014–2020.

Conclusion: The findings highlight the significant burden, especially in younger age groups, and it was observed concerning comorbidity patterns, particularly the high prevalence of mental and behavioral conditions in the epilepsy cohort

Disclosure: Nothing to disclose.

EPR-069 | Brain 18F-FDG PET: an efficient tool at the initial diagnosis of non-lesional late-onset epilepsy

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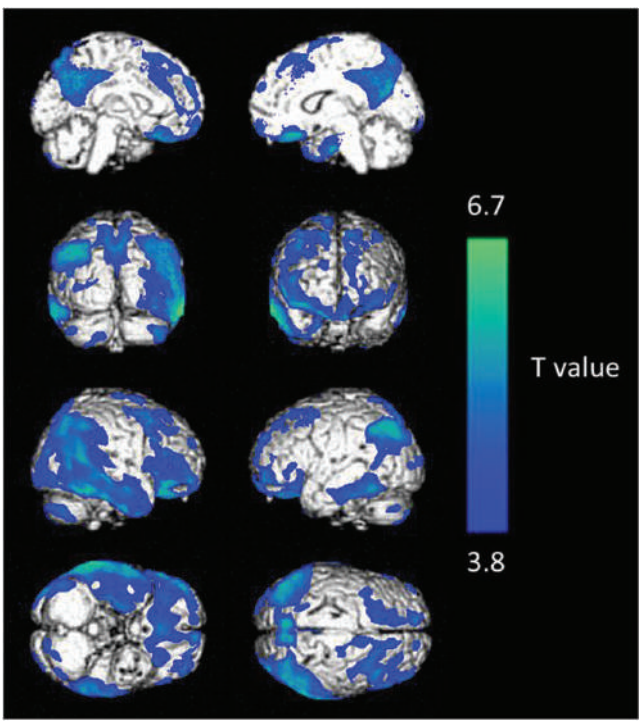
Background and Aims: This study evaluates the diagnostic performance and prognostic value of brain 18F-FDG PET at the initial diagnosis of patients with non-lesional late-onset epilepsy (NLLOE).
Methods: Eighty-seven, newly diagnosed NLLOE patients, >50 yo, with brain 18F-FDG PET scans, were prospectively included from June 2017 to January 2021 at the University Hospital of Nancy (maximum follow-up; 3 years) and categorized by clinical NLLOE subtype aetiology. Brain 18F-FDG PET scans were analysed using a combined visual and semi-quantitative approach at the individual level and a quantitative voxel-to-voxel comparison to sex- and age-matched controls at the group level.
Results: A normal 18F-FDG PET was observed in 46% of patients, with the final diagnosis of 88% of these patients excluding a neurodegenerative or inflammatory disorder. A normal 18F-FDG PET had a negative predictive value of 87% for a cognitive decline at follow-up. Moreover, a PET hypometabolic pattern suggestive of a neurodegenerative disorder had a 77% accuracy of identifying a cognitive decline at follow-up. At the group level, 18F-FDG PET identified a typical neurodegenerative pattern in patients with neurodegenerative disorders (p-voxel <0.001, corrected for cluster volume).



Statistical Z-score maps of brain 18F-FDG PET hypometabolism in the NDS-PET group represented in 3D rendered volume. The Z-score maps show the regions with significantly reduced metabolism compared to the normal database.
Conclusion: A 18F-FDG PET as part of the initial diagnosis of NLLOE patients has a significant impact on both NLLOE diagnosis and cognitive prognosis. For almost half of NLLOE patients, a normal 18F-FDG PET scan is able to exclude, neurodegenerative and inflammatory epilepsy aetiologies as well as a future cognitive decline, with a high level of certainty. In addition, 18F-FDG PET can identify neurodegenerative diseases with high diagnostic performances.
Disclosure: None.

EPR-070 | Psychosocial problems of epilepsy in Georgia – changes over the time (preliminary data)

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Background and Aims: The low quality of life in people with epilepsy (PWE) is largely determined by the problems of the patient's education, employment, social relations, family formation and other barriers, that were dramatically lower in the late 90s in Georgia (1). Since the beginning of the 21st century, many measures have been implemented to solve the psychosocial problems of people with epilepsy, although the actual results of these measures are unknown. Aim: To assess the dynamics of psychosocial problems of PWE in Georgia.
Methods: The study was conducted at the Institute of Neurology and Neuropsychology using the adapted survey QOL31, that was used in previous study (1). 305 PWE (Female – 171), aged 18–65 years, without severe cognitive dysfunctions were assessed. Indicators of patients' education, employment, marital status, satisfaction with their own health and social relationships were evaluated.
Results: Compared to the previous date indicators of the higher education (from 19.84% to 44.5%), employment (from 17% to 56%), general emotional well-being (from 9.39% to 80%) and in terms of social relations (from 15.1% to 88.9%) was significantly increased in PWE. The cases of satisfaction with one's own situation increased from 9.1% to 45%; As on marriage rate remained virtually unchanged (48.2% and 47%, respectively).
Conclusion: In general, the psychosocial problems of PWE have improved in Georgia, although some of the problems needs more active anti-stigma actions. Acknowledgments: The study was performed on the bases of Ph.D. educational programs grant funding from Sh. Rustaveli National Science Foundation of Georgia (PHDF-23-1911).
Disclosure: Nothing to disclose.

Headache 1

EPR-071 | Anti-CGRP Monoclonal Antibody Response After Switching (AMARAS) study

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Background and Aims: We aimed to evaluate whether migraine patients with lack of response to a first anti-CGRP monoclonal antibody (mAb) respond to a second mAb. Thus, the effectiveness was evaluated between weeks 8–12 of treatment, compared to the month prior to the mAb onset.
Methods: Observational multicenter study with an ambisective cohort design. Adult patients with a confirmed diagnosis of migraine were included if they were treated with a mAb after the failure to a prior mAb. A structured questionnaire was administered, encompassing demographic and clinical variables. All consecutive patients were screened for eligibility. The endpoints recommended by the International Headache Society were evaluated. The study was approved by the Ethics review board (PI-22-2658) and the study protocol is public (NCT05785988).
Results: In 247 patients a second mAb was used, 48 discontinued due to inadequate tolerability: constipation ($n=17$), injection site reactions ($n=12$), lightheadedness ($n=10$); 10 withdrew the consent and 189 provided valid data. Patients were aged 49.8 (SD: 11.3) years and were female in 86.2% cases. Migraine subtype corresponded to chronic (85.2%), with aura (20.6%), with a median number of prior preventive drugs of 6 [IQR: 5–7]. Between weeks 8–12, 30%, 50% and 75% responses were achieved by 32.3%, 19% and 5.3% patients. The mean reduction of headache days per month was 3.6 (SD: 8.3).
Conclusion: Lack of efficacy to anti-CGRP mAbs does not preclude the lack of efficacy to a second mAb, albeit only a minority of patients respond. Predictors of response are needed to optimize the patients' selection.
Disclosure: Nothing to disclose.

EPR-072 | Assessing Migraine Stigma in Europe: Insights and Implications for Support

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Background and Aims: Migraine is the most common cause of neurological referral in most practices. Stigma around migraine has been discussed broadly over some time. We sought to evaluate the stigma of migraine patients in Europe
Methods: The European Migraine & Headache Alliance (EMHA), a patient association umbrella alliance, collaborated with migraine experts to develop an anonymous and voluntary survey. Stigma Scale for Chronic Illness (SSCI) scales were used to assess migraine stigma and correlated with frequency, severity, and medication use. The survey was distributed through EMHA's European network. Data were analyzed in Excel.
Results: People with migraine ($n=4{,}210$) from around Europe completed the survey: Spain 22%, France 12%, Italy 11%, Germany 10%, Portugal 8%, and were predominantly women aged 25–64 years. Of respondents, 90% were migraine sufferers, with 50% considering themselves severe and 57% having ≥8 migraine days/month. Medical and workplace settings were identified as primary sources of stigma. Of responders, 74% felt medical professionals lacked an understanding of what it means to live with migraine, and 79% reported a negative impact on their careers. Migraine stigma was seen as more pronounced than for other neurological conditions but less than mental health conditions. Terms, such as severe, had no clear unifying definition, and diagnostic terminology, such as chronic migraine were poorly understood.
Conclusion: Migraine stigma impacts personal and professional lives. Broader education on migraine and changes in terminology used may limit stigma and improve quality of life people with migraine
Disclosure: Nothing to disclose.

EPR-073 | Prevalence and characteristics of women with menstrually-related migraine in the 2022 National Health & Wellness Survey

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Background and Aims: Menstrually related migraine (MRM) occurs in approximately 60% of women with migraine and is associated with attacks of longer duration, greater severity, and symptom burden than non-MRM attacks. There is a lack of evidence on the real-world utilization of migraine treatments among women with MRM.
Methods: This retrospective cross-sectional study used the five-country 2022 European National Health and Wellness Survey (NHWS, Cerner Enviza) to identify female participants who self-reported having a migraine diagnosis by a doctor and migraines related to menstruation. Respondents reported their migraine frequency, disability via the Migraine Disability Assessment Test (MIDAS), and current migraine treatments.
Results: Of 18.9 million women with diagnosed migraine, 10.6 million were pre-menopausal, and MRM was reported by nearly half (47.0%; mean age [SD], 35.5 [9.4] years). For women with MRM versus those without, 51.5% (vs. 42.4%) had moderate-to-severe migraine-specific disability, although monthly migraine (3.7 [5.0] vs. 3.5 [5.9] days) and headache frequencies were similar (7.1 [6.8] vs. 8.2 [7.5] days). Women with MRM had higher use of prescription migraine treatments (56.7 vs. 48.6%); non-steroidal anti-inflammatory drugs (60.4%), triptans (32.2%), and opioids (18.0%) were the most commonly used acute treatments. A smaller proportion of women with MRM used preventive treatments compared to women without MRM (16.6% vs. 19.1%).
Conclusion: The prevalence of MRM was 47.0% among pre-menopausal women. Women with MRM reported greater migraine-related disability and prescription medication use but had less preventive treatment use compared to their non-MRM counterparts.
Disclosure: GMT reports consultancy or industry support from Abbvie, Lilly, Lundbeck, Novartis, Pfizer, Teva, and Interactive Studios BV, and independent research support from the European Community, Dutch Heart and Brain Foundations, Dutch Research Council, Dioraphte, and the International Retinal Research Foundation. ML, AJ, JC, KHB, JY, LA, and JB are employees of Pfizer.

EPR-074 | Long-term improvements following >=50% migraine response in eptinezumab-treated patients with migraine

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Background and Aims: The DELIVER trial examined long-term (72-week) patient response to eptinezumab preventive treatment. For eptinezumab-treated patients demonstrating an initial migraine response (i.e., response over the placebo-controlled period, Weeks [Wks] 1–12), changes from baseline in monthly migraine days (MMDs), 6-item Headache Impact Test (HIT-6) total score, presenteeism, and percentage of severe migraine attacks are reported.
Methods: DELIVER included patients with migraine and 2–4 prior preventive migraine treatment failures, with the long-term population ($n=865$) including those completing the 24-week placebo-controlled period and continuing into the 48-week dose-blinded period. Post hoc analysis followed eptinezumab-treated patients with a >=50% migraine response during the first dosing interval (Wks1–12) across subsequent 12-week dosing intervals for the 72-week trial duration.
Results: Over Wks1-12, 123/286 (43.0%, 100 mg) and 141/282 (50.0%, 300mg) eptinezumab-treated patients in the long-term full analysis set experienced >=50% migraine response. Eptinezumab-treated patients with initial >=50% migraine response showed sustained reductions in migraine frequency, with mean reductions of 7.8 (100 mg) and 8.1 (300 mg) MMDs over Wks1–12 and 8.2 (100 mg) and 8.6 (300 mg) over Wks61–72. Also shown were sustained improvements from baseline in headache-related impact (HIT-6 total score: baseline 66.1–66.5; reduction 13.3–15.1 [Wk12] and 14.1–15.9 [Wk72]); presenteeism-affected working time (baseline 52.2%–52.4%; reduction 35.7%–37.8% [Wk12] and 34.7%–35.4% [Wk72]); and percentage of severe migraine attacks (baseline 45.0%–47.9%; reduction 28.7%–29.5% [Wks1–12] and 29.6%–33.4% [Wks61–72]).
Conclusion: Patients with >=50% migraine response following one eptinezumab dose experienced improvements over Wks1–12 in MMDs, headache-related impact, presenteeism, and percentage of severe migraine attacks. Benefits of eptinezumab (100mg and 300mg) were maintained for 72 weeks.
Disclosure: MA-personal fees from AbbVie, Amgen, Eli Lilly, GlaxoSmithKline, Lundbeck, Novartis, Pfizer, and Teva Pharmaceuticals during the conduct of the study. Research support-Lundbeck Foundation, Novo Nordisk Foundation, and Novartis. Associate editor of Cephalalgia, associate editor of The Journal of Headache and Pain, and associate editor of Brain. SA-Lundbeck employee. XYL-Lundbeck employee. LPB-Lundbeck employee. BP-Lundbeck employee RBL-has been a consultant, advisory board member, and/or has received honoraria from Allergan/

AbbVie, American Academy of Neurology, American Headache Society, Amgen, BioDelivery Sciences, Biohaven Pharmaceuticals, BioVision, electroCore, Eli Lilly, GlaxoSmithKline, Impel, Lundbeck Seattle BioPharmaceuticals, Merck, Pernix, Pfizer, Supernus, Teva, Trigemina, Vector, and Vedanta; has stock or stock options in Biohaven Pharmaceuticals and Manistee; and has received research support from Amgen, the FDA, the National Headache Foundation, and the NIH. JA-Consulting/Honoraria-Abbvie, Amgen, Aeon (data monitoring board 2022), Axsome, Biohaven, Biodelivery Scientific International (2022), Eli Lilly, Glaxo-Smithkline, Lundbeck, LinPharma, Impel, Ipsen, Merz, Miravio, Pfizer, Neurolief, Neso, Gore, Satsuma, Theranica, and Teva. Clinical trials grant to institution- Abbvie (2021), Biohaven (2021), Eli Lilly (2021), Satsuma (2022), Zosano (2021), Parema, and Ipsen. Editorial boards/steering committees- Medscape, SELF Magazine (medical editor).

EPR-075 | Insufficient sleep cause cognitive impairment in interictal migraine patients

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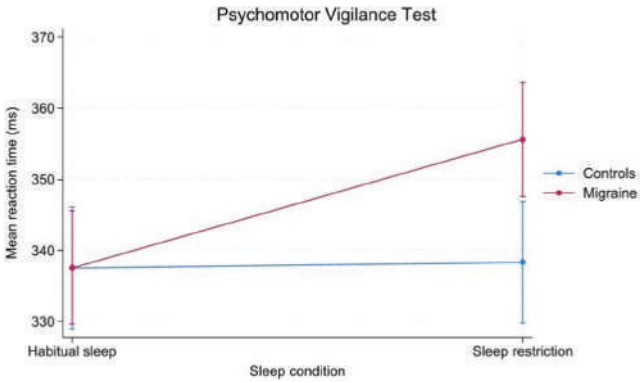
Background and Aims: There is a well-known, but unexplained connection between migraine and sleep. Whether migraine patients are more prone to cognitive effects of insufficient sleep between attacks is not known. We aimed to investigate attention as a measure of cognitive function after insufficient sleep, both in migraine patients and healthy controls.

Methods: We collected data from two studies with a corresponding study design. A total of eighty-five interictal migraine patients and sixty-three controls were examined after both two nights of eight-hour habitual sleep (HS) and two nights of four-hour restricted sleep (SR). All subjects performed a 10-min psychomotor vigilance test (PVT) the morning after the second sleep-controlled night. Sleep time was measured with actigraphy and a sleep diary. We applied linear mixed models to evaluate if the effect of sleep condition/measured sleep time differed between patients and controls.

Results: We found a significant effect of the interaction diagnosis x sleep condition for mean reaction time during PVT ($p=0.001$). Mean reaction time was increased after SR in the migraine group (estimated marginal mean; HS 337.6 ms, SR 355.6 ms), but not in the control group (estimated marginal mean; HS 337.6 ms, SR 338.4 ms). The corresponding interaction was also significant when exchanging sleep condition with measured sleep time ($p=0.016$).



Mean reaction time in milliseconds (ms) during a 10-min psychomotor vigilance test.

Conclusion: Insufficient sleep cause greater cognitive impairment in form of reduced attention in migraine patients compared to healthy controls.

Disclosure: Nothing to disclose.

EPR-076 | CGRP levels in peripheral blood in patients with idiopathic intracranial hypertension and migraine

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Background and Aims: Calcitonin gene-related peptide (CGRP) plays a dominant role in migraine. This prospective study was designed to investigate CGRP levels in patients with idiopathic intracranial hypertension (IIH) and compare the results of migraine patients and healthy controls (HC). As a second objective, CGRP levels obtained from IIH patients defining sustained headache after the resolution of papilledema were compared with those not defining post-IIH headache.

Methods: Thirty-six patients with IIH, 36 with episodic migraine (EM), 18 with chronic migraine (CM), and 36 HC were included in the study. CGRP levels were studied from blood samples obtained from the antecubital vein by using a commercial ELISA kit.

Results: Serum CGRP levels of the patient groups were significantly higher than the HC ($p<0.001$). As compared with controls, both CM (p Adj <0.001) and IIH (p Adj $=0.039$) had significantly increased levels of CGRP. Levels recorded from EM patients did not differ from the HC (p Adj $=0.661$). In 16 IIH patients, persistent headache was reported after the normalization of intracranial pressure (ICP). Twenty patients did not report post-IIH headaches. Comparison of serum CGRP levels of these two groups revealed significantly higher CGRP levels in patients with sustained headaches obtained from blood samples both at the initial and control visit (p Adj <0.001).

Conclusion: CGRP levels of the patient groups were higher than the HC. High levels recorded in patients with IIH indicates the role

of CGRP in IIH-related headache and even higher levels in patients with sustained headache after normalization of ICP strengthens this finding.

Disclosure: Nothing to disclose.

EPR-077 | Sexuality and sexual function in females with migraine versus controls

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Background and Aims: For females, migraine traditionally has been assumed to convey a relative decrease in libido. We compared the level of sexuality and various aspects of sexual function in two female migraine populations relative to a matched female population without migraine.

Methods: A consecutive series of heterosexually self-identifying and sexually active female patients ages 25–45 receiving care at a university-based headache clinic for migraine were asked to complete anonymously a set of surveys that included the Female Sexual Function Inventory (FSFI), From a general population sample we recruited females similar to the migraine group in age, race/ethnicity, marital status, educational background and socioeconomic status and asked them to complete the same surveys.

Results: In addition to 150 clinic-based migraine subjects (group 1) we evaluated 150 matched migraine-free controls (group 2) and 67 individuals with migraine from the general population (group 3). Relative to the control subjects (group 2), the clinic-based migraine group recorded a significantly higher mean FSFI score ($p < 0.05$). Patients with EM reported a higher monthly frequency of intercourse and a higher likelihood of intercourse resulting in orgasm. The mean FSFI score for the clinic-based migraine subjects did not differ significantly from the score for the 67 migraine patients from the general/non-clinic population (group 3). Mean FSFI scores from all three groups were above the level considered indicative of sexual dysfunction.

Conclusion: We found that heterosexually self-identifying and sexually active females with migraine reported a higher level of self-perceived sexuality and more positive sexual function than matched controls free of migraine.

Disclosure: None

EPR-078 | Corticosteroids and Galcanezumab in medication overuse headache: A three-arm head-to-head prospective cohort study

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Background and Aims: Medication Overuse Headache (MOH) is a condition where pain relief medications cause chronic headaches due to excessive use. Recent advancements highlight the effectiveness of preventive treatments like anti-CGRP monoclonal antibodies. Current strategies combine medication withdrawal and preventive treatments, with corticosteroids traditionally used to ease withdrawal symptoms.

Methods: This is a prospective three-arm observational cohort study comparing the effectiveness and safety of galcanezumab alone, galcanezumab plus prednisone and prednisone alone for the treatment of MOH. We enrolled 75 patients. Prednisone was administered at an initial dose of 50 mg daily, and then tapered off over 28 days. Duration of follow-up was 3 months.

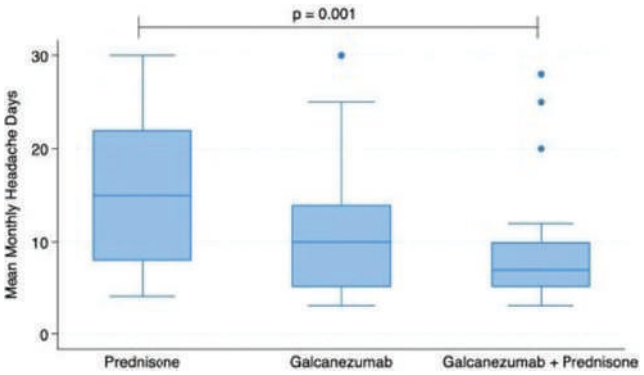
Results: All treatments proved effective ($p < 0.001$). We found a significant reduction of mean monthly days with headache in the Galcanezumab plus Prednisone group (baseline: 25, IQR: 20–30; after 3 months: 7, IQR: 5–10), in the Galcanezumab group (baseline: 25, IQR: 20–30; after 3 months: 10, IQR: 5–14) and in the Prednisone group (baseline: 20, IQR: 20–28; after 3 months: (median: 15 days, IQR: 8–22 days). Patients treated with Prednisone reported a higher incidence of side effects ($p = 0.002$).

Table 1 - Patients characteristics

	Overall (n = 75)	Group 1 (n = 25)	Group 2 (n = 25)	Group 3 (n = 25)	p-value
Age (years)					
Median	48	48	46	49	0.846
25th-75th	38-56	37-57	38-62	39-55	
Disease Duration (months)					
Median	23	24	26	22	0.957
25th-75th	13-33	12-34	9-33	17-30	
Sex, n (%)					
Female	58 (77.3)	18 (72.0)	21 (84.0)	19 (76.0)	0.694
Male	17 (22.7)	7 (28.0)	4 (16.0)	6 (24.0)	
Comorbidities, n (%)	42 (56.0)	13 (52.0)	15 (60.0)	14 (56.0)	0.931
Baseline Values					
Migraine days	25 (20-30)	25 (20-28)	25 (20-30)	25 (20-30)	0.788
MIDAS	65 (55-78)	66 (58-72)	64 (59-81)	65 (53-81)	0.914
Days of Acute Medication Intake	38 (25-60)	43 (25-55)	35 (25-55)	30 (30-60)	0.991
Medication Type, n (%)					
FANS	58 (77.3)	18 (72.0)	21 (84.0)	19 (76.0)	0.752
FANS + Triptans	1 (1.3)	1 (4.0)	0 (0.0)	0 (0.0)	
Opiates	1 (1.3)	0 (0.0)	0 (0.0)	1 (4.0)	
Triptans	15 (20.0)	6 (24.0)	4 (16.0)	5 (20.0)	

Legend. Group 1 = Prednisone; Group 2 = Galcanezumab; Group 3 = Prednisone + Galcanezumab

Demographic and Baseline Features.



Mean Monthly Days Reduction of Headaches.

Conclusion: Our study indicates that both Galcanezumab and Prednisone effectively decrease the frequency of headaches in patients with MOH. The combined usage of these treatments showed the highest reduction in mean monthly headache days. However, treatment with Prednisone determined a significant rate of adverse events, therefore we suggest its use only in unresponsive patients. In all other patients Galcanezumab appears to be a safe and effective option.

Disclosure: Nothing to disclose.

EPR-079 | Repeated onabotulinum Toxin A injections towards the sphenopalatine ganglion in chronic cluster and chronic migraine

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Background and Aims: This study explores onabotulinum toxin A (BTA) injections towards the sphenopalatine ganglion (SPG) in treatment-resistant chronic migraine (CM) and chronic cluster headache (CCH).

Methods: We included patients who had received at least one injection and completed headache diaries. We administered 25 units of BTA with navigated injections towards the SPG in local anaesthesia. Safety data were gathered from prior pilot trials and clinical records.

Results: The study involved 12 CM patients and 31 CCH patients. After a single injection, 81% of CM and 69% of CCH achieved a 50% reduction. Between weeks five and eight after injection, CM patients experienced a significant decrease of 9 moderate-to-severe headache days per month, while CCH patients saw an 8.9-attack reduction per month ($p < 0.001$). The 50% response rates persisted consistently over four consecutive injections in both groups, ranging between 67 and 81% in CM and 69%–89% in CCH. In the safety analysis, we evaluated 261 injections, and 123 linked adverse events (AE). One serious AE was reported with hospitalisation for investigation of facial weakness. The most frequent AEs was jaw pain/weakness ($n = 35$), localized pain/swelling the injection site ($n = 22$), and mild intermittent visual disturbances ($n = 28$). Four patients experienced facial weakness, and five reported transient diplopia. All these side effects resolved, with most resolving within 12 weeks, and none resulted in patients refusing further treatment.

Conclusion: This open-label study demonstrates that BTA injections targeting the SPG effectively treat both resistant CM and refractory CCH, providing sustained relief for at least three months.

Disclosure: Dr Bratbak and Prof Tronvik may benefit financially from a commercialization of a proposed treatment targeting the SPG and the intervention device used to perform the treatment through intellectual properties rights and has consulted for Man & Science within the past 12 months.

Movement disorders 1

EPR-080 | The phase 3 PROOF-HD trial demonstrates efficacy in Huntington disease participants without antidopaminergic medications

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Background and Aims: The PROOF-HD trial evaluated the safety and efficacy of pridopidine (45mg bid) in patients with early HD (TFC>7).

Methods: Primary and key secondary endpoints were change to week 65 in total functional capacity (TFC) and clinical progression (cUHDRS)(respectively). Other endpoints included cognition (SWR), motor (Q-Motor) and Quality-of-Life (HD-QoL). Prespecified subgroup analyses excluded participants on antidopaminergic medication (ADMs)(neuroleptics and anti-chorea medications).

Results: Pridopidine was well tolerated with a safety profile comparable to placebo. The primary and key secondary endpoints were not met in all patients. Nominal p-values are reported. In analyses excluding participants on ADMs (placebo $n = 99$, pridopidine $n = 79$), the placebo group showed an expected decline in all measures. Pridopidine shows improvement from baseline in cUHDRS at week 26 (Δ0.46, $p = 0.006$), week 39 (Δ0.60, $p = 0.003$), and week 52 (Δ0.43, $p = 0.04$) with sustained benefit to week 78 (Δ0.50, $p = 0.08$). Pridopidine demonstrates an improvement from baseline in SWR at week 26 (Δ3.32, $p = 0.03$), week 39 (Δ4.14, $p = 0.02$), and week 52 (Δ4.22, $p = 0.02$) and maintained to week 78 (Δ2.82, $p = 0.2$) never falling below baseline. In Q-Motor measures, including finger tapping, pridopidine shows improvement from baseline at week 26 (Δ-31.96msec, $p = 0.00008$), week 39 (Δ-22.84msec, $p = 0.04$), and to

week 78 (Δ-34.23msec, $p=0.005$). Pridopidine preserved quality-of-life (HD-QoL) through week 78.

Conclusion: Pridopidine showed improvement over placebo on all endpoints, at every timepoint in participants off ADMs. PROOF-HD is the first trial to demonstrate consistent, meaningful, and sustained benefits on clinical progression in HD.

Disclosure: The PROOF-HD study was sponsored by Prilenia Therapeutics.

EPR-081 | The impact of antidopaminergic medication on longitudinal clinical progression in early Huntington disease (HD)

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Background and Aims: Antidopaminergic medications (ADMs), comprised of anti-chorea medications (VMAT2 inhibitors (VMAT2i)) and neuroleptics (off-label), are used for the symptomatic treatment of HD. No prospective, double-blind studies have assessed the long-term effects of ADMs on disease progression in HD.

Methods: Rates of progression up to six years were assessed in an early manifest population (TFC >=7, DCL=4) from ENROLL-HD using the inclusion criteria of the PROOF-HD study. Each comparison involved a matching group On and Off the medication of interest (On vs. Off). The four comparisons were ADMs ($n=853$ per group), neuroleptics ($n=495$ per group), VMAT2i ($n=198$ per group), and antidepressants ($n=331$ per group). Pairs were matched at baseline using a propensity score constructed with 12 covariates.

Results: Participants on ADMs had faster disease progression across multiple measures including total functional capacity (TFC) ($p<0.001$), symbol digit modalities test (SDMT) ($p<0.001$), Stroop Word test (SWR) ($p<0.001$), and the composite UHDRS (cUHDRS) ($p<0.001$). Similar results were observed, when assessing neuroleptics and VMAT2i alone. On TMS subscales, ADM use was associated with improvement of chorea and, with worsening of bradykinesia ($p=0.001$). Participants on antidepressants showed no difference in progression rate.

Conclusion: ADMs use may be associated with adverse effects that alter disease progression, including cognition and function. Additional analyses will assess the impact of specific ADM medications/doses to identify treatments with minimal impact on disease progression. These observations have important implications for the design, conduct, and interpretation of investigational studies of disease-modifying agents in HD.

Disclosure: Prilenia Therapeutics sponsored this study.

EPR-082 | Subgroup analyses of a phase 3, randomized study of levodopa/carbidopa infusion (ND0612) for Parkinson's patients

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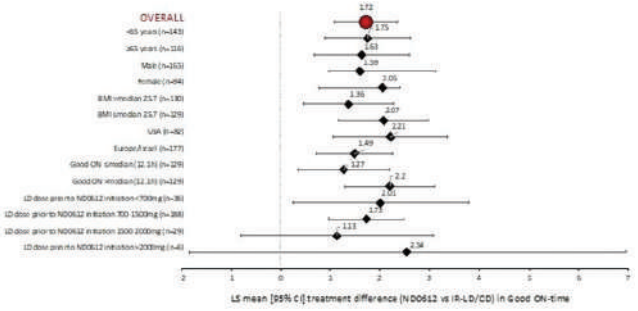
Background and Aims: Primary analyses from this Phase 3 study (NCT04006210) showed that treatment with an investigational, subcutaneous infusion of levodopa/carbidopa (ND0612, doses up to 720/90mg/day) supplemented with oral levodopa, provided an additional 1.72h [95%CI: 1.08h, 2.36h] of ON-time without troublesome dyskinesia (Good-ON) compared with immediate-release levodopa/carbidopa (IR-LD/CD; $p<0.0001$) at week 12. We present efficacy and safety findings for different patient subgroups categorized according to their baseline characteristics.

Methods: This was a randomized, double-blind, active-controlled trial in patients with Parkinson's disease experiencing motor fluctuations. Subgroups were analyzed separately for Good-ON using ANCOVA on multiply imputed data, with additional fixed factors for the subgroup variable and interaction term between the treatment group and subgroup variable. The influence of each subgroup factor was investigated by the interaction terms using Type III p-value combined for multiple imputation.

Results: The adjusted mean [95%CI] treatment effect of ND0612 for Good-ON was homogeneous across the different analyzed subgroups (Figure). Occurrence of adverse events (AEs) and serious AEs were generally consistent across subgroups (age, gender, region, and BMI). Consistent with the data for the full safety population, the most common AEs with ND0612 treatment across all subgroups were infusion site reactions. Overall, no relevant differences between subgroups were observed for AEs of particular interest, including dyskinesia, hallucinations, or falls.

Conclusion: The overall treatment effect was homogenous across different analyzed subgroups. Findings from these analyses support improved Good ON time, consistent with the overall effect of 1.72h, and no relevant differences in safety or tolerability were observed.



Subgroup analyses of Good ON time (primary endpoint).

Disclosure: Funded by NeuroDerm, a Mitsubishi Tanabe Pharma Group Company. Nelson Lopes is employed by NeuroDerm. Werner Poewe is an investigator in the study and he/his institution received fees for participation, and is a consultant for NeuroDerm. Joaquim J. Ferreria is an investigator in the study and he/his institution received fees for participation, and is a consultant for NeuroDerm.

EPR-083 | Onset of efficacy with levodopa/carbidopa infusion (ND0612) for Parkinson's patients

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Background and Aims: Primary results from this Phase 2 study (NCT02577523) demonstrated that 28 days of treatment with 24h subcutaneous levodopa/carbidopa infusion (with investigational ND0612) increased ON-time with no/mild dyskinesia (Good ON) by a LS mean of 3.7 [1.9, 5.6]h ($p < 0.001$) in levodopa-treated patients with Parkinson's disease experiencing motor fluctuations. We report data from a secondary analysis which evaluated the onset of efficacy for the 24h ND0612 regimen ($N = 19$) as rated by patients and clinicians.

Methods: This was a 28-day, open-label study in patients with ≥2.5h/day of OFF-time despite optimized treatment. Patients treated with 24h ND0612 infusion received a daily levodopa/carbidopa dose of 720/90 mg plus adjunct oral levodopa/carbidopa as needed.

Results: Significant improvements versus baseline in daily Good ON-time (LS mean change: 1.83 [0.30, 3.35]h, $p = 0.02$) and ON-time with moderate-severe dyskinesia (LS mean change: −1.36 [−2.29, −0.42] h, $p = 0.006$) were observed at Day 3, as were improvements in Unified Parkinson's Disease Rating Scale motor scores (reduced from 37.4 to 26.6 at 8AM and from 28.3 to 19.2 at 4PM). Overall, 73.7% of patients self-reported an improvement (including 36.8% very much/much improved) in their global impression of health on Day 3. By day 7 of treatment, the proportion of patients who reported achieving a full ON at 9AM increased from 31.6% at baseline to 72.2%.

Conclusion: Results of this analysis demonstrate that significant and clinically relevant improvements in ON-time can be detected as early as Day 3 after ND0612 initiation that further improved by Day 28.

Disclosure: Funded by NeuroDerm, a Mitsubishi Tanabe Pharma Group Company. Nelson Lopes is employed by NeuroDerm. Fabrizio Stocchi is an investigator in the study and he/his institution received fees for participation, and is a consultant for NeuroDerm.

EPR-084 | Characterization of infusion site reactions with 24-hour subcutaneous infusion of ND0612

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Background and Aims: ND0612 is an investigational, subcutaneous infusion of levodopa/carbidopa (max dose 720/90mg/day), supplemented with oral therapies, delivered via 2 cannulas to reduce skin burden. Here, we characterize infusion site reactions (ISRs) reported as adverse events (AEs) in clinical studies.

Methods: Integrated analysis of ISRs reported as AEs in patients with Parkinson's disease treated with a 24h regimen of ND0612 in two Phase 2 studies (NCT02577523 and NCT02726386) and one Phase 3 (NCT04006210) study. 'Grouped preferred terms' were defined for infusion site reactions including nodules, haematoma, swelling, eschar, erythema, infection, and pain.

Results: This analysis included 419 patients with a mean ± SD exposure of 395 ± 471 days [max 6.2 years]. Overall, 369 (88.1%) patients reported at least one ISR-AE, including 15 (3.6%) patients with serious ISR-AEs; 49 (11.7%) patients discontinued due to an ISR. Of 2461 ISRs-AEs, the most common were nodules (1065 events, 43.3%), haematoma (815 events, 33.1%), pain (141 events, 5.7%), and infection (134 events, 5.4%). Most ISR-AEs were mild (2079 events, 84.5%); 347 (14.1%) and 34 (1.4%) were moderate or severe, respectively. Most (88.1%) cases of infusion site infection were mild-moderate in severity, with a median time to resolution of 15 days. Infusion site infection led to discontinuation in only 12 (2.9%) patients.

Conclusion: While ISRs were commonly reported as AEs, 99% of ISR AEs were mild or moderate in severity and resolved with or without treatment. Despite the incidence of ISR events, most patients continued in the trials.

Disclosure: Funded by NeuroDerm, a Mitsubishi Tanabe Pharma Group Company. Werner Poewe is an investigator in the study and he/his institution received fees for participation, and is a consultant for NeuroDerm. Nelson Lopes is employed by NeuroDerm. Rajesh Pahwa is an investigator in the study and he/his institution received fees for participation, and is a consultant for NeuroDerm.

EPR-085 | Neural correlates of bradykinesia in Parkinson's disease: A kinematic and fMRI study

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Background and Aims: Bradykinesia defines a "complex" of motor alterations including reduced movement amplitude and/or speed and tendency to reduce them with task repetition (sequence effect). We aimed at investigating the neural correlates of bradykinesia during a hand-tapping performance in people with Parkinson's disease (pwPD) relative to healthy controls.
Methods: Twenty-five pwPD and 25 age/sex-matched healthy controls were included. Subjects underwent brain functional magnetic resonance imaging (fMRI) including a hand-tapping task: alternatively opening and closing the right hand as fast and ample as possible. Hand-tapping speed and amplitude were measured during fMRI task using an optical fiber data glove.
Results: During the fMRI hand-tapping task, pwPD showed reduced hand-tapping amplitude (hypokinesia) and a greater sequence effect. PwPD relative to healthy controls showed reduced activity of frontoparietal areas, supplementary motor area, middle cingulum, parahippocampus, pallidum, thalamus, and motor cerebellar areas. PwPD showed an increased activity of cognitive areas: superior temporal gyrus, posterior cingulum, and cerebellum crus I. The decreased activity of cerebellum IV-V-VI, vermis IV-V, inferior frontal gyrus, and cingulum correlated with hypokinesia and with the sequence effect.
Conclusion: PwPD showed a worse hand-tapping performance relative to healthy controls. Interestingly, a reduced activity of areas involved in motor planning and timing correlated both with hypokinesia and with the presence of the sequence effect in pwPD. This study has the major strength of collecting objective motor parameters and brain activity simultaneously, providing a unique opportunity to investigate the neural correlates of the "bradykinesia complex".
Funding: Italian Ministry of Health grant GR-2018-12366005.
Disclosure: Nothing to disclose.

EPR-086 | Motion analysis and MRI characteristics in patients with isolated REM sleep behavior disorder

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Background and Aims: Subtle signs in isolated REM sleep behavioral disorder (iRBD) patients may predict conversion to parkinsonisms. We aimed at assessing motor, non-motor, and magnetic resonance imaging (MRI) characteristics in iRBD patients.
Methods: Thirty-eight polysomnography-confirmed iRBD patients and 28 age/sex-matched healthy controls (HC) underwent neurological, cognitive, and motor functional evaluations including Nine-Hole Peg Test (9HPT), 5-Time Sit-To-Stand (5TSTS), Timed Up and Go test (TUG) and 4-Meter Walking Test (4MWT) with and without cognitive dual-task (TUG-COG;4MWT-COG). Spatio-temporal gait parameters during 4MWT(-COG) and TUG(-COG) were collected using a stereophotogrammetric system. We obtained functional connectivity (FC) maps of the main resting-state networks, brain structural alterations using whole-brain voxel-based morphometry, deep grey matter volumes using FIRST, cortical thickness and brainstem volumes using Freesurfer. Analyses were corrected for age, sex and education.
Results: IRBD patients relative to HC showed worse performance during 9HPT and 5TSTS, higher asymmetry of arm-swing amplitude (4MWT) and higher stride length variability (4MWT-COG). Dual-task significantly worsened walking performance of iRBD more than HC. IRBD patients showed non-motor symptoms, worse memory, abstract reasoning and visuo-spatial abilities. IRBD patients showed decreased FC of pallidum and putamen within the basal ganglia network and of occipital and temporal areas within the visuo-associative

network, and reduced volume of the supramarginal gyrus. Structural/functional alterations correlated with clinical changes.

Conclusion: We found subtle motor and non-motor alterations together with structural/functional MRI changes that may represent initial manifestations of neurodegeneration in iRBD patients. Longitudinal data will help developing a conversion prediction model.

Funding: Italian Ministry of Health [grant #RF-2018-12366746]

Disclosure: Nothing to disclose.

EPR-087 | Real-world clinical outcomes for Duchenne muscular dystrophy patients in Europe: results from a multi-national survey

V. Merla[1]; N. Posner[1]; J. Cappelleri[1]; A. Talaga[1]; S. Dukacz[1]; Z. Aslam[1]; E. Morton[2]; E. Chatterton[2]; H. Iqbal[2]; N. Hatchell[2]
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Background and Aims: Duchenne muscular dystrophy (DMD) is associated with progressive loss of muscle function, resulting in loss of ambulation and use of extremities. As data surrounding real-world outcomes for patients with DMD (pDMD) is limited, we aimed to outline clinical outcomes for these patients in Europe.

Methods: Neurologist-reported data were drawn from the Adelphi DMD Disease Specific Programme™, a cross-sectional survey with retrospective data collection in France, Germany, Italy, Spain, and the UK from October 2022–September 2023. Neurologists reported demographics and clinical characteristics of their pDMD. Analyses were descriptive.

Results: 90 neurologists provided data for 564 male pDMD. Mean (standard deviation; SD) age was 15.2 (7.9) years, mean (SD) time since symptom onset was 9.0 (7.5) years, 38% were non-ambulatory, and 21% had ≥1 diagnosed comorbidity. Difficulty climbing stairs (53%), and fatigue (41%) were the most frequently reported motor and non-motor symptoms, respectively. Mean (SD) North Star Ambulatory Assessment (NSAA) and Brooke upper extremity scale scores were 11.8 (9.6) and 2.8 (1.4), respectively. Difference in mean NSAA and Brooke upper extremity scores between ambulatory and non-ambulatory pDMD was 13.4 (16.6 vs. 3.2), and 1.9 (2.1 vs. 4.0), respectively. Mobility/support aids and respiratory aids were used by 73% and 32% pDMD, respectively.

Conclusion: Motor and non-motor symptoms were common, use of supportive aids/devices was high, and clinical testing scores suggested depletion of functional skills in pDMD. This indicates a high disease burden, which was greater for non-ambulatory pDMD. Additionally, this highlights a need for new therapies to address the high clinical burden of DMD.

Disclosure: VM, NP, JCC, AT, SD, and ZA are paid employees/stockholders of Pfizer. EM, EC, HI, and NH are paid employees of Adelphi Real World.

EPR-088 | Impact of Duchenne muscular dystrophy on caregiver employment and quality of life: A real-world survey in Europe

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Background and Aims: Duchenne muscular dystrophy (DMD) has a degenerative nature whereby patients often rely on caregiver assistance. As little is known about the effect of caregiving for people with DMD (pDMD), this study aims to understand the impact on caregiver quality of life (QoL) and employment.

Methods: Data were drawn from the Adelphi DMD Disease Specific Programme™, a cross-sectional survey with retrospective data collection conducted in France, Germany, and Spain from October 2022–September 2023. Caregivers reported demographics, employment status and completed EQ-5D-5L (German tariff), EQ-5D Visual Analogue Scale (VAS) and the Work Productivity and Activity Impairment (WPAI) questionnaire. Analyses were descriptive.

Results: Overall, 99 caregivers had a mean (standard deviation; SD) age of 44.0 (9.9) years, 82% were women and 86% were parents of pDMD. pDMD had a mean (SD) age 12.9 (8.0) years; 68% were ambulatory. Overall, 42% of caregivers were employed (full/part-time) and provided care for a mean (SD) of 50.5 (33.4) hours per week. Caregivers (35%) changed their pattern of work due to caring. In the last seven days, caregiver overall work impairment was 46.6%, percentage impairment while working was 42.9%, work time missed was 5.6%, and activity impairment was 49.4%. Caregiver EQ-5D-5L and EQ-VAS scores were 0.88 (0.1) and 76.0 (15.9), respectively.

Conclusion: Over half of caregivers were not employed, and those who were employed experienced impairment while working. Caregivers also experienced an impact on ability to perform activities of daily living and QoL. This highlights a significant caregiver burden that needs addressing within the treatment and management of pDMD.

Disclosure: VM, NP, JCC, AT, SD, ZA are paid employees/stockholders of Pfizer. EM, EC, HI, and NH are paid employees of Adelphi Real World.

Movement disorders 2

EPR-089 | Blood D-serine levels correlate with aging and dopaminergic treatment in Parkinson's disease

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Background and Aims: We recently described increased D- and L-serine concentrations in the putamen of parkinsonian monkeys and the striatum and cerebrospinal fluid of Parkinson's disease (PD) patients compared to controls. However, data regarding peripheral D-serine levels in PD are scarce. Here, we assessed whether the serum levels of serine enantiomers and the other N-methyl-D-aspartate receptor (NMDAR)-related aminoacids (i) differ between PD patients and controls and (ii) correlate with clinical features and levodopa equivalent daily dose (LEDD) in PD.

Methods: We recruited 83 PD patients and 41 healthy controls (HC). PD cohort underwent an extensive motor, cognitive and quality of life characterization. The serum levels of D- and L-serine, L-glutamate, L-glutamine, L-aspartate, L-asparagine and glycine were determined using High Performance Liquid Chromatography.

Results: In age- and sex-adjusted analyses, no differences emerged in the serum levels of D-serine, L-serine or the other aminoacids between PD and HC. D-serine and D-/Total serine positively correlated with age in PD ($r=0.313$, $p=0.004$ and $r=0.311$, $p=0.004$) but not in HC. Moreover, we found that (i) D-serine and D-/Total serine increase with older age at PD onset ($r=0.379$, $p<0.001$ and $r=0.325$, $p=0.003$) (Fig. 1); (ii) LEDD negatively correlate with D-serine ($r=-0.248$, $p=0.027$) and the other excitatory aminoacids (Fig. 2). Finally, the addition of LEDD as covariate disclosed higher D-serine in PD compared to HC (Table).

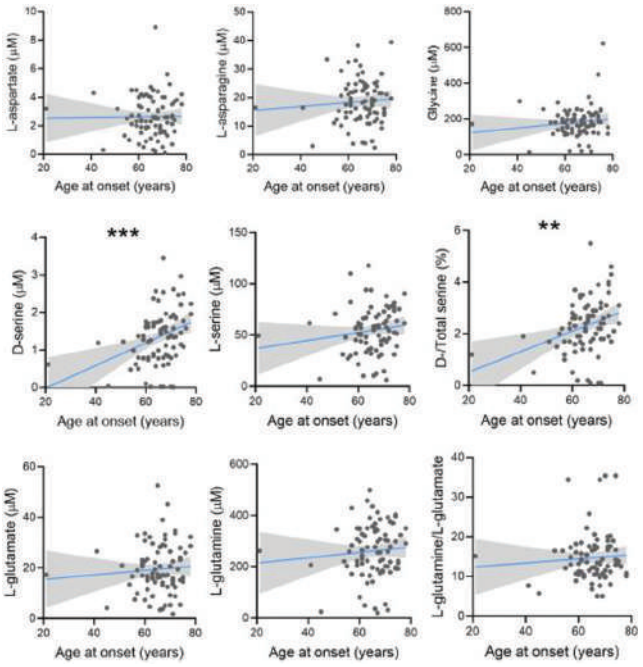

FIGURE 1. Scatterplots representing correlations between age at onset and serum neuroactive amino acid levels in PD group. $^{**}p<0.01$; $^{***}p<0.001$, Spearman's correlation. Blue lines and grey shadows represent the best fit line and its 95% CI.

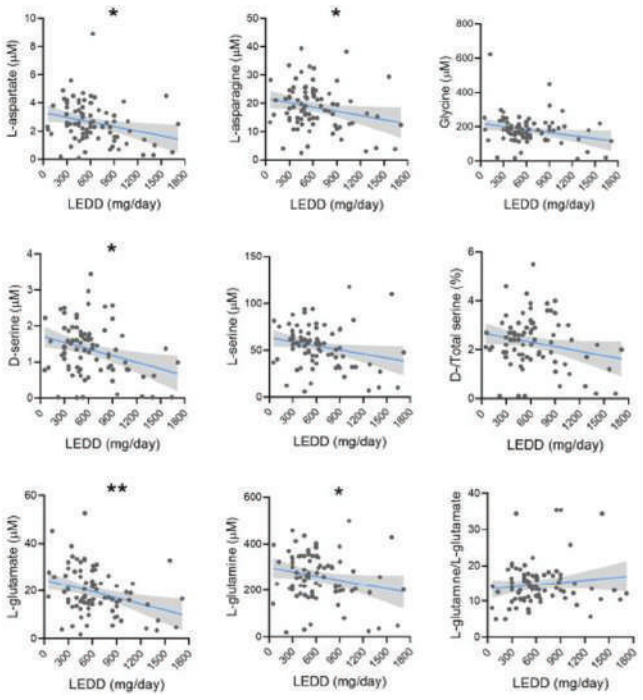

FIGURE 2. Correlations between LEDD and serum neuroactive amino acid levels in PD. $^{*}p<0.05$; $^{**}p<0.01$; age-, sex- and disease duration-adjusted partial correlations. Blue lines and grey shadows represent the best fit line and its 95% CI.

Table. Estimated serum levels of neuroactive amino acids in PD and HC extracted from ANCOVA models adjusted for the effect of age, sex and LEDD. Data are shown as estimated mean (standard error) of amino acids concentration. Significant p-values are shown in bold.

	HC (n = 41)	PD (n = 83)	p[a]
L-aspartate (μM)	2.7 (0.3)	2.9 (0.2)	0.724
L-asparagine (μM)	16.4 (1.6)	19.5 (1.0)	0.159
Glycine (μM)	155.2 (23.5)	194.8 (14.3)	0.206
D-serine (μM)	1.1 (0.1)	1.5 (0.1)	**0.038**
L-serine (μM)	48.9 (4.8)	57.2 (2.9)	0.192
D-/Total serine (%)	2.0 (0.2)	2.4 (0.1)	0.116
L-glutamate (μM)	20.3 (2.2)	21.0 (1.3)	0.792
L-glutamine (μM)	238.4 (22.0)	272.4 (13.5)	0.246
L-glutamine/L-glutamate	13.5 (1.3)	14.2 (0.8)	0.663

[a] PD compared to HC. Two-way ANCOVA with diagnosis and sex as factors; age and LEDD as covariates

Estimated serum levels of amino acids in PD and HC extracted from ANCOVA models adjusted for the effect of age, sex and LEDD. Data are shown as mean (standard error). a, Two-way ANCOVA with diagnosis and sex as factors, age as covariate.

Conclusion: Increased serum D-serine levels represent a putative biochemical signature of PD. The positive correlation between D-serine and age at PD onset supports the hypothesis that D-serine may play a neuroprotective role in PD.

Disclosure: This study was financially supported by Cariplo Foundation (Call 2017 – Scientific Research "Biomedical research on aging-related diseases", grant no. 2017-0575).

EPR-090 | Identification of Parkinson's disease biomarkers in a multi-modal AI framework using raw MRI and clinical data

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Background and Aims: The aims of this study were to develop a 3D Convolutional Neural Network (CNN) based on multimodal MRI to distinguish controls and PD patients and to employ CNN to predict the progression of PD.

Methods: Three cohorts were selected: (1) 86 mild, 62 moderate-to-severe PD patients and 60 controls; (2) 56 mild-PD subjects and 20 controls from PPMI database and (3) 91 mild-PD subjects and 38 controls. All participants underwent an MRI scan at baseline and a clinical evaluation at baseline and at 2-years follow-up. All the mild-PD subjects were classified stable or worsening using a k-means clustering based on baseline and follow-up UDPRS-III value. CNN were applied.

Results: CNN model demonstrated the capability to differentiate moderate-to-severe PD subjects from controls, achieving a good level of performance. Considering moderate-to-severe PD patients relative to controls, the accuracy rate on the test dataset reached nearly 75%, only relying on MRI data for classification. However, considering mild-PD versus controls, the accuracy rate was around 65% on the test set, highlighting challenges in the extraction of discriminative features during the initial stages of the disease. In the differentiation between stable and worsening PD, CNN reached over 70% accuracy rate on the test set by combining raw MRI and clinical data.

Conclusion: By integrating MRI data with clinical and demographic information, our CNN demonstrated promising results and offers a valuable tool for early diagnosis and personalized treatment planning for PD patients. Funding: Italian Ministry of Health (GR-2018-12366005, RF-2018-12366746, GR-2021-12374601).

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SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM.

EPR-091 | Peripheral immune response pattern in a genetic cohort of p.A53T alpha-synuclein Parkinson's disease

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Background and aims: Previous research has shown that inflammatory immune biomarkers including peripheral white blood cell subpopulations differ between Parkinson's disease (PD) patients and healthy controls (HC), with idiopathic PD patients exhibiting higher neutrophil to lymphocyte ratio (NLR). The aim of our present report was to assess the peripheral immune profile in patients harboring the p.A53T alpha-synuclein (SNCA) mutation.

Methods: Data regarding 30 p.A53T SNCA PD patients and 194 HCs were obtained from the database of the Parkinson's Progression Markers Initiative (PPMI). Focus was placed on peripheral immune blood cells subpopulations during the initial study assessment.

Results: NLR, Absolute Neutrophil cell count and Neutrophil to total Leukocytes ratio were increased in the p.A53T SNCA PD group as compared to HCs [2.74 vs. 2.18 ($p < 0.001$), 4.328 x 10^3 cells/μL vs. 3.674 x 10^3 cells/μL ($p = 0.001$), 65.47% vs. 59.55% ($p < 0.001$) respectively]. Absolute Lymphocyte cell count and Lymphocyte to total leukocytes ratio showed a trend towards being decreased in p.A53T PD. Monocyte to total Leukocytes ratio was lower in p.A53T PD ($p = 0.007$) and Neutrophil to Monocyte ratio (NMR) was increased as compared to HCs ($p < 0.001$). Differences in NLR were mainly driven by the male patient subgroup.

Conclusion: Our current study provides evidence of a specific pattern of peripheral immune response in the p.A53T SNCA PD group which aligns well with literature data in idiopathic and other genetic PD forms. Furthermore, given former evidence that alpha-synuclein represents an immune target in PD, we can speculate a putative underlying inflammatory pathway in this archetypal form of genetic synucleinopathy.

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EPR-092 | Safety and efficacy of sublingual apomorphine in Parkinson's patients with or without concomitant dopamine agonists use

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Background and Aims: In Study CTH-301, apomorphine sublingual film (SL-APO) was generally well tolerated and efficacious over the long term as treatment for OFF-episodes in patients with Parkinson's disease. This post-hoc analysis assessed SL-APO in patients from Study CTH-301 with or without concurrent dopamine agonists (DA) use at baseline.

Methods: Study CTH-301 included a dose-optimisation (DO) and long-term safety (LTS) phase. Safety/tolerability assessments included incidence of treatment-emergent adverse events (TEAEs)/DA-related TEAEs, discontinuation rates due to adverse events (AEs), and time to discontinuation due to TEAEs. Efficacy assessments included optimized SL-APO dose, discontinuation rate due to lack of efficacy, changes in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III scores from pre- to post-dose and percentage of patients with a full-ON response within 30 minutes post-dose at weeks 24, 36 and 48.

Results: DA versus non-DA users demonstrated lower incidence of most common (>5%) TEAEs, including DA-related TEAEs, and lower discontinuation rates due to TEAEs in both the DO and LTS phases, and remained longer in the study (median 148.0 vs. 114.0 days; LTS phase) (Table 1). Non-DA users had a lower SL-APO mean dose (18.0 vs. 21.2 mg) and lower discontinuation rate due to lack of efficacy (4.8 vs. 7.2%). For both groups, a clinically meaningful reduction in MDS-UPDRS Part III was reached (Figure 1) and the percentage of patients reporting full-ON response was >75% at all visits (Figure 2).

TABLE 1. Safety/tolerability summary in DA users and non-DA users during the dose-optimisation and long-term safety phases*

Table 1. Safety/tolerability summary in DA users and non-DA users during the dose-optimisation and long-term safety phases*

	Dose-optimisation phase		Long-term safety phase	
	Non-DA users n=146	DA users n=223	Non-DA users n=112	DA users n=193
Most commonly reported AEs (≥5% in any group), n (%)				
Nausea	38 (26.0)	18 (8.1)	41 (36.6)	26 (13.5)
Fatigue	10 (6.8)	5 (2.2)	8 (7.1)	10 (5.2)
Dizziness	15 (10.1)	7 (3.1)	14 (12.5)	3 (1.6)
Headache	14 (9.6)	7 (3.1)	6 (5.4)	6 (3.1)
Somnolence	15 (10.1)	10 (4.5)	11 (9.8)	12 (6.2)
Yawning	22 (15.1)	13 (5.8)	11 (9.8)	9 (4.7)
Mouth ulceration	1 (0.7)	2 (0.9)	8 (7.1)	11 (5.7)
Oral mucosal erythema	5 (3.4)	10 (4.5)	8 (7.1)	13 (6.7)
Vomiting	6 (4.1)	0	8 (7.1)	5 (2.6)
Urinary tract infection	0	0	6 (5.4)	4 (2.1)
Fall	1 (0.7)	3 (1.3)	6 (5.4)	16 (8.3)
Dysgeusia	2 (1.4)	2 (0.9)	7 (6.3)	4 (2.1)
On and off phenomenon	0	1 (0.4)	6 (5.4)	8 (4.1)
Hyperhidrosis	7 (4.8)	1 (0.4)	6 (5.4)	2 (1.0)
Orthostatic hypotension	3 (2.1)	7 (3.1)	7 (6.3)	7 (3.6)
Stomatitis	0	2 (0.9)	5 (4.5)	11 (5.7)
Dyskinesia	6 (4.1)	5 (2.2)	5 (4.3)	14 (7.3)
Discontinuations due to AEs, n (%)	19 (13.0)	6 (2.7)	47 (42.0)	61 (31.6)
p-value	<0.001[4]		0.08929[5]	
DA-related TEAEs[a], n (%)	65 (44.5)	39 (17.5)	68 (58.0)	64 (33.2)
p-value	<0.0001[5]		<0.0001[5]	
Time to discontinuation due to TEAEs, days				
Median (range)	-	-	114.0 (34–560)	148.0 (23–955)
p-value			0.09245[5]	

*The analysis included de novo patients only (i.e. those who were exposed to the study drug for the first time); [a]DA-related TEAEs were defined by the authors; [4]Chi-squared test; [5]Wilcoxon rank sum test. p-values were not adjusted for multiplicity. AE, adverse events; DA, dopamine agonist; TEAE, treatment-emergent adverse event

Figure 1. Mean change (SD) in MDS-UPDRS Part III score from pre-dose to 15/30/60 and 90 minutes post-dose in DA and non-DA users at 24 weeks (A); 36 weeks (B); and 48 weeks (C) (long-term safety phase).* DA, dopamine agonists; MCID, minimal clinically important difference; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; SD, standard deviation. *The analysis included de-novo patients only (i.e. those who were exposed to the study drug for the first time)

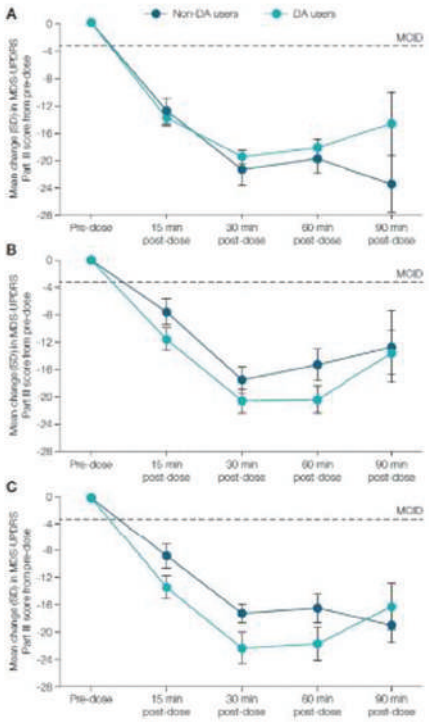

FIGURE 1. Mean change (SD) in MDS-UPDRS Part III score from pre-dose to 15/30/60 and 90 minutes post-dose in DA and non-DA users at 24 weeks (A); 36 weeks (B); and 48 weeks (C) (long-term safety phase).*

Figure 2. Patients achieving self-rated full-ON response within 30 minutes post-dose at 24, 36 and 48 weeks during the long-term safety phase: (A) non-DA users; (B) DA users.* DA, dopamine agonists. *The analysis included de-novo patients only (i.e. those who were exposed to the study drug for the first time)

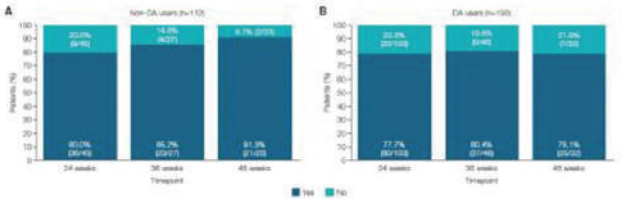

FIGURE 2. Patients achieving self-rated full-ON response within 30 minutes post-dose at 24, 36 and 48 weeks during the long-term safety phase: (A) non-DA users; (B) DA users.*

Conclusion: While SL-APO was found to be better tolerated in DA users, it demonstrated efficacy in both DA and non-DA users.
Disclosure: Supported by Bial

EPR-093 | Exploring implication of dysfunctional cellular pathways in Parkinson's disease: Lysosomal-PD and mitochondrial-PD

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Background and Aims: Lysosomal and mitochondrial dysfunction are possible pathogenetic mechanisms in Parkinson's disease (PD). The aim of this study is to examine phenotypic differences between mutated-PD patients according to the dysfunctional cellular pathway underlying the disease: the mitochondrial (mito-PD) or endolysosomal (lyso-PD) pathways.

Methods: PD patients carrying pathogenetic variant in different PD-associated genes (LRRK2, GBA1, PRKN, PINK1, DJ-1, RAB39B, POLG, TWNK, OPA1, mtDNA) were included in this retrospective observational study. We collected data about demographic characteristics, clinical features (presence of motor/non-motor symptoms, levodopa-induced dyskinesias (LID) and motor fluctuation (MF)) and Total Levodopa Equivalent Daily Dose (LEDD) at disease onset, 5- and 10-years follow-up. Patients were split in mito-PD (PRKN, PINK1, DJ-1, TWNK, POLG, OPA1, mtDNA) or lyso-PD (GBA1, LRRK2, RAB39B) groups depending on the cellular pathway most affected by the mutated gene.

Results: 135 PD patients were included: 99 lyso-PD (male: 65, age at onset: 55 years), and 36 mito-PD (male: 19, age at onset: 41 years). Mito-PD had higher prevalence of dystonia, while lyso-PD of bradykinesia and rigidity. Non-motor symptoms other than psychiatric and sleep disorders (namely dysautonomia, hyposmia, cognitive impairment, hallucinations, urinary symptoms, sialorrhea) had higher prevalence in lyso-PD, as well as MF and LID. LEDD was lower in

mito-PD (5y: 358 mg; 10y: 480 mg) than lyso-PD (5y: 500 mg; 10y: 645 mg) at 5-($p=0.05$) and 10- years ($p=0.06$) follow-up.

Conclusion: This study showed that lyso-PD patients had more frequently non-motor symptoms, MF and LID, whereas mito-PD patients had a prolonged response to low doses of levodopa.

Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPR-094 | Opicapone effect on sleep disorders in fluctuating Parkinson's disease patients: Findings from the OASIS trial

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Background and Aims: Motor fluctuations (MF) and associated sleep disorders are common in Parkinson's disease (PD) patients receiving levodopa/dopa decarboxylase inhibitors, negatively affecting their quality of life. Opicapone (OPC) proved to be effective in reducing end-of-dose MF in patients with PD. The OASIS study evaluated OPC's effects on sleep disorders in PD patients with MF.

Methods: In the exploratory, open-label, single-arm pilot OASIS trial, all patients ($N=16$) received OPC 50 mg once-daily as add-on to levodopa therapy for 6 weeks. Primary endpoint was change from baseline in PD Sleep Scale-2 (PDSS-2). Secondary endpoints included tolerability, functional motor and non-motor assessments (Movement Disorder Society [MDS]-Unified Parkinson's Disease Rating Scale [UPDRS], MDS-Non-motor Scale [NMS], 8-item PD Questionnaire [PDQ-8], 16-item PD Fatigue Scale [PFS-16], ON/OFF home diary), and Clinical and Patient Global Impression of Change (CGI-C; PGI-C).

Results: At week 6, there was a significant reduction of −7.9 points (95% CI −13.6, −2.2; $p=0.0099$) in total PDSS-2 score. Significant reductions were also observed in PFS-16 (−9.6 [95% CI −17.5, −1.7; $p=0.0211$]), MDS-NMS total score (-28.9 [95% CI −44.7, −13.2; $p=0.0052$]), MDS-UPDRS-III and IV (-6.3 [95% CI −11.6, −0.9; $p=0.0253$] and −1.2 [95% CI −2.0, −0.4; $p=0.0044$], respectively) and PDQ-8 (-14.2 [95% CI −23.3, −5.0; $p=0.0051$]). Absolute OFF-time was reduced (-142.1 mins), while ON-time without dyskinesia was increased (+127.1 mins). Most patients (93.3%) and most clinicians (80.0%) reported an improvement as evaluated by the PGI-C and CGI-C, respectively. OPC 50 mg was well tolerated.

Conclusion: Adding OPC to levodopa therapy improved sleep disturbances and other non-motor symptoms, supporting OPC's potential to treat MF in patients with PD-related sleep disorders.

Disclosure: Supported by Bial.

EPR-095 | Opicapone as add-on to levodopa in Parkinson's patients without motor complications: Preliminary data from EPSILON

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Background and Aims: Opicapone (OPC) demonstrated efficacy in reducing OFF-time in levodopa/dopa decarboxylase inhibitor (DDCi)-treated patients with Parkinson's disease (PD) and end-of-dose motor fluctuations (MF) and is generally well-tolerated. The EPSILON study explored OPC's potential to enhance the clinical benefit of levodopa/DDCi in PD patients without motor complications.

Methods: In this double-blind, multicentre, randomized, placebo-controlled study, 355 PD patients without MF treated with levodopa/DDCi and other anti-PD medications were randomized (1:1) to OPC 50 mg once-daily or placebo. A 4-week screening period was followed by a 24-week maintenance phase. Primary efficacy endpoint was change from baseline to week 24 in Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS)-III. Secondary endpoints included tolerability, Clinical and Patient Global Impression of Improvement/Change (CGI-I/PGI-C) and MDS-UPDRS-IV.

Results: At week 24, mean (standard error[SE]) change from baseline in MDS-UPDRS-III score for the OPC group was −6.5(0.7) versus −4.3(0.7) for the placebo group, with a significant −2.2(0.9) difference favouring OPC ($p=0.010$). Compared with placebo-treated patients, significantly more OPC-treated patients reported improvements on PGI-C (58% vs. 46%), with a similar trend observed for CGI-I (50% vs. 46%; p = not significant). Motor complications (MDS-UPDRS-IV items 1–6 score ≥1) were reported in fewer patients in the OPC than the placebo group (5.5% vs. 9.7%), with mean scores of 0.3 and 0.4 points, respectively. Frequency and types of adverse events were similar between the two groups; no dyskinesia was reported in either group.

Conclusion: Adjunct OPC significantly improved motor impairment in levodopa-treated PD patients without motor complications, with no dyskinesia reported as adverse event.

Disclosure: Supported by Bial

EPR-096 | Opicapone as first-line strategy for the treatment of wearing-off in patients with Parkinson's disease

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Background and Aims: Opicapone (OPC) has proven efficacy for treating end-of-dose motor fluctuations in levodopa/dopa decarboxylase inhibitor (DDCi)-treated patients with Parkinson's disease (PD). The Korean and European ADOPTION studies explored the efficacy of OPC 50 mg versus an additional 100 mg levodopa dose to treat early wearing-off in patients with PD.

Methods: Patient-level data from matching treatment arms in the two ADOPTION studies were combined. Trials had similar designs, eligibility criteria and methods. Both were prospective, multicentre, randomized, active-controlled, 4-week studies that recruited patients on stable regimen of immediate-release levodopa/DDCi (3–4 daily intakes, maximum 600 mg of levodopa, for ≥4 weeks pre-screening). Patients with an average daily OFF-time >5 hours while awake were excluded. Primary endpoint was change from baseline in absolute OFF-time. Secondary endpoints included tolerability, Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS), 8-item PD Questionnaire (PDQ-8), Clinical Global Impression of Improvement (CGI-I) and Patient Global Impression of Change (PGI-C).

Results: At week 4, mean (standard error[SE]) change from baseline in absolute OFF-time was −68.1 min(7.8) for OPC 50 mg and −33.6 min (9.7) for levodopa 100 mg, resulting in a significant difference of −34.6 min ($p=0.0056$). Numerically greater differences in favour of OPC were observed for MDS-UPDRS-III and IV, and PDQ-8. OPC-treated patients tended to show greater improvements on CGI-I and PGI-C. OPC was generally well-tolerated.

Conclusion: OPC 50 mg was superior to an increased daily levodopa dose in reducing wearing-off, suggesting that adding OPC may also be considered as first-line therapeutic option in PD patients with early/less severe motor fluctuations.

Disclosure: Supported by Bial.

EPR-097 | sGFAP – A possible hint for cerebellar neurodegeneration in essential tremor?

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Background and Aims: Essential tremor (ET) is considered a heterogeneous syndrome and a possible neurodegenerative process has been debated. Diffusion tensor imaging (DTI) studies consistently revealed microstructural alterations in cerebellar regions like the cerebellar peduncles. In a pilot study, we found higher serum glial fibrillary acidic protein (sGFAP) in elderly, late-onset compared to younger, early-onset ET-patients. Higher sGFAP-levels have previously been found in other neurological disorders, inlcuding Parkinson's disease. We therefore aimed to investigate associations of sGFAP with cerebellar microstructural tissue damage in ET-patients.

Methods: 34 ET-patients underwent blood sampling and 3-Tesla cerebral MRI including DTI-sequences at the same visit. sGFAP was quantified by single-molecule-array. FA- and MD-values of inferior (ICP), middle (MCP) and superior (SCP) cerebellar peduncles were obtained from DTI-sequences.

Results: Higher sGFAP-levels correlated with lower FA-values in right (rs=-0.465, $p=0.006$) and left (rs=-0.563, $p<0.001$) ICP, right SCP (rs=-0.397, $p=0.020$) and right (rs=-0.375, $p=0.029$) and left (rs=-0.421, $p=0.013$) MCP. Increased sGFAP-levels correlated with increased MD in right (rs=0.468, $p=0.005$) and left (rs=0.376, $p=0.028$) ICP and right SCP (rs=0.347, $p=0.044$). Patients with sGFAP-levels above median (124.2 pg/mL) demonstrated significantly lower FA in bilateral ICP and MCP and right SCP and higher MD in right ICP compared to patients with sGFAP-levels below median.

Conclusion: Higher sGFAP-levels were associated with cerebellar microstructural white matter damage in ET. Together with our finding of elevated sGFAP-levels in elderly, late-onset ET-patients, these results support the hypothesis of a neurodegenerative process contributing to ET-pathophysiology at least in a subgroup of patients. Larger, prospective studies including MRI control groups are warranted.

Disclosure: Nothing to disclose.

MS and related disorders 1

EPR-098 | Impact of serum neurofilament-light on clinical decision making in a tertiary multiple sclerosis clinic

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Background and Aims: Serum neurofilament light (sNfL) is an established biomarker for neuro-axonal damage in multiple sclerosis (MS). Clinical implementation remains relatively limited. We investigated the impact of sNfL implementation on clinical decision making in a tertiary MS clinic for different contexts.

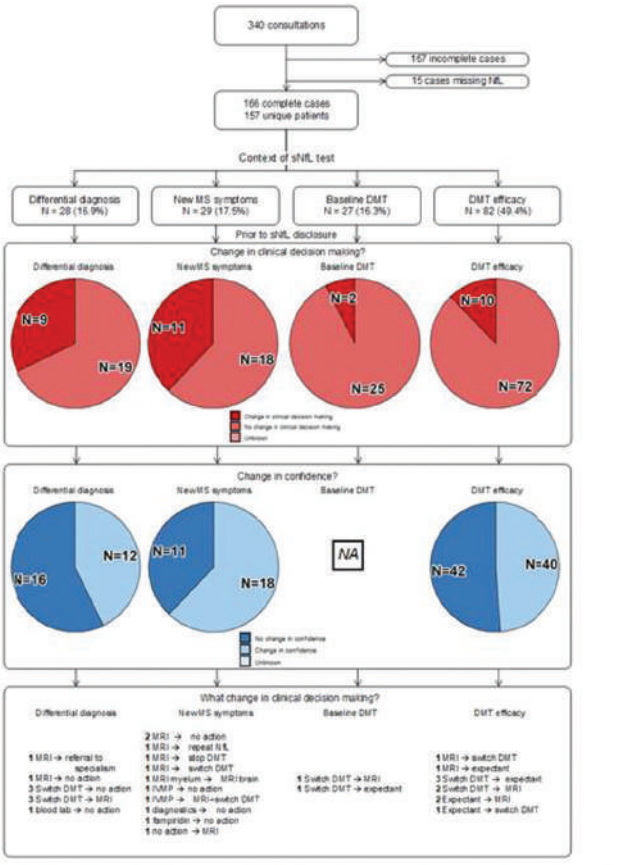
Methods: sNfL measurements were added to routine practice between August 2021 and December 2022 for context 'differential diagnosis'(17%), 'new symptoms in MS'(18%), 'disease-modifying treatment (DMT) monitoring'(55%), and 'DMT baseline'(11%). Physicians filled in questionnaires on clinical decision making, expectations of MRI-activity, certainty regarding decision making, and how this changed after disclosure of the sNfL results. Characteristics associated with changes in scores and the perceived value of sNfL were investigated.

Results: 166 Questionnaires were completed (157 unique MS-patients, age 41±12 years, 68% female). Adding sNfL to the diagnostic tools influenced clinical decisions in 19.3% of cases. Clinicians' certainty significantly increased after disclosure of the sNfL result ($p = 0.004$), lower sNfL levels were associated with higher levels of certainty ($p = 0.044$). Expectation of activity on follow-up brain-MRI significantly decreased after the sNfL disclosure ($p = 0.008$), in accordance with significantly lower sNfL levels in those cases. Urgency and perceived value of the sNfL result was highest in the context of 'new symptoms' ($p = 0.017$), the motivation to measure sNfL was highest in the context of 'differential diagnosis' ($p < 0.001$).

TABLE 1.

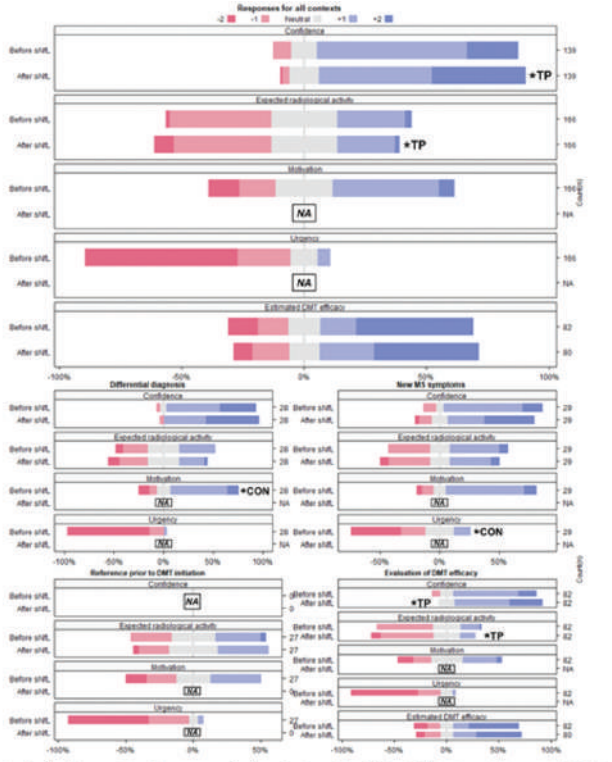
Baseline[1] characteristics	Total (n=166)[2]	DMT efficacy (n=82, 49%)	New MS symptoms (n=29, 18%)	Differential diagnosis (n=28, 17%)		Screening DMT (n=27, 16%)
				CIS or MS (n=20)	No MS (n=8)	
Females (n, %)	112 (68)	56 (68)	20 (69)	11 (55)	5 (63)	20 (74)
Age at sNfL blood sample (years ± SD)	41 ± 12	42 ± 11	39 ± 13	44 ± 13	41 ± 15	37 ± 11
Subtypes (n, %)						
CIS	3 (2)	0	0	2 (10)		1 (4)
RRMS	132 (80)	73 (89)	24 (83)	12 (60)		23 (85)
SPMS	10 (6)	5 (6)	4 (14)	1 (5)		0
PPMS	13 (8)	4 (5)	1 (3)	5 (25)		3 (11)
Disease modifying therapies (%)						
None	60 (36)	4 (5)	8 (28)	16 (80)	8 (100)	23 (85)
Ocrelizumab	44 (27)	32 (39)	10 (35)	1 (5)		1 (4)
Dimethyl fumarate	26 (16)	17 (21)	6 (21)	1 (5)		2 (7)
Teriflunomide	9 (5)	8 (10)	1 (3)	0		0
Interferon-beta	9 (5)	5 (7)	1 (3)	1 (5)		1 (4)
Fingolimod	5 (3)	4 (5)	1 (3)	0		0
Natalizumab	4 (2)	3 (4)	1 (3)	0		0
Glatiramer acetate	3 (2)	3 (4)	0	0		0
Cladribin	3 (2)	3 (4)	0	0		0
Ozanimod	2 (1)	1 (1)	1 (3)	0		0
Rituximab	1 (1)	1 (1)	0	0		0
sNfL – mean ± SD (pg/mL)	12 ± 17	10 ± 5.8	15 ± 19	25 ± 39	16 ± 14	11 ± 8
sNfL - age corrected percentiles (%)[3]						
<5th percentile	1 (1)	0	0	1 (5)	0	0
5-10th percentile	4 (2)	3 (4)	1 (3)	0	0	0
10-25th percentile	13 (8)	9 (11)	3 (10)	0	0	1 (4)
25-50th percentile	42 (25)	24 (29)	6 (21)	3 (15)	2 (25)	7 (26)
50-75th percentile	60 (36)	29 (35)	12 (41)	6 (30)	2 (25)	11 (41)
75-90th percentile	15 (9)	5 (6)	2 (7)	2 (10)	0	6 (22)
90-95th percentile	8 (5)	3 (4)	1 (3)	3 (15)	1 (13)	0
>95th percentile	23 (14)	9 (11)	4 (14)	5 (25)	3 (38)	2 (7)

Baseline characteristics for the 166 included cases.
1 The date of the blood draw for sNfL measurement was defined as baseline time point.
2 This included 157 unique patients, for sNfL were measured in 3 separate consultations by 1 patient, and 2 separate consultations in 7 patients.
3 Calculated using the NIL interface for physicians.17 For patients with CIS or MS, we calculated age corrected percentiles based on a reference cohort of patients with MS. For some age groups of patients with MS (below 20 and above 62 years), age corrected percentiles are technically unknown because of insufficient data. In this study, we therefore extrapolated age corrected percentiles based on the available data for MS patients7. For patients without MS, we calculated age corrected percentiles based on a reference cohort of controls (i.e. without a neurological diagnosis).



Flowchart with piecharts depicting inclusions, divisions into contexts of use, change in confidence and changes in clinical decision making after sNfL disclosure. sNfL = serum neurofilament light chain, DMT = disease modifying treatment, MS = multiple sclerosis, NA = not applicable.

FIGURE 1.



Likert-scale showing questionnaire response for all contexts combined (A) and different context separately (B-D). The median scores of questionnaire items were compared before and after sNfL disclosure, significant differences ($p<0.05$) are indicated with *TP. The median scores were furthermore compared between contexts, significant differences ($p<0.05$) are indicated with *CON. Three Likert-scale items (level of confidence, estimated DMT efficacy and expected radiological activity) were repeated in part 2 of the questionnaire. Median scores for these three items were compared between part 1 (prior to sNfL disclosure) and part 2 (after sNfL disclosure) of the questionnaire, and significant differences (p-value <0.05) are indicated in bold and by two asterisks (**). sNfL = serum neurofilament light, DMT = disease modifying treatment, MS = multiple sclerosis.

FIGURE 2.

Conclusion: sNfL implementation may have considerable impact on clinical decision making and certainty herein, depending on different contexts. Standard and regular implementation of sNfL in clinical practice and daily analysis may complement patient management; particularly in patients with new symptoms or suspicion of disease activity.

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EPR-099 | Serum NfL and GFAP is not associated with wearing-off symptoms in natalizumab treated multiple sclerosis patients

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Background and Aims: Wearing-off symptoms (WoS) are reported by more than 50% of people with multiple sclerosis (MS) during treatment with natalizumab. Biomarkers of neuro-axonal damage (serum neurofilament light (sNfL) and glial fibrillary acidic protein (sGFAP)) could provide insight in the etiology of wearing-off symptoms with natalizumab. We investigated the association between these biomarkers and the occurrence of WoS in natalizumab treated MS patients, and the predictive value of these biomarkers on the occurrence of WoS during further treatment.

Methods: We performed longitudinal measurements of sNfL and sGFAP, using Simoa, in 364 participants (79.1% female, median age 40 years, median Expanded Disability Status Scale (EDSS) 3.0)

treated with natalizumab who participated in the NEXT-MS trial and completed a questionnaire about WoS. Association of sNfL and sGFAP levels with experiencing WoS were assessed, both cross-sectional at timepoints and longitudinal during follow-up. In addition, the predictive value of baseline sNfL and sGFAP for first time WoS occurence was investigated.

Results: 55.5% of patients treated with natalizumab experienced WoS. EDSS scores at baseline were higher in patients with WoS. Repeated analysis showed that sNfL and sGFAP levels were not associated with WoS at any timepoint. No association was found between changes in biomarker levels and first time WoS occurrence, neither were baseline sNfL and sGFAP levels predictive of first time WoS occurrence.

Conclusion: sNfL and sGFAP levels were not associated with natalizumab WoS, underpinning that acute and chronic neuro-axonal damage are most likely not the underlying cause of experiencing WoS.

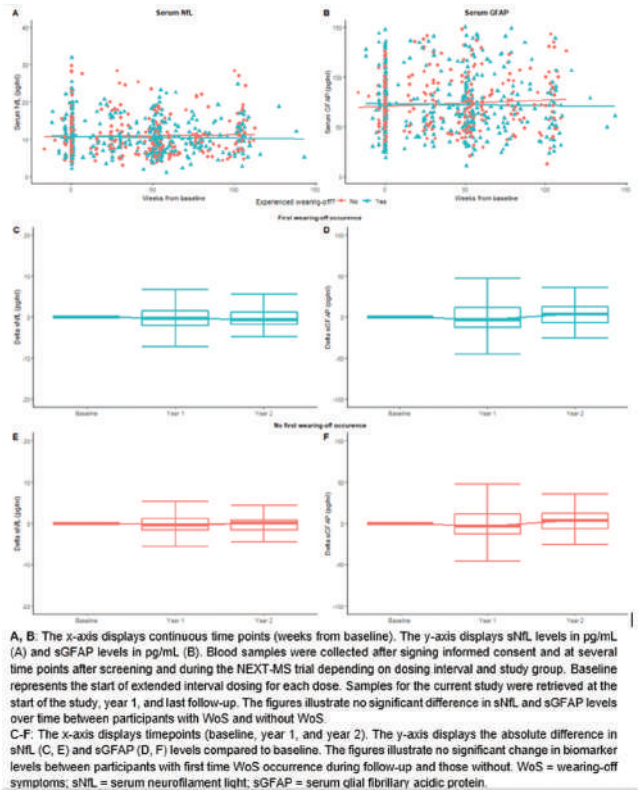
TABLE 1. Baseline characteristics of included participants.

Ever experienced WoS	No (N=162)	Yes (N=202)	Total (N=364)	P-value
Sex, n (%)				
Male	33 (20.4%)	43 (21.3%)	76 (20.9%)	.93
Female	129 (79.6%)	159 (78.7%)	288 (79.1%)	
Age, years (IQR)	39.0 (33.0 - 49.0)	40.0 (33.0 - 50.0)	40.00 (33.0- 50.0)	.91
BMI at baseline, kg/m2 (IQR)	24.44 (21.95 - 27.70)	24.86 (21.50 - 28.18)	24.69 (21.60 – 28.04)	.91
EDSS, (IQR)	2.5 (1.5 - 4.0)	3.0 (2.0 - 4.4)	3.0 (2.0 - 4.0)	.0022
JCV-status, n (%)				
Negative	138 (85.2%)	169 (83.7%)	307 (84.3%)	.8
Positive	24 (14.8%)	33 (16.3%)	57 (15.7%)	
New/newly enlarged T2 lesions on MRI[a], n (%)				
No activity	145 (89.5%)	181 (89.6%)	326 (89.6%)	1
Activity	17 (10.5%)	21 (10.4%)	38 (10.4%)	
Extended dosing group, n (%)				
SID group	18 (11.1%)	39 (19.3%)	57 (15.7%)	.098
EID10 group	113 (69.8%)	130 (64.4%)	243 (66.8%)	
EID5 group	31 (19.1%)	33 (16.3%)	64 (17.6%)	
Duration NTZ treatment, years (IQR)	4.22 (1.31 - 8.71)	3.98 (1.67 - 7.50)	4.05 (1.50 - 8.20)	.85
NfL at baseline, pg/mL (IQR)	9.51 (7.17 - 13.02)	10.22 (7.40 - 13.16)	9.81 (7.22 - 13.1)	.5
GFAP at baseline, pg/mL (IQR)	66.86 (50.95 - 90.83)	70.75 (53.41 - 94.36)	68.03 (51.70 - 92.71)	.71
First time WoS occurrence during follow-up[b], n (%)	0 (0%)	33 (16.4%)	33 (9.09%)	<0.001

Values are depicted as medians with interquartile ranges or frequencies with percentages. Clinical characteristics were compared between groups using the Chi-Square test for categorical variables, the t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous variables. WoS = Wearing-off symptoms; BMI = Body Mass Index; JCV = John-Cunningham Virus; sNfL = serum neurofilament light; sGFAP = serum glial fibrillary acidic protein; EDSS = Expanded Disability Status Scale; NTZ = natalizumab; SID = standard interval dosing (treatment every 4 weeks); EID10 = extended interval dosing with an aim drug trough concentration of 10 µg/mL; EID5 = extended interval dosing with an aim drug trough concentration of 5 µg/mL.[8]

[a]Baseline MRI scan of the NEXT-MS trial

[b]Participants that did not experience WoS at baseline, but reported WoS during follow-up.



A, B. The x-axis displays continuous time points (weeks from baseline). The y-axis displays sNfL levels in pg/mL (A) and sGFAP levels in pg/mL (B). Blood samples were collected after signing informed consent and at several time points after screening and during the NEXT-MS trial depending on dosing interval and study group. Baseline represents the start of extended interval dosing for each dose. Samples for the current study were retrieved at the start of the study, year 1, and last follow-up. The figures illustrate no significant difference in sNfL and sGFAP levels over time between participants with WoS and without WoS.

C-F. The x-axis displays timepoints (baseline, year 1, and year 2). The y-axis displays the absolute difference in sNfL (C, E) and sGFAP (D, F) levels compared to baseline. The figures illustrate no significant change in biomarker levels between participants with first time WoS occurrence during follow-up and those without. WoS = wearing-off symptoms; sNfL = serum neurofilament light; sGFAP = serum glial fibrillary acidic protein.

FIGURE 1. sNfL and sGFAP levels over time.

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EPR-100 | Cognitive-motor interference predicts disease activity and progression in early-stage multiple sclerosis patients

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Background and Aims: Abnormalities of gait are present in 50%–80% of people with multiple sclerosis (pwMS), particularly in more disabled patients and during dual task (DT) conditions. The aim of this study, performed on a cohort of very early stage and non-disabled pwMS, was to evaluate cross-sectionally the relationship between gait and cognitive performance and longitudinally between the cognitive-motor interference (CMI) and disease progression.

Methods: 70 pwMS (age 36.5 ±11 years; female $n=49$, 70%) with disease duration <3 years and EDSS </=1.5 performed a 1-minute overground walking trial in a hallway in single and DT conditions at comfortable speed; spatio-temporal gait parameters were evaluated with two optoeletronic bars. Patients underwent also a neuropsychological assessment with Rao's battery. 38 pwMS completed the same evaluation after 1 year (T1). We performed Spearman correlation analysis of gait and cognitive parameters at baseline (T0) and a Mann–Whitney *U*-test to compare them in worsened (either MRI activity, EDSS >1, relapse) and non-worsened patients after 1-year follow-up.

Results: At T0 we found a relationship between symbol digit modalities test (SDMT) and the main spatio-temporal parameters of gait (step length, velocity) in single ($r=0.369$, $p=0.007$; $r=0.342$, $p=0.012$) and dual task conditions ($r=0.392$, $p=0.004$; $r=0.284$, $p=0.039$). 11/38 pwMS worsened at T1; greater DT costs of cadence (9.97 vs. 6.03; $p=0.017$) and velocity (0.176 vs. 0.088; $p=0.013$) were significantly related to disease worsening.

Conclusion: Even in very early and non-disabled pwMS gait performance is related to cognitive function. Dual task performance could reveal pwMS at greater risk of disease progression.

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EPR-101 | Evaluation of brain atrophy in multiple sclerosis patients. Comparison between manual and volumetric measures

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Background and Aims: manual measures such as corpus callosum index (CCI), normalized central corpus callosum area (CCAc), normalized mean corpus callosum area (CCAm), corpus callosum index (CCI) are potential biomarkers for brain atrophy. We investigate their suitability to assess the neurodegenerative component of multiple sclerosis (MS) by comparing them to volumetric measure (nBV) and expanded disability status scale (EDSS).

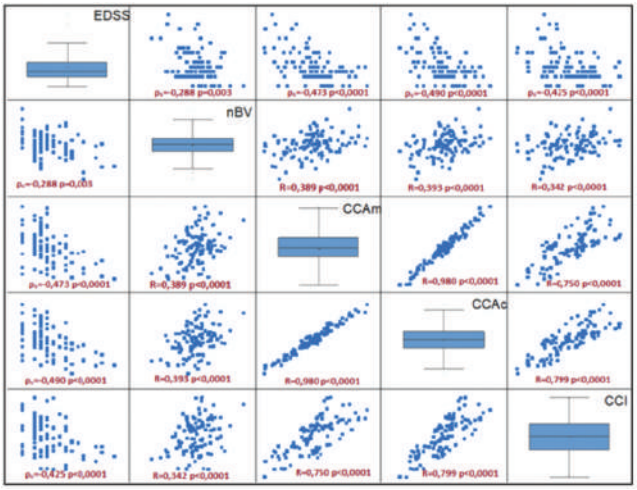
Methods: Fifty-three patients were included in this observational retrospective study. For each patient clinical and radiological data (nBV, CCAm, CCAc, CCI) were collected at two-time points, baseline (T0) and last follow-up (TX). All the MRi scans were performed with the same acquisition protocol.

Results: Inter-rater reliability between 2 examiners was excellent (0.98 inter-class correlation coefficient with absolute agreement (95% confidence interval, p-value <0.001)) for all the manual measures analyzed; Manual and volumetric measures showed statistically significant correlation between them, and with clinical measure (EDSS) at cross-sectional analysis. Manual measures showed better correlation with clinical measure (EDSS) compared with volumetric measure (ρs=-0,288 for NBV, ρs=-0,473 for CCAm, ρs=-0,490 for CCAc, ρs=-0,425 for CCI). At longitudinal analysis manual and volumetric (anBV) measures showed statistically significant correlation between them; aNBV was superior to manual measures in reducing the required sample size required to detect pre-specified treatment effects.

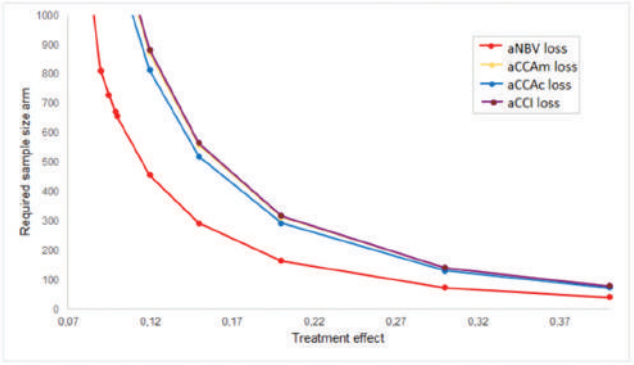
N = 53	T0	TX
EDSS (range)	1,5 (0,0 – 6,5)	2,0 (0,0 – 7,5)
Age (median years, range)	33,3 (22 – 64)	38,77 (24 – 69)
Gender (female %)	36 (67,9)	
Normalized Brain Volume (nBV), *median, range*	1577575 (1336697 – 1820497)	1537315 (1285398 – 1712687)
Annualized Normalized Brain Volume loss (aNBV loss) *Mean (2SD)* *Median (range)* *Coefficient of Variation (CV)*	 -0,27 (0,36) -0,24 (-0,65, -0,01) 0,67	
mean Corpus Callosus Area (mCCA), *median %, range*	2,71 (1,59 – 4,05)	2,55 (1,34 – 4,00)
Annualized mean Corpus Callosum Area loss (aCCAm loss) *Mean (2SD)* *Median (range)* *Coefficient of Variation (CV)*	 -1,27 (2,34) -0,89 (-5,19, -0,03) 0,92	
central Corpus Callosus Area, (eCCA), *median %, range*	2,89 (1,60 – 4,25)	2,63 (1,24 -3,93)
Annualized central Corpus Callosum Area loss (aCCAc loss) *Mean (2SD)* *Median (range)* *Coefficient of Variation (CV)*	 -1,36 (2,42) -1,01 (-7,6, -0,02) 0,89	
Corpus Callosus Index (CCI); *median, interval range*	0,29 (0,16 – 0,41)	0,268 (0,136 – 0,41)
Annualized Corpus Callosus Index (aCCI loss) *Mean (2SD)* *Median (range)* *Coefficient of Variation (CV)*	 -1,23 (2,28) -0,99 (-5,21, -0,03) 0,93	
Follow-up, *median years, range*		5,4 (1,5 – 13,28)

Abbreviations: Normalized Brain Volume (nBV); Annualized Normalized Brain Volume loss (aNBV loss); mean Corpus Callosus Area (mCCA); Annualized mean Corpus Callosum Area loss (aCCAm loss); central Corpus Callosus Area (eCCA); Annualized central Corpus Callosum Area loss (aCCAc loss); Corpus Callosus Index (CCI); Annualized central Corpus Callosum Area loss (aCCAc loss)

Demographic, clinical and MRi data at baseline (T0) and at follow-up (TX).



Correlation matrix of clinical, MRi manual and volumetric measures cross-sectional data. I MRi measures showed statistically significant correlation with EDSS, with manual measures showing better correlation compared with volumetric measure.



The required sample size per arm for each measure, for varying treatment effects with fixed power of 80% and 0.05 significance level. aNBV was superior to manual measures in reducing the required sample size required.

Conclusion: This study provides a direct comparison between manual and volumetric measurements, with the former being easy to use and showing better correlation with EDSS. Volumetric measure (nBV) have less variability in the sample size analysis, and are mostly recommended for clinical trials.

Disclosure: Nothing to disclose.

EPR-102 | Safety and efficacy of frexalimab in relapsing multiple sclerosis: 48-week results from the phase 2 open-label extension

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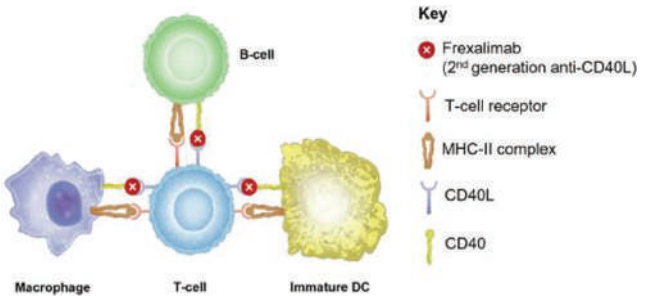
Background and Aims: Frexalimab, a second-generation anti-CD40L monoclonal antibody, blocks the costimulatory CD40/CD40L pathway, which is important for activation and function of adaptive and innate immunity. In the 12-week (W) double-blind-period (DBP) of a Phase 2 trial (NCT04879628), frexalimab demonstrated safety and efficacy with high-dose treatment showing an 89% reduction in new gadolinium-enhancing (Gd+) T1-lesions in participants with relapsing multiple sclerosis (RMS). Efficacy and safety were further

sustained over W24 in the open-label extension (OLE). Here, we report W48 results.



Inhibition of the CD40/CD40L interaction with frexalimab.

Methods: In the DBP, participants were randomized to frexalimab-high ($N=52$), frexalimab-low ($N=51$), or matching placebo (placebo-high, $N=12$; placebo-low, $N=14$). At W12, participants receiving placebos switched to respective frexalimab arms. Key assessments during the OLE included safety and efficacy (number of Gd+ T1-lesions and new/enlarging T2-lesions).

Results: 125/129 (97%) participants completed the DBP and entered the OLE; 112 (87%) remained in the study at W48. At W48, the number of Gd+ T1-lesions (mean±SD) remained low in participants who continued receiving frexalimab and in those who switched from placebo to frexalimab at W12 (frexalimab-high: 0.0±0.2; frexalimab-low: 0.2±0.5; placebo-high/frexalimab-high: 0.2±0.6; placebo-low/frexalimab-low: 0.1±0.3). Furthermore, 96% of participants in frexalimab-high, 87% in frexalimab-low, 90% in placebo-high/frexalimab-high, and 92% in placebo-low/frexalimab-low were free of Gd+ T1-lesions at W48. New/enlarging T2-lesions and T2-lesion volume change remained low with frexalimab-high through W48. Lymphocyte counts were stable over W48. Overall, frexalimab was well-tolerated through W48.

Conclusion: Frexalimab continued to show favorable safety and efficacy in RMS participants through W48. These data support its further development as a potential high-efficacy, non-lymphocyte-depleting treatment option in MS.

Disclosure: PV: honoraria/consultant/research: Janssen, Biogen, Sanofi, Novartis (NVS), Teva, Merck, Roche, Imcyse, AB Sci, BMS-Celgene. CG: adboard/consultant/speaker/research: Actelion, NVS, Sanofi, GeNeuro, Roche, Siemens, Biogen, Teva, Merck, Janssen. YMD: consultant/speaker/research: Acorda, Bayer, Biogen, BMS-Celgene, Chugai, EMD Serono, Genentech-Roche, Horizon/Amgen, Janssen, NVS, Sanofi, Teva, NIAID, NIH NINDS, PCORI. GC: DSMB: APLT, AI Therap, AMO, AZ, Avexis, Biolinerx, BrainStorm Cell, BMS-Celgene, CSL Behring, Galmed, Green Valley, Horizon, Immunic, Karuna Therap, Mapi, Merck, Mitsubishi Tanabe, Opko Biol, Prothena, NVS, REGN, Sanofi, Reata, Teva, NHLBI, UTSouthwestern, UPenn, VTI; consultant/adboard: Alexion, Antisense Therap, Biogen, CliniTrialSolutions, Entelexo, Sanofi, Genentech, GW, Immunic, Immunosis, Klein Buendel, Merck/Serono, NVS, Perception NS, Protalix, REGN, Roche, SAB Bio; employee UAB; president Pythagoras. OK: honoraria/consultant/speaker: Sanofi, Roche, Genentech, Merck, NVS, GeNeuro, BMS-Celgene, Mapi, VielaBio, Teva. IS: travel/consultant/speaker: Sanofi, Ewopharma-Biogen, Shire, Gedeon-Richter, Teva, BI, Pfizer, Bayer, Roche, Mylan, Polpharma, Penumbra, Adapt, Merck, GL Pharma, Medochemie, NVS, Viatris, NobelPharma. MD: coordinator Sanofi. SS, RB, BD, PT, EW: Sanofi employee. GG: research/consultant/speaker: AbbVie, Actelion, Atara, Biogen, Canbex, Celgene, EMD Serono, Japan Tobacco, Sanofi, Genentech, GSK, GW, Merck, NVS, Roche, Synthon, Teva.

EPR-103 | Pediatric onset multiple sclerosis is associated with parental smoking: Insights from the PEDIGREE study

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Background and Aims: Assessing the environmental impact on adult multiple sclerosis (MS) is complex due to long disease latency and risk for recall bias, and especially for perinatal exposures. We aimed to investigate the association between parental smoking habit and the development of pediatric-onset MS (POMS).

Methods: As a part of the Italian multicenter case-control PEDIGREE Study, the PEQ-IT questionnaire for prospective data collection was used. Subjects aged less than 18 years with POMS (2013 Krupp's diagnostic criteria) and with disease duration of up to 5 years from onset, and matched controls were enrolled.

Results: The study included 116 participants with POMS and 116 controls. Among them, 76.7% of cases and 54.3% of controls were females with a mean (SD) age of 16.6 (2.9) and 13.4 (5.0) years, respectively. The mean (SD) age at MS onset was 13.9 (3.0) years, median EDSS score was 1.0 (range 0–4.0), and the mean (SD) disease

duration was 33.3 (28.3) months. The crude odds ratio (OR) for risk of POMS among subjects with fathers being current smokers was 2.05 (95%IC 1.17–5.58) and 2.70 (95%IC 1.15–6.35) having been smokers pre-pregnancy. The OR was 5.10 (95%IC 1.07–24.23) when both parents smoked before pregnancy. No significant association was found with maternal smoking or children's smoking habits.

Table 1. Distribution of the main clinical and demographic characteristics of the study sample by status.

	Controls N=116	MS cases N=116	*p*
Sex: F, N (%)	63 (54.3)	89 (76.7)	*0.001*[a]
Age at study time (mean, SD), years[b]	13.4 (5.0)	16.6 (2.9)	*0.000001*
Males	13.9 (5.0)	16.2 (3.2)	*0.016*
Females	13.4 (4.8)	16.7 (2.8)	*0.000004*
Age at MS onset (mean, SD), years[b]	-	13.9 (3.0)	-
MS duration (mean, SD), months[b]	-	33.3 (28.3)	-
EDSS at study time (median, range)[b]	-	1.0 (0-4.0)	-
Educational level			
No education, Primary School, Junior School	16 (15.1)	41 (42.3)	*0.000007*
High School, Vocational School	54 (50.9)	44 (45.4)	
University, Post-Graduate Studies	36 (34.0)	21 (12.4)	

[a] Fisher Test
[b] No statistically significant difference by sex

Distribution of the main clinical and demographic characteristics of the study sample by status.

	Controls N=116	MS Cases N=116	OR	*p*	OR_{adj}	*p*
Active cigarette smoking habit[a]						
Never smokers	73 (81.1)	73 (74.5)	1	*0.298*[c]	1	*0.997*[d]
Ever smokers	17 (18.9)	25 (25.5)	1.65 (0.77, 3.56)		1.00 (0.47, 2.12)	
Mother's smoking history						
Never smoker	78 (67.8)	62 (57.4)	1	*0.108*	1	*0.479*[d]
Ever smoker	37 (32.2)	46 (42.6)	1.56 (0.91, 2.70)		0.34 (0.18, 6.64)	
No smoking during pregnancy	95 (88.0)	92 (89.3)	1	*0.756*	1	*0.949*[d]
Smoking during pregnancy	13 (12.0)	11 (10.7)	0.87 (0.37, 2.05)		0.97 (0.38, 2.44)	
No smoking 3 months before pregnancy	96 (97.0)	94 (91.3)	1	*0.135*		
Smoking 3 months before pregnancy	3 (3.0)	9 (8.7)	3.06 (0.80, 11.67)			
No smoking at all prior to pregnancy	95 (95.0)	90 (87.4)	1	*0.082*[c]	1	*0.173*[c]
Smoking prior to pregnancy	5 (5.0)	13 (12.6)	2.74 (0.94, 8.01)		2.33 (0.69, 7.83)	
No smoking when participant is aged 1 year	95 (89.6)	86 (89.6)	1	*0.993*	1	*0.125*[c]
Smoking when participant is aged 1 year	11 (10.4)	10 (10.4)	1.00 (0.41, 2.48)		3.46 (0.71, 16.94)	
No smoking when participant is aged 2-5 years	84 (78.5)	84 (81.6)	1	*0.609*	1	*0.760*[c]
Smoking when participant is aged 2-5 years	23 (21.5)	19 (18.4)	0.83 (0.42, 1.63)		0.87 (0.41, 1.93)	
No smoking when participant is aged 6-10 years	82 (78.8)	78 (78.0)	1	*0.883*	1	*0.785*[c]
Smoking when participant is aged 6-10 years	22 (21.2)	22 (22.0)	1.05 (0.54, 2.05)		0.90 (0.43, 1.88)	
Father's smoking history						
Never smoker	57 (51.4)	34 (34.0)	1	*0.012*[c]	1	*0.022*[c]
Ever smoker	54 (48.6)	66 (66.0)	**2.05 (1.17, 3.58)**		**2.07 (1.11, 3.85)**	
No smoking 3 months prior to pregnancy	100 (91.7)	74 (80.4)	1	*0.023*[c]	1	*0.109*[c]
Smoking within 3 months before pregnancy	9 (8.3)	18 (19.6)	**2.70 (1.15, 6.35)**		2.23 (0.84, 5.91)	
Mother and father smoking habit						
No smoking at all prior to pregnancy	102 (98.1)	90 (90.9)	1	*0.030*[c]	1	*0.201*[c]
Smoking prior to pregnancy	2 (1.9)	9 (9.1)	**5.10 (1.07, 24.23)**		2.91 (0.57, 15.02)	

[a] investigated in subjects aged 10 to 17 years
[b] logistic regression: Odds Ratio (OR) adjusted for age at study time
[c] logistic regression: Odds Ratio (OR) adjusted for participant's smoking habit
[d] Fisher test

Association between active and passive cigarette smoking habit within families of MS cases and controls.

Conclusion: Our findings point to parental, and particularly paternal, smoking exposure, as a potential risk factor for POMS. The disparity in the impact of maternal versus paternal smoking could be attributed to a quantitative factor, social pressures and awareness influencing maternal smoking behaviors during and after pregnancy.

Disclosure: Pilotto S. has received compensations for research activities from FISM – Fondazione Italiana Sclerosi Multipla. Other authors have nothing to disclose.

EPR-104 | Time spent outdoors and risk of pediatric onset MS: The PEDIGREE study

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Background and Aims: Evaluating environmental influence on adult multiple sclerosis (MS) presents complexities, particularly with exposures during the perinatal period. This study aims to investigate how time spent outdoors, considered as a proxy for sun exposure, may contribute to the development of pediatric-onset MS (POMS).

Methods: As a part of the Italian multicenter case-control PEDIGREE Study, the PEQ-IT questionnaire for prospective data collection was used. Subjects aged less than 18 years with POMS and with disease duration of up to 5 years from onset, and matched controls were enrolled.

Results: The study included 117 participants with POMS and 123 controls. Among them, 76.9% of cases and 55.1% of controls were females with a mean (SD) age of 16.6 (2.9) and 13.4 (4.9) years, respectively. The mean (SD) age at MS onset was 13.9 (3.0) years, median EDSS score was 1.0 (range 0–4.0), and the mean (SD) disease duration was 29.3 (23.5) months. In our analysis, reduced (less than 60 minutes per week) time spent outdoors during spring in the first five years of life was associated with a significant risk of developing POMS (OR 2.26 (95%CI:1.25–4.07) (between 0 and 1 years: OR = 1.93(95%CI: 1.09–3.39); between 1 and 2 year: OR = 2.22 (95%CI:1.005–4.84); between 3 and 5 years: OR 4.82 (95%CI: 1.02–22.85). Less time spent outdoors resulted to be associated with a 2–3 times increased risk of POMS even when considering other seasons in the first 5 years of life ($p < 0.05$).

Conclusion: Spending more time in the sun in the first 5 years of life is associated with a reduced risk of developing POMS.

Disclosure: Pilotto S. has received compensations for research activities from FISM – Fondazione Italiana Sclerosi Multipla. Other authors have nothing to disclose in relation to this work. This study was supported by FISM – Fondazione Italiana Sclerosi Multipla – (grant N. 12/18/F14, P.I. Angelo Ghezzi) and financed or cofinanced with the "5 per mille" public funding.

EPR-105 | Functional connectivity modifications in monoaminergic circuits underpin fatigue development in MS patients

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Background and Aims: In multiple sclerosis (MS), monoaminergic network dysregulation may contribute to fatigue pathogenesis. Here, we investigated changes over time in monoaminergic-related resting state (RS) functional connectivity (FC) and its association with fatigue development in MS.

Methods: Eighty-nine right-handed MS patients and 49 healthy controls underwent neurological, fatigue and 3.0T RS functional MRI assessment at baseline and after 1.3-year median follow-up (interquartile range = 1.01–2.01 years). Fatigue was evaluated using the modified fatigue impact scale (MFIS) score. Patients were considered as fatigued if MFIS was >38. Independent component analysis constrained to PET atlases for dopamine, noradrenaline and serotonin transporters estimated monoaminergic-related RS FC.

Results: At baseline, 24 (27%) MS patients were fatigued (F) and 65 were non-fatigued (NF). Of these, 22 (34%) developed fatigue (devFAT) at follow-up and 43 remained NF (noFAT). At baseline, F-MS patients showed increased monoaminergic-related RS FC in hippocampal, postcentral and temporo-occipital cortices, as well as decreased insular RS FC. During the follow-up, devFAT MS patients showed increased dopamine-related hippocampal RS FC, significant at time-by-group interaction analysis. NoFAT patients showed decreased noradrenaline-related RS FC over time in superior frontal regions, while both devFAT and F-MS patients showed increased RS FC in the same regions; this divergent behavior was significant at time-by-group interaction analysis. DevFAT MS patients presented increased serotonin-related RS FC over time in the angular and middle occipital gyri; this latter region showed decreased serotonin-related RS FC at follow-up versus baseline in F-MS.

Conclusion: Specific monoaminergic networks changes over time characterized MS patients according to fatigue status.

Disclosure: MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. M. Margoni reports grants and personal fees from Sanofi Genzyme, Merck Serono, Novartis and Almiral. P Valsasina, A Bacchetti, D Mistri, N Tedone have nothing to disclose. M. Filippi received compensation for consulting or speaking activities from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPR-106 | Evaluation of sleep disorders in neuromyelitis optica spectrum disorder

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Background and Aims: We aimed to investigate the structure of sleep, sleep disorders, and the relationship between abnormalities and brain lesions in neuromyelitis optica spectrum disorder(NMOSD).

Methods: 26 patients with NMOSD and 20 healthy individuals were enrolled. Questionnaires were used to evaluate sleep quality, daytime sleepiness, restless legs syndrome(RSL). Night polysomnography (PSG) and multiple sleep latency tests(MSLT) were performed.

Results: Diencephalic lesions were present in 23.1% of patients, and infratentorial lesions were observed in 84.6%. NREM1 percentage, general AHI, REM-AHI, and NREM-AHI averages were higher in NMOSD patients. The obstructive sleep apnea syndrome(OSAS) and were more common in NMOSD patients ($p = 0.001$; $p < 0.001$). Mild obstructive apnea (OA) was detected in general AHI, and moderate OA was found in REM-AHI ($p = 0.002$; $p = 0.001$). Hypersomnia was detected in 30.8% of patients, narcolepsy in 11.5% and neither was observed in the control group. Sleep latency was shorter, and SOREM was higher in the NMOSD group ($p = 0.001$; $p = 0.001$). High REM-AHI was associated with short sleep latency and hypersomnia ($p = 0.010$; $p = 0.012$). No relationship was found between sleep changes and the presence of diencephalic lesion/infratentorial lesion. Epworth Sleepiness Scale, Beck Depression Scale, and

Pittsburgh Sleep Quality Index were higher in the patient group. There was a relationship between PSQI general score and EDSS ($p=0.023$). RLS were observed more frequently in the NMOSD group ($p=0.031$; $p<0.001$).

Conclusion: REM-related OA and hypersomnia are common in NMOSD patients. Therefore, NMOSD patients need objective evaluations such as PSG and MSLT. Our study is the first study conducted with MSLT in addition to PSG and shows the importance of quantitative examinations in NMOSD patients.

Disclosure: Nothing to disclose

MS and related disorders 2

EPR-107 | Landscapes of gut microbiome and blood metabolomic signatures in relapsing-remitting multiple sclerosis

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Background and Aims: Gut microbiome disturbances have been implicated in multiple sclerosis (MS), little is known about the changes and interactions between gut microbiome and blood metabolome, and how these changes affect the disease-modifying therapy (DMT) drugs in preventing the progression of MS.

Methods: The structure and composition of the gut microbiota were evaluated using 16S rRNA gene sequencing while an untargeted metabolomics approach was also used to compare the serum metabolite profiles from patients with relapsing-remitting MS ($n=154$) and healthy controls (HC; $n=81$).

Results: MS is characterized by increased α-phylogenetic diversity and significantly disturbed serum glycerophospholipid metabolism. Compared to MS patients in the acute phase (AMS), α-phylogenetic diversity in MS patients in the chronic phase (CMS) was significantly decreased. Serum glycerophospholipid metabolism also differed significantly between AMS and CMS. Moreover, a combination of two increased genera (Slackia, Lactobacillus) and five glycerophospholipid metabolism-associated metabolites (four increased: GPCho(22:5/20:3), PC(18:2(9Z,12Z)/16:0), PE(16:0/18:2(9Z,12Z)), PE(18:1(11Z)/18:2(9Z,12Z)); one decreased: PS(15:0/22:1(13Z))) in MS patients would enable distinguishing MS from HC; and a biomarker panel consists of four microbial genera (three decreased: Lysinibacillus, Parabacteroides, UBA1819; one increased: Lachnoanaerobaculum) and two glycerophospholipid metabolism-associated metabolites (one increased: PE(P-16:0/22:6); one decreased: CL(i-12:0/i-16:0/i-17:0/i-12:0)) in CMS patients would discriminate CMS from AMS in both the training and testing sets. Furthermore, DMT drugs inhibit the development of AMS via downregulating UBA1819 and upregulating CL(i-12:0/i-16:0/i-17:0/i-12:0).

Conclusion: We provide a deep insight into understanding the roles of microbiome and metabolome in MS and explore potential biomarkers, therefore further development of promising therapeutic targets for MS based on gut microbiota and metabolites.

Disclosure: All of the authors report no disclosures relevant to this research.

EPR-108 | Autologous hematopoietic stem cell transplantation in aggressive multiple sclerosis – a 25-year monocentric experience

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Background and Aims: Autologous haematopoietic stem-cell transplantation (AHSCT) is a treatment option in aggressive relapsing-remitting (RR-) multiple sclerosis (MS) refractory to conventional disease-modifying treatments (DMTs). Here we report long-term outcomes from our 25-year experience.

Methods: Monocentric retrospective study including relapsing (R-) MS patients (primary-progressive MS excluded) treated with AHSCT in Florence between 1998 and 2023 with the same AHSCT protocol (mobilization: cyclophosphamide 4 g/sqm and G-CSF; conditioning: BEAM/ATG). Variables are reported as median (range) or number (frequency). Efficacy outcomes include survival free from relapses (RFS), disability worsening (PFS) and clinical-radiological disease activity (NEDA-3). The primary safety endpoint was 100-days transplant-related mortality (TRM).

Results: Ninety-three R-MS patients were included (Table 1). Follow-up duration was 57 months (1 – 262). PFS at 3, 5 and 10 years was 71%, 69% and 62%, respectively, being higher in RR-MS than in secondary-progressive (SP-)MS (at year 5: 88% vs. 48%; $p<0.0001$; Fig. 1a-b). RFS was 98% and 90% at year 3–5 and 10, respectively. NEDA-3 survival at 3, 5 and 10 years was 70%, 68%, and 52%, respectively, being higher in RR-MS than in SP-MS (at year 5: 86% vs. 48%; $p<0.0001$; Fig. 1c-d). NEDA-3 failure was mostly caused by disability worsening, with sparse events of new focal inflammatory activity, being 6 events observed over 575 patient-years of follow-up. TRM was 0%.

TABLE 1. Baseline clinical-demographic characteristics of the R-MS patients included.

	MS overall (n=93)		RR-MS (n = 50)		SP-MS (n = 43)	
	median	(range)	median	(range)	median	(range)
Age, y	36	(20 – 57)	36	(20 – 53)	40	(27 – 57)
Disease duration (onset), y	11	(1 – 33)	9.5	(1 – 29)	13	(6 – 33)
Number of previous DMTs	3	(0 – 7)	3	(0 – 7)	3	(1 – 6)
ARR in the prior 2 y	1	(0 – 4.5)	1.25	(0 – 4.5)	0.5	(0 – 2)
EDSS	5.0	(1.0 – 7.5)	3.0	(1.0 – 7.0)	6.0	(3.5 – 7.5)
			n	(%)	n	(%)
Gender, female	70	(75%)	37	(74%)	33	(77%)

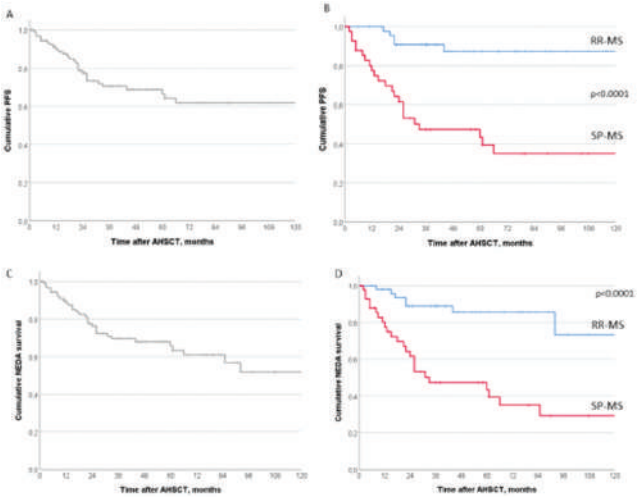

FIGURE 1. Cumulative proportion of patients free from EDSS worsening (PFS; A, B) and evidence of clinical-radiological disease activity (NEDA-3; C, D) over follow-up. RR-MS patients showed lower rates of treatment failure compared to SP-MS both for PFS an.

Conclusion: AHSCT is an effective treatment for patients with aggressive R-MS, with an acceptable safety profile, likely more effective than high-efficacy (HE-)DMTs over long-term. Definite evidence on this issue is awaited from ongoing randomized trials with HE-DMTs.

Disclosure: Nothing to disclose.

EPR-109 | Spinal cord gray matter atrophy predicts disability progression in multiple sclerosis

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Background and Aims: Cervical spinal cord (cSC) gray matter (GM) damage is associated with more severe disability in multiple sclerosis (MS), but its relevance in predicting disability worsening is unclear. Here, we investigated whether cSC GM damage predicts disability progression in MS patients.

Methods: Eighty MS patients and 33 healthy controls (HC) underwent brain and cSC MRI scans at baseline, and neurological evaluations at baseline and after a median follow-up of 1.35 years. Global and GM cSC lesions were identified on axial T2-weighted sequences. Whole and GM cSC cross-sectional area (CSA) were manually quantified at C3–C4 level on phase-sensitive inversion recovery images. Brain T2-hyperintense lesion volume, normalized brain, thalamic and cortical volumes were also obtained. At follow-up, disability worsening was defined as progression on >=1/3 components of the Expanded Disability Status Scale (EDSS)-plus (EDSS worsening or >=20% threshold change for timed 25-foot walk or 9-hole peg test).

Results: Compared with HC, MS patients showed significantly higher brain and cSC lesions ($p < 0.001$), and lower normalized brain, thalamic and cortical volumes, and whole and GM cSC CSA ($p <= 0.03$). At follow-up, 34/80 (43.6%) MS patients showed EDSS-plus worsening. At univariate analysis, baseline predictors of disability worsening were cSC GM CSA ($\beta = -0.71$, $p = 0.02$) and NBV ($\beta = -0.01$, $p = 0.04$); at multivariate analysis, only cSC GM CSA was retained in the model ($\beta = -0.70$, $p = 0.02$, Nagelkerke-R^2=0.358).

Conclusion: cSC GM atrophy emerged as the only independent predictor of disability progression in MS, highlighting its clinical relevance in identifying patients at higher risk of disease worsening at short term.

Disclosure: M Azzimonti received travel grants from Novartis. P Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck Serono, Bristol Myers Squibb, Genzyme, Horizon and Sanofi, and research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). E Pagani, A Meani, M Rubin, M Gueye have nothing to disclose. M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPR-110 | Ocrelizumab and ofatumumab comparison: an Italian real-world propensity score matched study

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Background and Aims: The management of Multiple Sclerosis (MS) has undergone transformative evolution with the introduction of high-efficacy disease-modifying therapies (DMTs), specifically anti-CD20 monoclonal antibodies such as ocrelizumab (OCR) and ofatumumab (OFA).

Methods: This is an independent retrospective cohort study in Relapsing MS (RMS) patients followed at eight Italian MS centres who initiated treatment with OCR or OFA in the participating centres and with at least 12 months on therapy. A generalized linear regression model inverse probability of treatment weight (IPTW) PS-adjusted was performed to evaluate the relationship between annualized relapse rate (ARR) and treatment groups. No evidence of disease activity-NEDA3 at 12-months score was also collected. Safety profile of the investigated DMTs was recorded.

Results: A total cohort of 396 RMS patients fulfilled the required criteria and were enrolled in the study. Out of them, 216 had a prescription of OCR and 180 of OFA. The mean follow-up was 13.2±1.9 months. The estimated means for ARR did not show differences between the two groups, 0.059 for patients on OCR and 0.038 for patients on OFA ($p=0.185$). The generalized regression model IPTW PS-adjusted did not reveal differences between patients on OCR and OFA (ExpBOFA 0.974, 95%CI 0.934–1.015, $p=0.207$). NEDA-3 at 12-months was experienced by 199(92.1%) patients on OCR and 170(94.4%) patients on OFA ($p=0.368$). Generally, both therapies exhibit good tolerability.

Conclusion: The treatment with OCR and OFA resulted in comparable control of disease activity with good safety profile. Our results need further validation in larger multicentre studies with long-term follow-up.

Disclosure: Nothing to disclose.

EPR-111 | Secondary progression in a 30 years cohort from Italian MS registry

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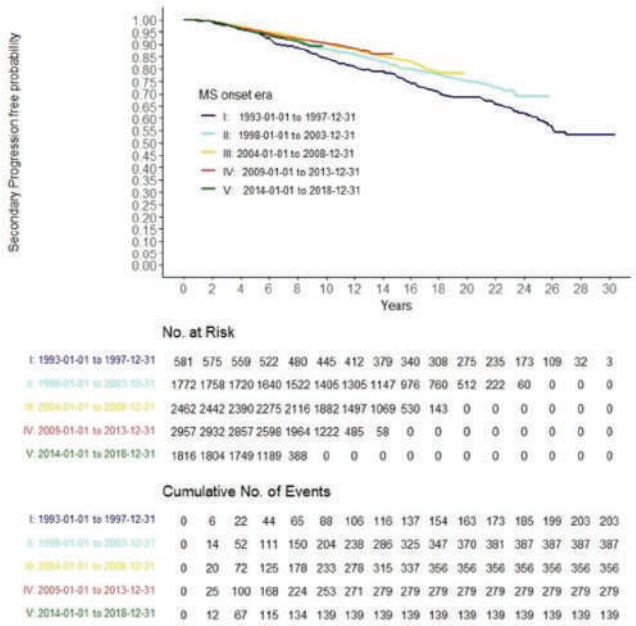
Background and Aims: Contemporary research in MS field emphasizes strategies to prevent or delay secondary progression advocating for early and aggressive interventions. Precision medicine, tailored to individual characteristics such as genetic profiles and biomarkers, holds promise in optimizing treatment outcomes.

Methods: This cohort study using prospectively acquired data from the Italian MS register (IMSR) extracted in November 2023. At the time of data extraction, longitudinal data of 73.564 patients from 120 MS centers were available in the IMSR. Secondary progressive Multiple Sclerosis (SPMS) was defined according to Lorscheider criteria. Conversion to SP was analysed along a 30 years epoch from 1993 to 2023. Five therapeutic era are considered: from 1993 to 1998, 1999 to 2004, 2005 to 2009, 2009 to 2014, and 2015 to 2018. Normalized SP incidence at 5 and 10 years will be analyzed.

Results: A total cohort of 1364 patients, with at least 2 years of follow-up, converted to SPMS (see Figure 1). Generally, patients converting to SPMS during the first eras were younger and with lowest therapeutic coverage all over the investigated follow-up (respectively, first epoch 60.7 (3.7–78.5) vs. last epoch 71.5 (47.4–86.3) (median, Q1–Q3).



MS onset among therapeutic era and SP conversion.

Conclusion: During a 30-year era, the SP conversion rate changed significantly and also the therapeutic overall coverage.

Disclosure: Nothing to disclose.

EPR-112 | Disability progression is a question of definition – a methodological reappraisal in the AMSTR

G. Bsteh[1]; N. Krajnc[2]; S. Marti[3]; R. Hoepner[3]; M. Guger[4]; F. Di Pauli[5]; J. Kraus[6]; C. Enzinger[7]; T. Berger[1]

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Background and Aims: It is unclear whether different definitions of disability progression influence frequency of disability progression overall as well as regarding relapse associated disability worsening (RAW) and progression occurring independent of relapses (PIRA).

Methods: Using data from the Austrian MS treatment registry, we compared event frequency and time to event for 672 definitions of disability progression using a) different cut-offs for minimal EDSS increase, b) different definitions for required confirmation of EDSS increase (unconfirmed, confirmed after 12/24/48 weeks, sustained) and c) use of fixed versus roving baseline score models. Then, we classified each event as either RAW or PIRA using the two described definitions of minimal interval to last relapse (>30 or >90 days).

Results: We analyzed data from 6646 RMS patients (mean age at baseline 35.2 years [SD 10.2], 73.2% female, median baseline EDSS 2.5 [IQR 2.5 – 6.0], median follow-up duration 2.7 years [IQR 2.6 – 8.9]). Rates of disability progression ranged from 71.7% with the most sensitive definition to 6.7% with the least sensitive definition. Classification as RAW or PIRA varied from a distribution percentage of 87:13 to 31:69 depending on the definition of progression used. The >90 days threshold decreased PIRA events by a mean 54.3% (vs. >30 days, $p < 0.001$) over all progression definitions. Comparing roving versus fixed baseline, progression rates increased by a mean 111.8% with the mean proportion of PIRA increasing from 36.1% to 54.3%.

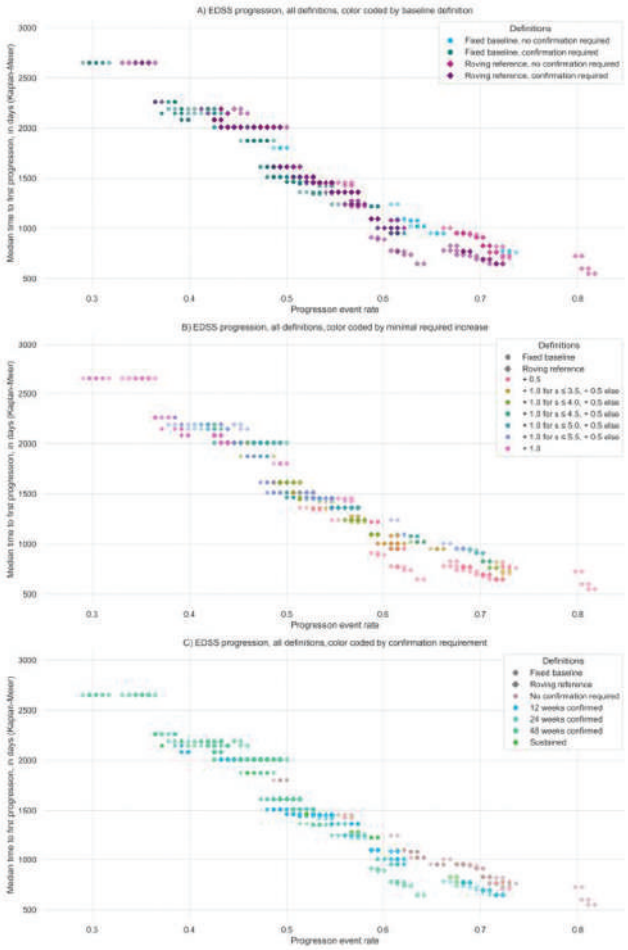

FIGURE 1. Impact of definition options on progression event rate versus time to progression.

Conclusion: The definition of disability progression strongly impacts rates of progression as well as observed proportions of RAW/PIRA.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by and received honoraria from Biogen, Celgene/BMS, Janssen, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva Nik Krajnc: nothing to disclose. Stefanie Marti: Nothing to disclose. Robert Hoepner: has received speaker/advisor honorary from Merck, Novartis, Roche, Biogen, Alexion, Sanofi, Janssen, Bristol-Myers Squibb, Teva/Mepha and Almirall. Michael Guger: has received support and honoraria from Almirall, Alexion, Bayer, Biogen, Bristol Myers Squibb, Genzyme, Horizon, Janssen, MedDay, Merck, Novartis, Octapharma, Roche, Sanofi Aventis, Shire and TEVA ratiopharm. Franziska Di Pauli: has received speaker/advisor honorary from Biogen, Celgene BMS, Horizon, Johnson&Johnson, Merck, Novartis, Sanofi-Genzyme, Teva, and Roche. Jörg Kraus: has received speaker/advisor honorary from Abbvie, Alexion, Almirall, Biogen, BMS, Cannaxan, Grünenthal, Horizon, Johnson&Johnson, Lilly, Merck, Novartis, Pharmgenetix, Roche, Sandoz, Sanofi, and Teva Christian Enzinger: has received speaker/advisor honorary from Biogen, Bayer, Merck, Novartis, Roche, Shire, Genzyme and Teva. Thomas Berger: has received speaker/advisor honorary from Allergan, Bayer, Biogen, Bionorica, BMS/Celgene, Genesis, GSK, GW/Jazz Pharma,

Horizon, Janssen-Cilag, MedDay, Merck, Novartis, Octapharma, Roche, Sandoz, Sanofi-Genzyme, Teva and UCB.

EPR-113 | Treatment escalation in multiple sclerosis based on isolated MRI activity – how much is too much?

G. Bsteh[1]; H. Hegen[3]; J. Walde[4]; L. Haider[5]; G. Traxler[6]; C. Gradl[7]; A. Salmen[8]; K. Riedl[1]; P. Leyendecker[5]; P. Poskaite[9]; P. Altmann[2]; M. Auer[3]; K. Berek[3]; F. Di Pauli[3]; F. Leutmezer[1]; N. Krajnc[2]; P. Rommer[1]; G. Zulehner[1]; T. Zrzavy[2]; F. Deisenhammer[3]; A. Chan[8]; T. Berger[1]; R. Hoepner[8]

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Background and Aims: Isolated value of MRI metrics in relapsing multiple sclerosis (RMS) as surrogate marker of response to disease-modifying treatment (DMT) is still a matter of debate.

Methods: We included RMS patients aged ≥18 years who i) had started moderately-effective DMT, ii) were clinically stable (no relapses/progression) on DMT for 12 months, iii) had MRI at DMT-start and after 12 months, and iv) had clinical follow-up for ≥2 years after the second MRI. The primary endpoint was occurrence of relapse during follow-up. Cox regression was employed including the number of new T2 lesions (T2L) as well as DMT strategy (continuing moderate DMT vs. escalating DMT) as independent covariates adjusting for age and sex.

Results: A total of 131 RMS patients (median age 36 [IQR 29–43] years, 73% females) were included and observed over a median 6 (5–9) years after second MRI. Sixty-two (47%) had relapse. Patients who continued moderate DMT had a three-fold increased risk of relapse given 2 new T2L and a four-fold increased risk given ≥3 new T2L. Escalation of DMT lowered the risk of relapse in patients with 2 new T2L by approximately 80% and with ≥3 new T2L by 65%. In case of only 1 new T2L, the increased risk of relapse as well as the treatment effect did not reach statistical significance of 5%.

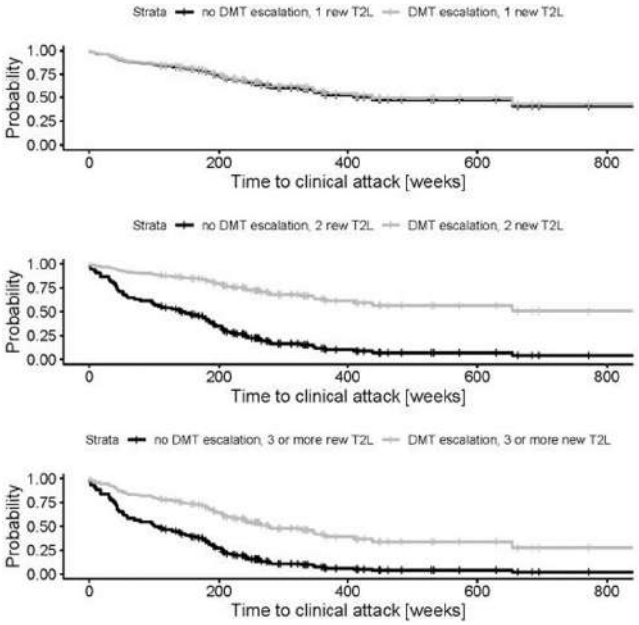

FIGURE 1. Probabilities for freedom of relapse depending on new T2 MRI lesions and DMT escalation.

Conclusion: In our real-world cohort of patients clinically stable under moderately effective DMT, escalation of DMT based on isolated MRI activity decreased risk of further relapse when ≥2 new T2L had occurred.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Janssen, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPR-114 | Headache disorders in multiple sclerosis: Is there an association? A systematic review and meta-analysis

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Background and Aims: The prevalence of headache disorders has been found to be increased in people with MS (pwMS), however, an association has not been established. Existing studies have provided conflicting results mostly because of methodological differences.

Methods: PubMed, Embase and Scopus were searched to identify eligible studies. Studies were included if they were cross-sectional, case-control or cohort. Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias of the included studies. Meta-analysis was conducted using StatsDirect by calculating the overall prevalence of headache disorders in pwMS as well as the Odds Ratio (OR) of headache disorders in pwMS versus controls.

Results: Twenty-three studies were included yielding a total of 5,440 MS patients and 28,0958 controls. The majority of them scored a NOS score between 5 and 6 (max 9), which indicates that they did not rank high in terms of quality, because most studies were cross-sectional and uncontrolled, and only one was prospective, controlled, and longitudinal, but with small population size. Pooled prevalence for all headache disorders, migraine and tension-type headache (TTH) in pwMS was 58%, 30% and 19% respectively. A significant association between migraine and MS was found (OR = 2.02, 95% CI = 1.14–3.57).

Figure 6. (A) Odds ratio forest plot for migraine in pwMS vs controls. **(B)** Funnel plot for odds ratio meta-analysis for migraine.

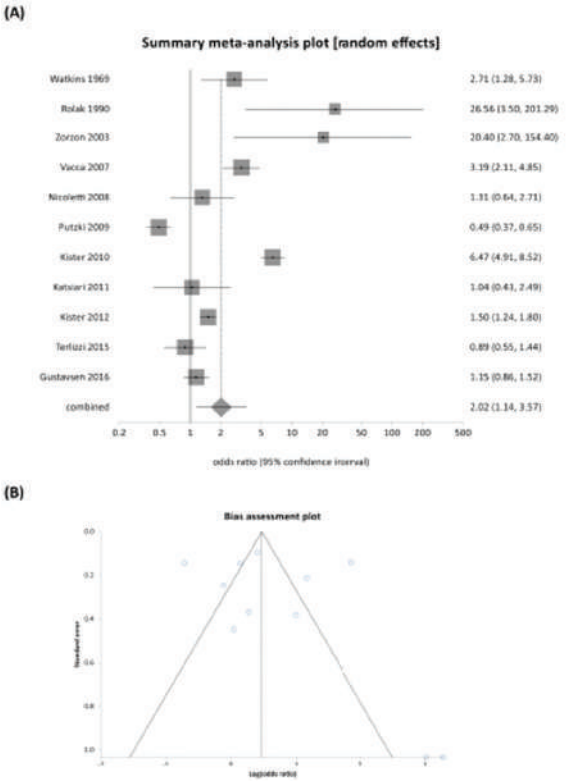


FIGURE 1. Odds ratio meta-analysis for migraine in multiple sclerosis versus controls.

Figure 3. (A) Forrest plot for overall migraine prevalence in pwMS **(B)** Funnel plot for migraine prevalence in pwMS

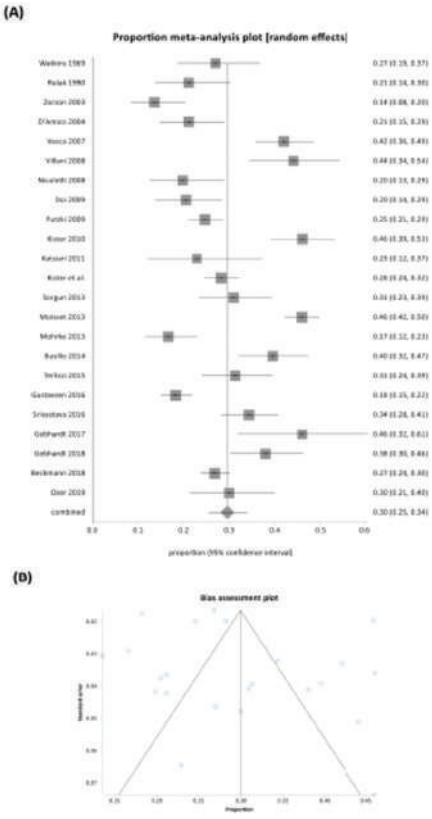
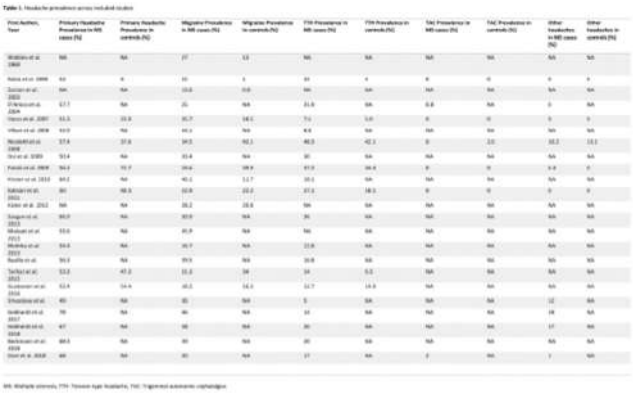


FIGURE 2. Prevalence meta-analysis for migraine in people with multiple sclerosis.

TABLE 1. Headache prevalence across included studies.



Conclusion: PwMS are twice as likely to experience migraine as controls, but the results need to be translated with caution since most of the studies included in the meta-analysis were of low or moderate quality. Larger prospective cohort, controlled, longitudinal studies are needed to confirm whether there is indeed an association between MS and migraine.

Disclosure: Nothing to disclose.

EPR-115 | Metabolomics of cerebrospinal fluid as a new potential source of biomarkers in early stages of multiple sclerosis

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[1]*Department of Neurology, Third Faculty of Medicine, Charles University and Faculty Hospital Kralovske Vinohrady, Prague, Czechia;* [2]*National Institute of Mental Health, Klecany, Czechia*

Background and Aims: Multiple sclerosis (MS) is a chronic autoimmune disease affecting predominantly the white matter of the CNS. The exact cause of MS is still unknown and its pathophysiology is very complex. Metabolomics is a systematic study that profiles endogenously small metabolites present in the examined substrate. Comparison of the metabolomic profiles represents an important strategy to understand the pathophysiology of the disease at the molecular level. The main goal of this study was to determine significant differences in the metabolome of the CSF of patients in the initial stage of MS compared to the controls, and to explain these differences from a pathophysiological point of view.
Methods: We collected CSF samples from 40 MS patients and 33 controls. The analysis was performed using high-performance liquid chromatography with tandem mass spectrophotometry with a high-resolution detector. After that, we correlated these findings with EDSS values at the time of examination, after 1 and 2 years.
Results: Statistically significant changes (p-value <0.05) were observed in arginine, histidine, spermidine, glutamate, choline, tyrosine, serine, oleic, stearic and linoleic acid. Additionally, we observed a significant negative correlation with the EDSS values at the time of examination and after 1 year in the case of histidine.

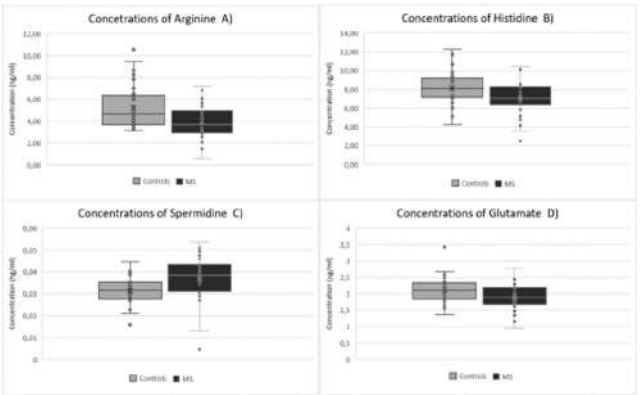

FIGURE 1. Comparison of concentrations between patients after the first clinical symptoms of MS and the control group in (A) arginine; (B) histidine; (C) spermidine; (D) glutamate.

Conclusion: In conclusion, we demonstrated significant differences in the concentrations of several metabolites in the CSF of patients in the early stages of MS, which could be used as new biomarkers of MS. These metabolites can potentially serve as prognostic indicators in the early stages of MS, markers of inflammation, ongoing demyelination or neurodegeneration.
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 1

EPR-116 | Nipocalimab in generalized myasthenia gravis: Results from a double-blind, placebo-controlled, randomized phase 3 study

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Background and Aims: Nipocalimab is a fully human, effectorless IgG1 anti-neonatal Fc receptor (FcRn) monoclonal antibody evaluated in a pivotal phase 3 study in generalized myasthenia gravis (gMG). Nipocalimab may ameliorate disease by selectively targeting FcRn IgG recycling and lowering circulating IgG, including pathogenic autoantibodies in gMG.
Methods: Seropositive (anti-AChR/MuSK/LRP4) or seronegative adult gMG patients (MGFA Class II-IV) with insufficient response (MG-ADL ≥6) to ongoing standard-of-care (SOC) therapy were enrolled in a 24-week double-blind placebo-controlled study. Randomization was 1:1 to SOC+ nipocalimab (30 mg/kg IV loading dose followed by 15mg/kg every two weeks) or SOC+ placebo. The primary endpoint was mean change in MG-ADL score from baseline over weeks 22, 23 and 24 in seropositive patients. Secondary endpoints included change in QMG score. Safety and tolerability were also assessed.
Results: Of 199 patients enrolled, 153 were seropositive. Baseline demographics were balanced across arms (77 nipocalimab, 76 placebo). Nipocalimab showed statistically significant improvement in clinical efficacy with mean change in MG-ADL score of -4.70 (SE 0.329) from baseline over weeks 22-24 on nipocalimab vs. -3.25 (SE 0.335) on placebo (difference of LS means -1.45; p=0.002). Statistically significant improvement was seen in mean change in QMG score of -4.86 (SE 0.504) from baseline over weeks 22-24 on

nipocalimab vs. -2.05 (SE 0.499) on placebo (difference of LS means -2.81, p<0.001). Nipocalimab was well-tolerated with incidence of adverse events comparable to placebo.

Conclusion: The efficacy and safety results of this pivotal phase 3 study of nipocalimab in gMG will be presented at the EAN 2024 Congress.

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EPR-117 | Minimal symptom expression in generalized myasthenia gravis: A post hoc analysis of MycarinG and open-label studies

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Background and Aims: High rates of Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis response were observed with rozanolixizumab across MycarinG (NCT03971422) and its open-label extension (OLE) studies in adults with generalized myasthenia gravis (MG). Attainment of minimal symptom expression (MSE; MG-ADL score: 0 or 1) is a stringent measure of therapeutic efficacy and a treatment goal in MG. A post hoc analysis of MSE is reported.

Methods: In MycarinG, patients received once-weekly placebo, rozanolixizumab 7mg/kg or 10mg/kg for 6 weeks. Patients could subsequently enrol in OLEs MG0004 (NCT04124965) then MG0007 (NCT04650854), or MG0007 directly. MG0004 comprised once-weekly rozanolixizumab 7mg/kg or 10mg/kg for <=52 weeks. In MG0007, after an initial 6-week cycle (rozanolixizumab 7mg/kg or 10mg/kg), cycles were administered on symptom worsening. Data were pooled across MycarinG, MG0004 (first 6 weeks) and MG0007 (data cut-off: 08 July 2022) for patients with >=2 symptom-driven cycles. The proportion of patients achieving MSE (MG-ADL score: 0 or 1) at any time in each cycle was analysed. Post hoc analysis of MSE rate was conducted based on achievement of MSE in Cycle 1.

Results: At data cut-off, 127 patients had >=2 symptom-driven cycles. MSE rates were 27.6% (35/127), 26.8% (34/127) and 25.5% (25/98) in Cycle 1, 2 and 3, respectively. For patients who achieved MSE in Cycle 1 and had further cycles, MSE rate was high over subsequent cycles (Cycle 2: 77.1% [27/35]; Cycle 3: 81.8% [18/22]).

Conclusion: The majority of patients achieving MSE in Cycle 1 continued to achieve MSE in subsequent rozanolixizumab treatment cycles.

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EPR-118 | DNTH103, a potentially safer and more convenient novel therapy for generalized myasthenia gravis

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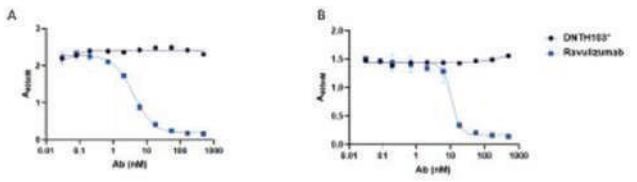
Background and Aims: Complement inhibition is an effective treatment pathway of generalized myasthenia gravis (gMG).1,2 DNTH103 is a fully human, potent, monoclonal antibody with a long half-life. It selectively binds to active human C1s to block only the classical complement pathway (CP), with the aim of maintaining complement mediated bacterial killing.

Methods: Three preclinical studies evaluated the efficacy or safety of DNTH103. Study 1: DNTH103 functional activity was characterized with Human-on-a-Chip Neuromuscular Junction (NMJ) System using healthy iPSC-derived motoneurons and skeletal muscle myotubes and sera from 3 healthy and 3 acetylcholine receptor-positive

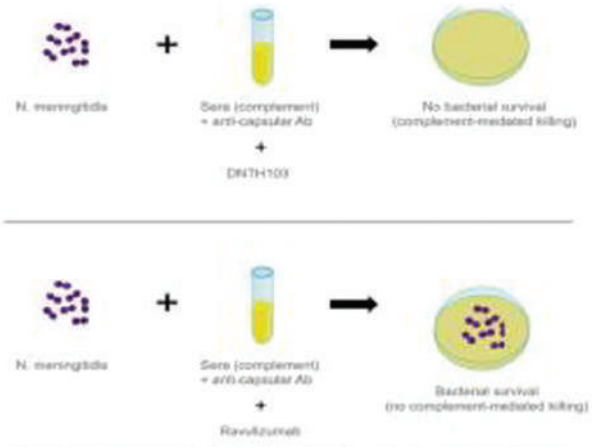
(AChR+) gMG patients. Fatigue index was calculated using continuous electrical stimulation of NMJs with or without DNTH103 or anti-C5. Study 2: complement assays using anti-C1s antibody (DNTH103*) and anti-C5 antibody (ravulizumab) evaluated their ability to inhibit the lectin and alternative pathways. Study 3: serum bactericidal assays with DNTH103, ravulizumab, or control were performed with 80% normal human sera and anti-capsular antibodies that mimic vaccination against Neisseria meningitidis.

Results: Treatment with DNTH103 at 0.1 and 1 μM reduced muscle fatigue index in AChR+ gMG samples by 24.8% and 27.8% respectively; similar results were observed with anti-C5. DNTH103* did not inhibit the lectin or alternative pathways or impede bacterial killing (similar to untreated control); ravulizumab inhibited all pathways and blocked bacterial killing by complement.



DNTH103* is an analogue and precursor to DNTH103 and differs in the N-terminal acid of the IgG4 heavy chain. Both have been shown to exhibit indistinguishable biophysical and functional properties.
Note: Data points represent mean (N=3) ± SD.
SD, standard deviation

FIGURE 1. Effect of Complement Inhibitory Antibodies on the Complement Lectin and Alternative Pathways in 1% Human Serum (mean ± SD).



*Serum bactericidal assay performed with 80% NHS and anti-capsular antibodies

FIGURE 2. High serum bactericidal assay to evaluate the effect of DNTH103 on N. meningitidis killing.

Conclusion: The ability of DNTH103 to improve neurotransmission and muscle contraction and selectively inhibit the CP makes it an attractive research candidate for gMG while potentially reducing the risk of severe infection seen with current gMG therapies.

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EPR-119 | Long-term safety outcomes of rozanolixizumab treatment in patients with generalized myasthenia gravis: A pooled analysis

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Background and Aims: The long-term safety of rozanolixizumab across MycarinG (NCT03971422) and ongoing open-label extension study MG0007 (NCT04650854) in adults with generalized myasthenia gravis has been previously presented (AANEM 2023). Here, predefined treatment-emergent adverse events (TEAEs) are evaluated.

Methods: In MycarinG, patients received one 6-week cycle of once-weekly placebo, rozanolixizumab 7mg/kg, or rozanolixizumab 10mg/kg. In MG0007, after an initial 6-week cycle (rozanolixizumab 7mg/kg or 10mg/kg), cycles were administered based on symptom worsening. Data were pooled across MycarinG and MG0007 (data cut-off: 08 July 2022) for patients receiving >=1 rozanolixizumab treatment cycle with a <=8-week follow-up period. Based on the mechanism of action of rozanolixizumab and pre-defined Medical Dictionary for Regulatory Activities search criteria, TEAEs including headaches, infections, hypersensitivity, anaphylactic reactions and gastrointestinal disorders were evaluated.

Results: Overall, 188 patients received >=1 rozanolixizumab treatment cycle (mean [standard deviation] cycles initiated: 3.6 [2.2]). TEAEs occurred in 89.9% (169/188) of patients (rozanolixizumab 7mg/kg: 77.4% [103/133]; 10mg/kg: 91.6% [120/131]). Incidence of pre-defined TEAEs was similar across repeated treatment cycles except for headaches and gastrointestinal disorders (more frequent in Cycle 1; Table); most were mild or moderate in intensity. Eight (4.3%) patients each experienced severe headaches and serious infections. One patient experienced serious aseptic meningitis which led them to discontinue the study. No serious hypersensitivity or anaphylactic reactions occurred. No potential risk for hepatotoxicity or renal toxicity or clinically meaningful changes in lipid or albumin levels were identified.

TABLE. Occurrence of pre-defined TEAEs by cycle in patients with at least one rozanolixizumab treatment cycle.

Category,* n/N (%)	Cycle	RLZ 7mg/kg	RLZ 10mg/kg	RLZ total
Headaches†	1	37/94 (39.4)	35/94 (37.2)	72/188 (38.3)
	2	17/69 (24.6)	17/74 (23.0)	34/143 (23.8)
	3	5/48 (10.4)	16/65 (24.6)	21/113 (18.6)
	4	6/40 (15.0)	11/52 (21.2)	17/92 (18.5)
	5	3/28 (10.7)	7/35 (20.0)	10/63 (15.9)
	6	3/17(17.6)	6/26 (23.1)	9/43 (20.9)
Infections‡	1	16/94 (17.0)	27/94 (28.7)	43/188 (22.9)
	2	10/69 (14.5)	14/74 (18.9)	24/143 (16.8)
	3	14/48 (29.2)	11/65 (16.9)	25/113 (22.1)
	4	8/40 (20.0)	8/52 (15.4)	16/92 (17.4)
	5	9/28 (32.1)	10/35 (28.6)	19/63 (30.2)
	6	3/17 (17.6)	5/26 (19.2)	8/43 (18.6)
Hypersensitivity-related TEAEs§	1	8/94 (8.5)	5/94 (5.3)	13/188 (6.9)
	2	3/69 (4.3)	4/74 (5.4)	7/143 (4.9)
	3	1/48 (2.1)	1/65 (1.5)	2/113 (1.8)
	4	2/40 (5.0)	1/52 (1.9)	3/92 (3.3)
	5	1/28 (3.6)	2/35 (5.7)	3/63 (4.8)
	6	0	0	0
Gastrointestinal disorders‖	1	26/94 (27.7)	25/94 (26.6)	51/188 (27.1)
	2	11/69 (15.9)	10/74 (13.5)	21/143 (14.7)
	3	2/48 (4.2)	12/65 (18.5)	14/113 (12.4)
	4	7/40 (17.5)	6/52 (11.5)	13/92 (14.1)
	5	3/28 (10.7)	7/35 (20.0)	10/63 (15.9)
	6	2/17 (11.8)	3/26 (11.5)	5/43 (11.6)

Most recent dose analysis. Patients who received both doses in any cycle are included in both 7mg/kg and 10mg/kg treatment groups. 'N' represents the number of patients in each cycle. *Categories based on pre-defined MedDRA search criteria. †The most common TEAE in this category was headache. ‡The most common TEAEs in this category were COVID-19, upper respiratory tract infection, nasopharyngitis and oral herpes. §Excluding injection-site reactions, the most common TEAEs in this category were rash and urticaria. ‖The most common TEAEs in this category were diarrhoea, nausea and abdominal pain. MedDRA, Medical Dictionary for Regulatory Activities; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.

Conclusion: Incidence of TEAEs did not increase with repeated rozanolixizumab treatment cycles; repeated treatment was well tolerated with an acceptable safety profile.

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EPR-120 | Safety and effectiveness of ravulizumab in generalized myasthenia gravis: Evidence from a global registry

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Background and Aims: Complement C5 inhibitor therapies (C5ITs) eculizumab and ravulizumab are approved in the US and EU for anti-acetylcholine-receptor-antibody-positive (AChR+) generalized myasthenia gravis (gMG). The ongoing, global MG-SPOTLIGHT Registry is assessing ravulizumab safety and effectiveness in patients with gMG in routine clinical practice using the MG Activities of Daily Living (MG-ADL; includes minimum symptom expression [MSE] outcome) and MG Foundation of America clinical class (MGFA-CC) assessments.

Methods: This interim analysis includes ravulizumab-treated patients with MG-ADL total scores or MGFA-CC data for >=2 time points (before and after initiating C5IT). Descriptive statistics were performed and presented as mean (SD). Safety was assessed by frequency of serious adverse events (SAEs).

Results: Of 70/204 enrolled patients (63% male; aged 60.4 [19.0] years at MG diagnosis), 17 received ravulizumab only and 53 transitioned to ravulizumab from eculizumab; ravulizumab treatment averaged 3–4 months. In ravulizumab-only patients, MG-ADL score decreased from 5.8 (3.4) to 3.4 (3.3) after ravulizumab initiation (Table 1); in ravulizumab-switch patients, MG-ADL scores remained stable from 3.7 (4.2) to 3.4 (3.2) following ravulizumab initiation (Table 2). In ravulizumab-only pts, the 66.7% with MGFA-CC 0-II increased to 88.9% after ravulizumab initiation; in ravulizumab-switch patients, the 92.0% with MGFA-CC 0-II remained stable at 96.0% following ravulizumab initiation. Similar patterns were observed in patients achieving MG-ADL MSE. SAEs were similar to previous findings. Limitations included no adjustment for confounders and small sample sizes.

TABLE 1. Outcomes in patients treated with ravulizumab only. Data shown as mean (SD) unless otherwise indicated.

	Before ravulizumab initiation	First assessment after ravulizumab initiation
Patients with MG-ADL total score assessments	n=10[a]	n=10[a]
MG-ADL total score	5.8 (3.4)	3.4 (3.3)
MG-ADL minimal symptom expression (MG-ADL ≤1), n (%)	0	3 (30.0)
Ravulizumab treatment duration at assessment, months	NA	3.6 (1.9)
Patients with MGFA clinical class assessments	n=9[b]	n=9[b]
MGFA clinical class, n (%)		
0	0	0
I	0	2 (22.2)
II (includes II, IIa, IIb)	6 (66.7)	6 (66.7)
III (includes III, IIIa, IIIb)	3 (33.3)	1 (11.1)
IV (includes IV, IVa, IVb)	0	0
V	0	0
Ravulizumab treatment duration at assessment, months	NA	3.6 (2.0)

[a]Of the patients treated with ravulizumab only (n=17), MG-ADL data were examined in the 10 patients with MG-ADL data available at the indicated time points.
[b]Of the patients treated with ravulizumab only (n=17), MGFA clinical class data were examined in the 9 patients with MGFA clinical class data available at the indicated time points.
MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NA, not applicable; SD, standard deviation.

TABLE 2. Outcomes in patients switched from eculizumab to ravulizumab. Data shown as mean (SD) unless otherwise indicated.

	Before eculizumab initiation	Last assessment after eculizumab initiation	First assessment after ravulizumab initiation
Patients with MG-ADL total score assessments	n=23[a]	n=23[a]	n=23[a]
MG-ADL total score	8.2 (3.5)	3.7 (4.2)	3.4 (3.2)
MG-ADL minimal symptom expression (MG-ADL ≤1), n (%)	1 (4.3)	9 (39.1)	9 (39.1)
Eculizumab treatment duration at assessment, months	NA	30.4 (21.0)	33.9 (20.3)
Ravulizumab treatment duration at assessment, months	NA	NA	3.9 (2.8)
Patients with MGFA clinical class assessments	n=25[a]	n=25[a]	n=25[a]
MGFA clinical class, n (%)			
0	0	1 (4.0)	1 (4.0)
I	0	9 (36.0)	11 (44.0)
II (includes II, IIa, IIb)	6 (24.0)	13 (52.0)	12 (48.0)
III (includes III, IIIa, IIIb)	16 (64.0)	1 (4.0)	1 (4.0)
IV (includes IV, IVa, IVb)	3 (12.0)	1 (4.0)	0
V	0	0	0
Eculizumab treatment duration at assessment, months	NA	31.3 (20.1)	34.2 (19.7)
Ravulizumab treatment duration at assessment, months	NA	NA	3.6 (2.8)

[a]Of the patients who transitioned from eculizumab to ravulizumab (n=53), MG-ADL data were examined in the 23 patients with MG-ADL data available at the indicated time points.
[b]Of the patients who transitioned from eculizumab to ravulizumab (n=53), MGFA clinical class data were examined in the 25 patients with MGFA clinical class data available at the indicated time points.
MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NA, not applicable; SD, standard deviation.

Conclusion: In clinical practice, ravulizumab was well tolerated and effective, with improved activities of daily living and MGFA-CC after initiating ravulizumab and sustained improvements when transitioning from eculizumab.

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EPR-121 | Pozelimab and cemdisiran combination therapy in patients with myasthenia gravis: Phase 3 NIMBLE trial design

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Background and Aims: Generalized myasthenia gravis (gMG) is a rare autoimmune disease of the neuromuscular junction predominantly due autoantibodies that bind to the acetylcholine receptor (AChR). IgG1 AChR (and less commonly anti-lipoprotein receptor-related protein 4, LRP4) antibodies are likely responsible for neuromuscular junction damage via terminal complement activation, in most patients with gMG. Pozelimab and cemdisiran are investigational agents for gMG that both inhibit the terminal complement. Cemdisiran is an N-acetylgalactosamine-conjugated small interfering RNA that suppresses liver production of C5, while pozelimab is a monoclonal antibody inhibitor to C5. We describe the design of the ongoing phase 3 NIMBLE trial (NCT05070858), which aims to evaluate the efficacy and safety of pozelimab plus cemdisiran in patients with symptomatic gMG.

Methods: This is a multinational, randomized, double-blind, placebo-controlled trial in patients with clinically confirmed gMG (seropositive for anti-AChR or anti-LRP4 antibodies). The study includes 5-week screening period; 24-week double-blind placebo-controlled treatment period; 28-week double-blind extension treatment period, 68-week open-label long-term treatment period; and a 52-week post-treatment follow-up period (Figure 1). On Day 1, patients will be randomized to one of four treatment arms (Figure 1). This study will enroll approximately 235 patients. The primary and secondary study endpoints are summarized in Table 1.

Results: The first patient was enrolled on December 14, 2021.

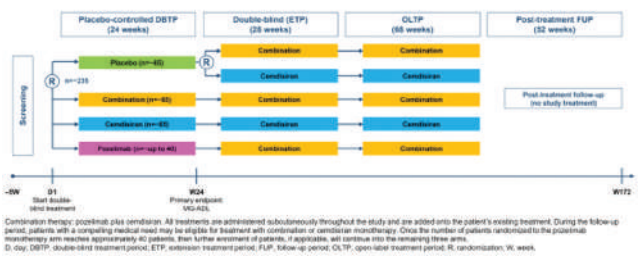
TABLE 1.

Table 1. Primary and secondary study endpoints of the NIMBLE trial

Endpoint
Primary endpoint
Change in MG-ADL total score from baseline to Week 24
Key secondary endpoint
Change from baseline in QMG score at Week 24
Other secondary endpoints
Proportion of patients:
• Responding on the MG-ADL, with a responder defined as one with a ≥3-point improvement from baseline to Week 24
• Responding on the QMG, with a responder defined as one with a ≥5-point improvement from baseline to Week 24
• With consistent response on the MG-ADL, defined as patients with ≥2-point MG-ADL improvement on ≥2 consecutive assessments spanning ≥4 weeks during the double-blind period
• With minimal symptom expression (defined by a score of 0–1 on the MG-ADL) at Week 24
• With improvement point thresholds of ≥2, 4, 5, 6, 7, 8, 9, or 10 on MG-ADL at Week 24
• With improvement point thresholds of ≥3, 4, 6, 7, 8, 9, or 10 on QMG at Week 24
Change from baseline in:
• MGC total score at Week 24
• MG-QOL15r total score at Week 24
• Incidence and severity of TEAEs, SAEs, and AESIs through Week 24
Concentrations of:
• Total pozelimab in serum at nominal time-points
• Cemdisiran and its metabolites in plasma at nominal time points
Incidence of:
• Treatment-emergent ADAs to pozelimab after repeated doses over time
• Treatment-emergent ADAs to cemdisiran after repeated doses over time
Change and percent change in CH50 over time

ADA, anti-drug antibody; AESI, adverse event of special interest; CH50, total complement hemolysis activity assay; MG-ADL, myasthenia gravis-activities of daily living; QMG, quantitative myasthenia gravis; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Figure 1. Study design



Combination therapy: pozelimab plus cemdisiran. All treatments are administered subcutaneously throughout the study and are added onto the patient's existing treatment. During the follow-up period, patients with a compelling medical need may be eligible for treatment with combination or cemdisiran monotherapy. Once the number of patients randomized to the pozelimab monotherapy arm reaches approximately 40 patients, then further enrollment of patients, if applicable, will continue into the remaining three arms.
D, day; DBTP, double-blind treatment period; ETP, extension treatment period; FUP, follow-up period; OLTP, open-label treatment period; R, randomization; W, week.

FIGURE 1.

Conclusion: This ongoing study (open for recruitment) is designed to evaluate the effect of pozelimab plus cemdisiran on daily functioning and other MG efficacy measures (including quality of life), as well as safety in patients with symptomatic gMG.

Disclosure: SJ has served as an international advisory board member for Alexion, Alnylam, argenx, Immunovant, Regeneron, and UCB; is currently an expert panel member of the Myasthenia Gravis Consortium for argenx; and has received speaker fees from Eisai Pharmaceuticals and Terumo BCT. UC, KM, LP, RP and CL are employees of and stockholders in Regeneron Pharmaceuticals, Inc. JFH has received research funding (paid to institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, and Takeda Pharmaceuticals; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc (now Amgen), Medscape CME, Merck EMB Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Ra Pharmaceuticals/UCB Bioscience, Regeneron Pharmaceuticals, Sanofi US, and Zai Labs; non-financial support from Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Bioscience and Zai Labs.

EPR-122 | Rozanolixizumab in generalized myasthenia gravis: Patient-reported outcomes in the randomized, Phase 3, MycarinG study

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Background and Aims: The five Myasthenia Gravis Symptoms Patient-Reported Outcome (MGSPRO) scales, developed to evaluate changes in severity of patient-relevant symptoms, were used to assess efficacy of rozanolixizumab in patients with generalized myasthenia gravis (gMG) in the MycarinG study.

Methods: The randomized, double-blind, placebo-controlled, Phase 3, MycarinG (NCT03971422) study enrolled adults with Myasthenia Gravis Foundation of America Disease Class II–IVa acetylcholine receptor or muscle-specific tyrosine kinase autoantibody-positive gMG. Patients were randomized 1:1:1 to weekly subcutaneous rozanolixizumab 7mg/kg, rozanolixizumab 10mg/kg, or placebo for 6 weeks. Primary endpoint was change from baseline (CFB) to Day 43 in Myasthenia Gravis Activities of Daily Living (MG-ADL) score. CFB to Day 43 in the five MGSPRO scale scores was assessed (secondary endpoints: Muscle Weakness Fatigability, Physical Fatigue, Bulbar Muscle Weakness; other endpoints: Respiratory and Ocular Muscle Weakness) . Safety was also assessed.

Results: Overall, 200 patients received rozanolixizumab 7mg/kg ($n=66$), 10 mg/kg ($n=67$) or placebo ($n=67$). At Day 43, least squares mean CFB in MG-ADL score was clinically meaningful and statistically significantly improved with rozanolixizumab versus placebo (Table). Improvements in MGSPRO Muscle Weakness Fatigability, Physical Fatigue and Bulbar Muscle Weakness scores were also statistically significant versus placebo, and improvements were observed in mean CFB to Day 43 for MGSPRO Respiratory and Ocular Muscle Weakness scores versus placebo (Table). Treatment-emergent adverse events occurred in 52 (81.3%), 57 (82.6%) and 45 (67.2%) patients in the rozanolixizumab 7 mg/kg, 10 mg/kg and placebo groups.

		Placebo (n=67)	RLZ 7mg/kg (n=66)	RLZ 10mg/kg (n=67)
MG-ADL (primary endpoint)	LS mean (SE)	−0.8 (0.5)	−3.4 (0.5)	−3.4 (0.5)
	LS mean difference vs placebo (95% CI)		−2.6 (−4.1, −1.2)	−2.6 (−4.0, −1.2)
	p-value		<0.001	<0.001
Muscle Weakness Fatigability	LS mean (SE)	−10.6 (3.0)	−23.0 (3.0)	−25.8 (3.1)
	LS mean difference vs placebo (95% CI)		−12.4 (−21.8, −4.1)	−15.2 (−23.6, −6.5)
	p-value		<0.001	<0.001
Physical Fatigue	LS mean (SE)	−10.6 (3.1)	−19.3 (3.0)	−25.5 (3.1)
	LS mean difference vs placebo (95% CI)		−8.7 (−18.1, −0.1)	−14.8 (−23.8, −5.9)
	p-value		0.012	<0.001
Bulbar Muscle Weakness	LS mean (SE)	−3.5 (2.4)	−14.8 (2.4)	−14.2 (2.5)
	LS mean difference vs placebo (95% CI)		−11.3 (−19.0, −5.0)	−10.7 (−17.8, −4.0)
	p-value		<0.001	<0.001
Respiratory Muscle Weakness*	Observed mean (SD)	−2.1 (22.5)	−12.5 (21.6)	−11.8 (16.5)
	Mean difference vs placebo		−10.4	−9.7
Ocular Muscle Weakness*	Observed mean (SD)	−3.4 (18.2)	−9.6 (16.8)	−11.9 (14.0)
	Mean difference vs placebo		−6.2	−8.5

*Results for these endpoints are descriptive.

CFB, change from baseline; CI, confidence interval; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGSPRO, Myasthenia Gravis Symptoms Patient-Reported Outcome; RLZ, rozanolixizumab; SD, standard deviation; SE, standard error.

CFB to Day 43 in MG-ADL score (primary endpoint) and MGSPRO scale scores

Conclusion: Rozanolixizumab demonstrated greater improvements in all five patient-relevant symptoms scales versus placebo, including Physical Fatigue, an important symptom for patients with gMG

Disclosure: Due to space constraints, full disclosures will be provided separately by email and will be included in the presentation if accepted. This study was funded by UCB Pharma. Sabrina Sacconi and Artur Drużdż have nothing to disclose. Marion Boehnlein, Asha Hareendran, Bernhard Greve, Thaïs Tarancón and Franz Woltering are employees and shareholders of UCB Pharma. The other authors' disclosures will be provided separately.

EPR-123 | Quality of life in generalized myasthenia gravis: Results from a global registry of eculizumab and ravulizumab treatment

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Background and Aims: Complement C5 inhibitor therapies (C5ITs) eculizumab and ravulizumab are approved in the US and EU for anti-acetylcholine receptor antibody-positive (AChR+) generalized myasthenia gravis (gMG). The global MG SPOTLIGHT Registry enrolled patients receiving C5ITs in clinical practice to assess eculizumab and ravulizumab safety and effectiveness in patients with gMG. This analysis examined quality of life (QOL) changes after C5IT initiation using Myasthenia Gravis Quality of Life 15-revised (MG-QOL15r) scores.

Methods: Enrolled registry patients were included if they had MG-QOL15r assessments before and after C5IT initiation. Descriptive statistics were performed and are presented as mean (SD). Safety was assessed by evaluating frequency and type of serious adverse events.

Results: The 47/204 (23%) enrolled registry patients with available data were 60% male (aged 46.5 [20.3] years at MG diagnosis). In eculizumab-only-treated patients ($n=30$), the MG-QOL15r score before eculizumab initiation, 18.2 (6.9), improved to 12.2 (8.5) after 30.9 (16.1) months of eculizumab treatment. Among eculizumab-to-ravulizumab switched patients ($n=10$), the MG-QOL15r score of 18.2 (7.9) before C5IT initiation improved to 11.2 (10.6) after 29.6 (25.4) months of eculizumab and to 8.7 (9.0) after 4.6 (3.1) months of ravulizumab. The C5IT safety profile within this patient cohort was similar to previous analyses, including clinical trial data. Limitations include the lower number of patients with MG-QOL15r data in routine clinical use and lack of adjustment for potential confounders.

Conclusion: These initial results underline clinically meaningful QOL improvements in patients with AChR+ gMG treated with C5ITs in clinical practice. Patients transitioned from eculizumab experienced further slight QOL improvements with ravulizumab.

Disclosure: CAS, NJ, GC, PN, RT, and AG, or their institutions, have received compensation from research and funding organisations and/or pharmaceutical companies for speaking, consulting, and contracted research. LZ, ER, and AY are employees of Alexion, AstraZeneca Rare Disease and hold stock options in AstraZeneca.

EPR-124 | Measuring change in OXPHOS-deficiency in skeletal muscle of patients with mitochondrial myopathy

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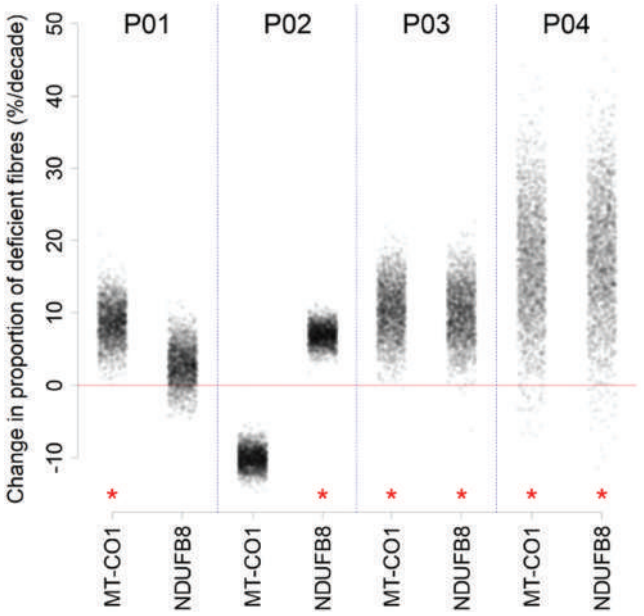
Background and Aims: Mitochondrial diseases affect ~1 in 5,000 adults and often cause skeletal muscle disease (i.e., weakness, fatigue, and exercise intolerance). Disrupted oxidative phosphorylation (OXPHOS), a hallmark of mitochondrial disease, is a commonly used surrogate of impaired muscle bioenergetics. However, standard immunofluorescence (IF) OXPHOS markers have not been systematically demonstrated to detect changes and predict disease progression in longitudinal studies.

Methods: So far, we selected 4 participants with progressive myopathy due to mitochondrial DNA (mtDNA) single, large-scale deletions (SLSD). We used IF to measure changes in proportions of muscle fibres deficient in the standard OXPHOS markers, MT-CO1 and NDUFB8, between muscle biopsies at two time points (>3.6 years apart). Fibre status per marker was determined using a Bayesian Inference and reference fibre data from healthy controls. We plan to extend our cohort to 20 participants.

Results: We detected an increase deficiency for both markers, except for participant 2, who shown a decrease in MT-CO1 deficiency (Fig.1). Rate of change was estimated, using sampling interval, and varied substantially between participants and markers. This variability is unsurprising because deletion size, position, and proportion vary and differentially affect OXPHOS markers, and compensatory overexpression is well documented.



Rate of change in proportions of OXPHOS-deficient fibres between time points per participant. Dots are Bayesian Inference simulations of fibre OXPHOS status capturing uncertainty of the analysis. (*) statistically significant increasing deficiency.

Conclusion: Standard IF protocols seem to detect changes in markers of OXPHOS deficiency in skeletal muscle tissue over time. We now aim to increase our cohort and study the effect of deletion size, position, and proportion on the trajectory of these biomarkers. We hope that our findings will support future studies into disease progression and clinical trials in mitochondrial diseases.

Disclosure: Nothing to disclose. Work funded by Wellcome.

Sunday, June 30 2024

Ageing and dementia 2

EPR-125 | **Predictive efficacy of atrophy rating scales and volumetric analysis for Aβ-CSF status and anti-Aβ treatment eligibility**

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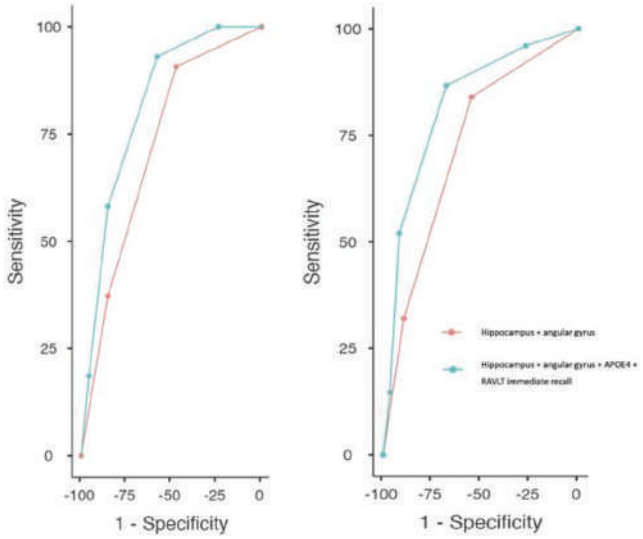
Background and Aims: Establishing tools that enable the prediction of amyloid status is of primary importance, especially considering the forthcoming availability of disease-modifying therapies and the need to identify eligible patients with Alzheimer's disease. We aim to predict CSF-amyloid status and eligibility for anti-amyloid treatment in a memory clinic by (I) comparing the predictive performances of visual, automated rating scales and volumetric analysis, and (II) combining MRI volumetric data with neuropsychological tests and Apoε4 status.

Methods: From the initial pool of 592 consecutive patients, 290 patients underwent a comprehensive assessment. Amyloid status was determined using data-driven CSF biomarker cutoffs (Ab42/Ab40 ratio). To assess eligibility for anti-Aβ treatment, we adhered to recent appropriate use recommendations published after the FDA approval of the anti-Aβ drug Aducanumab.

Results: The automated rating scales and volumetric analysis demonstrated higher performance compared to visual assessment in predicting Aβ status, particularly for parietal-GCA (AUC=0.699), MTA (AUC=0.663) scores, hippocampal (AUC=0.681), and angular gyrus (AUC=0.689) volumes. Combining hippocampal and angular gyrus volumes, with RAVLT immediate recall and Apoε4 status reached the highest accuracy (AUC=0.821), which remained high even in predicting anti-Aβ treatment eligibility (AUC=0.818).



ROC curves for the model combining hippocampus and angular gyrus volumes, and the comprehensive model adding neuropsychological and ApoE4 data. On the left in the global cohort, while the right in the prediction of the eligibility for anti-Aβ treatment.

Conclusion: Our study underscores the importance of employing automated neuroimaging assessment to quantify brain atrophy in a tertiary memory clinic. The integration of volumetric data with neuropsychological and genetic information results in a high level of accuracy for predicting amyloid-CSF status and anti-Aβ treatment eligibility, within the naturalistic and heterogeneous context of a memory clinic.

Disclosure: Nothing to disclose.

EPR-126 | 18F-fluorodeoxyglucose levels in cerebrospinal fluid are driven by glucose demand of the brain in Alzheimer's disease

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Background and Aims: Glucose delivery to the brain requires transport across blood-brain-barrier (BBB) through glucose transporters (GLUT). It has been suggested that GLUT downregulation may be linked to neuronal deficits in Alzheimer disease (AD), but it remains unclear whether it is caused by reduced demands in affected tissues or whether reduced glucose availability, linked to altered BBB, could induce neuronal degeneration. The study aimed to investigate, for the first time to our knowledge, the relationships between cerebrospinal fluid (CSF) [18F]fluorodeoxyglucose (18F-FDG), cortical and subcortical glucose metabolism and most relevant CSF parameters in a population of AD patients.
Methods: A total of 224 biologically defined AD patients underwent a complete clinical investigation, structural MRI, 18F-FDG PET/CT and CSF analysis 2 weeks before the PET/CT scan. Core AD biomarkers, glycorrhachia and Albumin Quotient (QAlb) were evaluated. 18F-FDG in CSF and in brain was quantified using WFUpickatlas toolkit implemented in statistical parametric mapping (SPM12). Normalization was performed using the pons as reference.
Results: 18F-FDG in CSF was positivley related to glucose metabolism in gray matter ($r=0.37$; $p<0.0001$) and white matter ($r=0.44$; $p<0.0001$). Instead, higher BBB permeability (Qalb) was associated with lower glucose uptake in gray matter ($r=-0.16$; $p=0.018$), white matter ($r=-0.14$; $p=0.040$) and 18F-FDG in CSF($r=-0.16$; $p=0.018$). The mediation analysis confirmed a significant total effect of 18F-FDG in CSF on glucose metabolism in gray matter ($p<0.001$) although not mediated by QAlb values ($p=0.104$).
Conclusion: The presence of 18F-FDG in CSF could be indicative of glucose uptake to meet energy demands of AD brains, independent of BBB permeability.
Disclosure: Nothing to disclose.

EPR-127 | Increased mortality in older adults with parkinsonian signs – A longitudinal study from the Good Aging in Skåne-cohort

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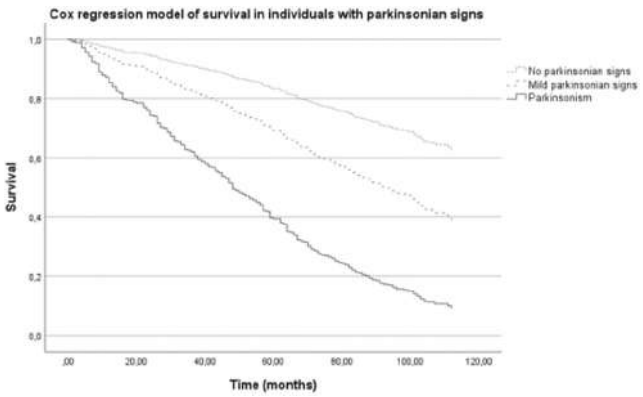
Background and Aims: Mild parkinsonian signs (MPS) are highly prevalent in older adults. The aim of this study was to investigate the associations between parkinsonian signs and mortality, risk factors and underlying cause of death in older adults.
Methods: Community-dwelling older adults without any previously diagnosed movement disorder ($n=480$, median age 85, range 80–101 years) were examined using United Parkinson's Disease Rating Scale (UPDRS) during 2010-2012. Data regarding mortality were collected until 2020-09-22 from the Swedish cause of death registry.
Results: MPS were present in 49.4% and parkinsonism in 28.6% of the cohort (missing UPDRS-score in 79 participants). Mortality rates were significantly increased in individuals with MPS (HR 2.0, CI 1.2–3.4, p-value 0.008) and parkinsonism (HR 5.1, CI 3.0–8.5, p-value <0.001). Preliminary results imply that the main causes of death were neoplasms, vascular disease, and neurologic disease.



Survival of individuals above 80 years of age with mild parkinsonian signs and parkinsonism. A follow-up of 480 individuals, mild parkinsonian signs present in 49.4% and parkinsonism in 28.6%.
Conclusion: In a population of older adults above 80 years, parkinsonian signs are associated with an increased mortality rate. Further research regarding pathophysiology of parkinsonian symptoms in older adults with MPS is needed to increase knowledge and provide adequate treatment.
Disclosure: The authors have nothing to disclose. The Good Aging in Skåne (GÅS-SNAC) project, part of the Swedish National Study on Aging and Care, was supported by the Swedish Ministry of Health and Social Affairs, the county Region Skåne, the Medical Faculty at Lund University, and the Swedish Research Council (grant number 2013-8604, 2017-01613, 2021-01437).

EPR-128 | Age of onset moderates the effects of Vascular Risk Factors in Alzheimer's disease

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Background and Aims: The role of Vascular risk factors (VRFs) in the progression of Alzheimer's disease (AD) is not cleared yet and could be influenced by age-specific mechanisms of resilience and vulnerability.

Methods: For 368 patients with AD, we computed eight risk factors in a cumulative measure (vascular score, VS). We regressed VS on CSF markers of amyloid deposition, neurodegeneration (t-tau), and blood-brain-barrier (BBB) permeability (Albumin-Quotient, Qalb), stratifying patients into early-onset (<65,EOAD), classic late-onset (65–75, cLOAD) and very late-onset (>75,vLOAD). Moreover, with bootstrapped mediation analysis we tested direct and indirect associations of VS with t-tau, using Qalb as mediator. In a subset of 105 patients, we performed multivariate backward regressions to assess the effects of Qalb, VS, and t-tau on ΔMMSE.

Results: Cumulative vascular risk (VS) was positively associated with t-tau in EOAD ($\beta = 0.256$, $p = 0.019$) and in vLOAD ($\beta = 0.007$, $p < 0.001$), but not in cLOAD ($\beta = 0.007$, $p = 0.925$). Conversely, VS was positively associated with Qalb only in cLOAD ($\beta = 0.173$, $p = 0.015$), where Qalb trends toward mediating the association between VS and t-tau. Longitudinally, ΔMMSE was not associated with VS in any of the subgroups. Instead, it was negatively associated with both CSF t-tau and Qalb in EOAD and vLOAD, while Qalb was the only determinant of cognitive decline in cLOAD.

Conclusion: VRFs do not influence cognitive decline in AD, but impact neurodegeneration differently depending on age-of-onset, and notably in patients with more aggressive progression (EOAD) or old age (vLOAD). Instead, in cLOAD, the modulation of BBB permeability could represent a resilience response to neurodegeneration, albeit causing relatively steeper cognitive decline.

Disclosure: Nothing to disclose.

EPR-129 | The role of astrocytes in vascular regulation along the Alzheimer's continuum: 18F-FDG-PET correlates

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Background and Aims: Astrocytes in Alzheimer's disease (AD) exert a pivotal role in blood-brain barrier (BBB) integrity and neurovascular unit (NVU) releasing soluble factors like Vascular Endothelial Growth Factor (VEGF), Matrix Metalloproteinases (MMP)-9, MMP-2 and Endothelin-1 (ET-1), all involved in mechanisms of neuroprotection in AD. In addition, astrocytes contribute to brain energy metabolism through glucose consumption. Here, we aimed at exploring the possible associations between CSF levels of the above-mentioned vascular factors and regional hypometabolism, evaluated via 18F-fluorodeoxyglucose Positron Emission Tomography (18F-FDG-PET).

Methods: We recruited 61 patients that fulfilled NIA-AA diagnostic criteria for AD and performed a 18F-FDG-PET scan and CSF evaluation of VEGF, MMP2/9 and ET-1 levels.

Results: ET-1 was positively associated to 18F-FDG uptake in right Broadman area (BA)13, BA 6 and BA 27, and left BA 22, BA 47 and BA 13 (see Figure 1). We also observed a trend of positive association between 18F-FDG uptake and MMP-2 CSF levels in left BA 20 and BA 21 (See Figure 2). No association was found with neither CSF VEGF nor MMP-9 levels (see Table).

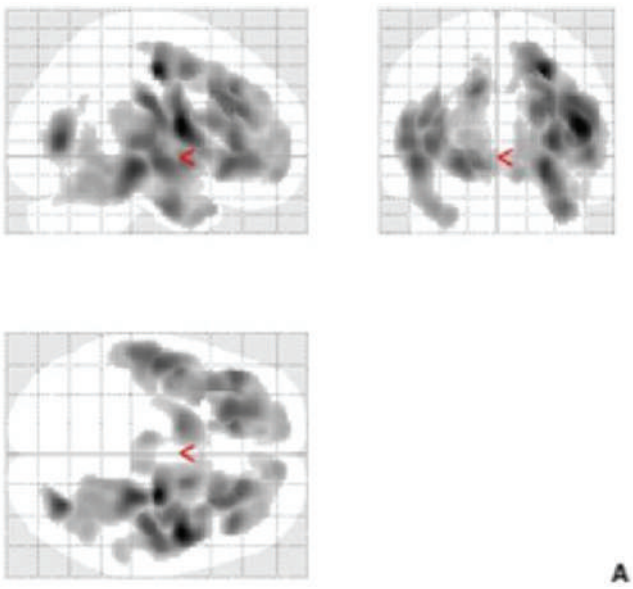

FIGURE 1. MNI projections showing cluster obtained in SPM regression analysis for the positive association between CSF ET-1 levels and glucose 18F-FDG uptake. The strength of correlation is represented in gray intensity scale.

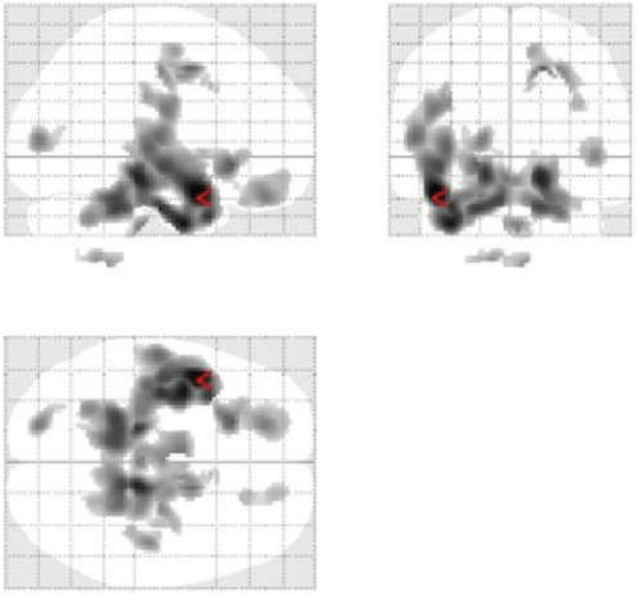

FIGURE 2. MNI projections showing cluster obtained in SPM regression analysis for the positive association between CSF MMP-2 levels and glucose 18F-FDG uptake. The strength of correlation is represented in gray intensity scale.

TABLE. Multivariate regression analysis showing associations between CSF vascular biomarkers and 18F-FDG uptake. L: left; R: right; FWE: Familywise error; FDR: False discovery rate; BA: Broadman Area; p unc: uncorrected p, n/a: not applicable.

	Cluster Level					Voxel Level		
	Cluster p (FWE)	Cluster p (FDR)	Cluster extent	p unc	Cortical region	z score	Talairach coordinates	Cortical region
VEGF								
	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
MMP-2								
Positive	0.074	0.088	6310	0.003	L Middle Temporal Gyrus L Inferior Temporal Gyrus R Cerebellum Culmen	3.57 3.31 3.20	-44 6 -22 -36 -2 -38 16 -28 -12	L BA 20 L BA 21 -
Negative	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
MMP-9								
	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
ET-1								
Positive	0.004	0.002	11535	0.000	R Sub-Lobar, Insula R Precentral Gyrus R Parahyppocampal Gyrus	4.26 4.08 3.64	46 -2 16 24 -14 46 26 -28 -8	R BA 13 R BA 6 R BA 27
	0.039	0.008	7312	0.001	L Superior Temporal Gyrus L Inferior Frontal Gyrus L Inferior Frontal Gyrus	3.54 3.46 3.40	-48 -14 -6 -24. 26 -6 -40 30 6	L BA 22 L BA 47 L BA 13
Negative	0.054	0.032	6772	0.002	L Precentral Gyrus R Precentral Gyrus L Precentral Gyrus	5.40 4.56 4.18	-38 -18 60 32 -14 64 -8 -2 66	L BA 4 R BA 6 L BA 6

Conclusion: The coexistence of positive associations between vascular factors and 18F-FDG uptake confirms that astrocytes can impact vascular regulation in a dynamic and heterogeneous process, where the positive association may represent a compensatory mechanism to counteract NVU dysregulation. This is in line with previous evidences that showed a positive correlation between CSF-GFAP and regional metabolism in key brain areas, suggesting a possible compensatory function of astrogliosis. To what extent such association can impact cognitive functions in AD remains elusive.

Disclosure: Nothing to disclose.

EPR-130 | Combined use of plasma p-tau181 and NfL chain in subjective cognitive decline and mild cognitive impairment

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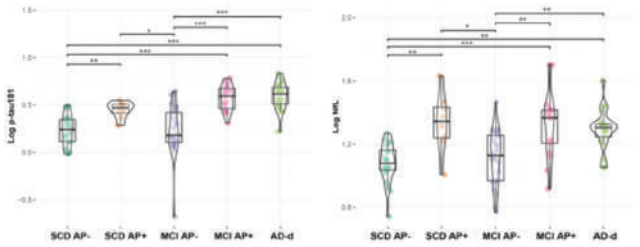
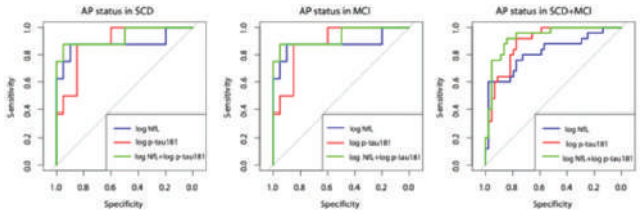
Background and Aims: We aimed to assess diagnostic accuracy of plasma p-tau181 and NfL separately and in combination in discriminating Subjective Cognitive Decline (SCD) and Mild Cognitive Impairment (MCI) patients carrying Alzheimer's disease (AD) pathology from non-carriers; to propose a flowchart for the interpretation of the results of plasma p-tau181 and NfL.

Methods: We included 43 SCD, 41 MCI and 21 AD-demented (AD-d) patients, who underwent plasma p-tau181 and NfL analysis. Twenty-eight SCD, 41 MCI and 21 AD-d patients underwent CSF biomarkers analysis (Aβ1-42, Aβ1-42/1-40, p-tau, t-tau) and were classified as carriers of AD pathology (AP+) it they were A+/T+ (regardless of N), or non-carriers (AP-) when they were A- (regardless of T and N), A+/T-/N-, or A+/T-/N+ according to the A/T(N) system.

Results: Plasma p-tau181 and NfL separately showed a good accuracy (AUC=0.88), while the combined model (NfL+p-tau181) showed an excellent accuracy (AUC=0.092) in discriminating AP+ from AP- patients. Plasma p-tau181 and NfL results were moderately concordant (Coehn's $k=0.50$, $p<0.001$). Based on a logistic regression model, we estimated the risk of AD pathology considering the two biomarkers: 10.91% if both p-tau181 and NfL were negative; 41.10% and 76.49% if only one biomarker was positive (respectively p-tau18 and NfL); 94.88% if both p-tau181 and NfL were positive.

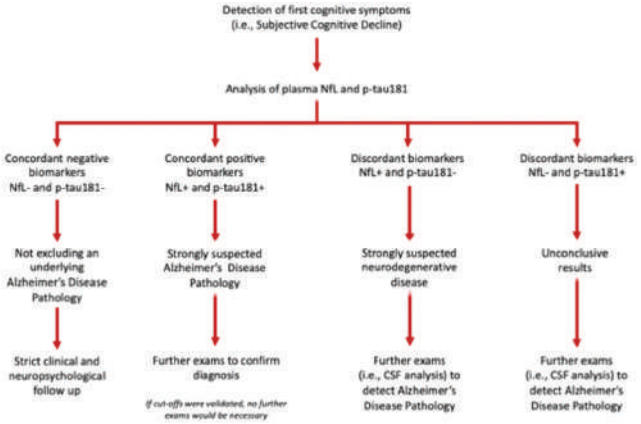


Plasma biomarkers levels across diagnosis/ATN groups.



ROC curves for accuracy of plasma p-tau181, NfL and the combined model (NfL+p-tau181) in distinguishing AP+ from AP- patients in SCD and MCI, considering both separately and together.

Conclusion: Considering the moderate concordance and the risk of presenting an underlying AD pathology according to the positivity of plasma p-tau181 and NfL, we proposed a flow chart to guide the combined use of plasma p-tau181 and NfL and the interpretation of biomarker results to detect AD pathology.



Flow chart for the potential use and interpretation of plasma biomarkers in clinical setting for the early detection of Alzheimer's disease

Disclosure: Nothing to disclose.

EPR-131 | Association between presence of alpha synuclein aggregates in the olfactory mucosa and DaT-SPECT patterns in DLB

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Background and Aims: Alpha-synucleinopathies, characterized by abnormal alpha-synuclein (a-syn) aggregates in the brain, exhibit varied clinical presentations, including distinct motor (Parkinson's Disease PD) and cognitive (Lewy Body Dementia DLB) forms. Pathological confirmation of a-syn-related pathology through minimally invasive techniques is crucial for neurodegenerative disease research. The Real-Time Quaking Induced Conversion assay (RT-QuIC) has been tested for a-syn detection in olfactory mucosa brushing (OMB) and cerebrospinal fluid (CSF), especially in PD patients. This study investigates dopamine transporter SPECT (DaT-SPECT) alterations' symmetry in DLB patients relative to RT-QuIC results in OMB.

Methods: Thirty-five DLB patients (27 males, 8 females) were enrolled, meeting McKeith's criteria. Mean age at OMB was 76 ±6 years, MMSE score 23.8 ±5. Patients were categorized into RT-QuIC-positive ($n=26$) and negative ($n=9$) groups. Thirty-one underwent DaT-SPECT; and BasGanV2 software was used for image post-processing, comparing them with normal controls to derive Z-scores. Non-parametric statistics assessed putamen and caudate Z-score asymmetry.

TABLE 1. Demographic characteristics of patients. Legend: DLB: Dementia with Lewy Bodies; pDLB: prodromal DLB; CCF: Core Clinical Features; VH: Visual Hallucinations; CF: Cognitive Fluctuations; Pk: Parkinsonism; RBD: Rem Sleep behavior Disorder; RWA: RE.

		Mean (SD)			CCF				
		Age, y	MMSE baseline	MMSE longitudinal	VH	CF	Pk	RBD_all	RWA
PDLB (n=18)		74.9 (5.3)	27 (1.9)	25.3 (4.3)	11/18 (61.1%)	9/18 (50%)	16/18 (88.9%)	12/18 (66.7%)	8/18 (44.4%)
	OMB +	74.7 (5.7)	26.9 (2.1)	25.6 (3.7)	10/14 (71.4%)	8/14 (57.1%)	12/14 (85.7%)	10/14 (71.4%)	7/15 (50%)
	OMB -	75.6 (4.5)	27.3 (1)	24.3 (6.8)	1/4 (25%)	1/4 (25%)	4/4 (100%)	2/4 (50%)	¼ (25%)
DLB (n=17)		77.6 (5.8)	20.5 (5)	13.8 (6.6)	12/17 (70.6%)	8/17 (47,1%)	15/17 (88.2%)	14/17 (82.4%)	9/17 (52.9%)
	OMB +	77.3 (6.2)	21.3 (5.5)	12.8 (7.2)	10/12 (83.3%)	5/12 (41.7%)	10/12 (83.3%)	10/12 (83.3%)	8/12 (66.7%)
	OMB -	78.6 (5.3)	18.6 (3.4)	16.8 (3.3)	2/5 (40%)	3/5 (60%)	5/5 (100%)	4/5 (80%)	1/5 (20%)

Results: Olfactory brushing was well tolerated by all participants. Statistically significant caudate asymmetry was found between RT-QuIC-positive and -negative OMB groups (positive: mean 0.1338 ±0.182, negative: mean 0.0337 ±0.187; $p=0.03$). No significant putamen difference was noted ($p=0.3$).

Conclusion: Our results confirm the frequent involvement of olfactory mucosa in DLB and validate RT-QuIC's diagnostic utility. OMB involvement can lead to a different spreading pattern of a-syn pathology. RT-QuIC in OMB is a novel diagnostic tool for alpha-synucleinopathies, well tolerated in DLB patients. Further research is needed to assess its prognostic value and correlations with other biomarkers.

Disclosure: Nothing to disclose.

EPR-132 | Sustained meningeal lymphatic vessel atrophy or expansion does not alter Alzheimer's disease-related amyloid pathology

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Background and Aims: The discovery of meningeal lymphatic vessels in dura mater, also known as dural lymphatic vessels (dLVs) that depend on vascular endothelial growth factor-C (VEGF-C) expression has raised interest in their possible involvement in Alzheimer's disease (AD).
Methods: Here we induce sustained dLV atrophy or hyperplasia, by blocking or overexpressing VEGF-C in the APdE9 and 5xFAD mouse models of AD, resulting in impaired or improved macromolecular cerebrospinal fluid (CSF) drainage to cervical lymph nodes.
Results: In the AD mice, dLV morphology or function was not altered, dural amyloid beta accumulation was confined to blood vessels, and sustained manipulation of dLVs did not lead to significant changes in overall brain amyloid beta plaque load. Moreover, dLV atrophy did not alter the behavioral phenotypes of the AD mice but, interestingly, it improved CSF-to-blood drainage.
Conclusion: Our results indicate that sustained dLV manipulation does not affect amyloid beta deposition in the brain and that compensatory mechanisms promote CSF clearance.
Disclosure: Nothing to disclose.

EPR-133 | Exploring the association between frailty and Alzheimer's disease biomarkers

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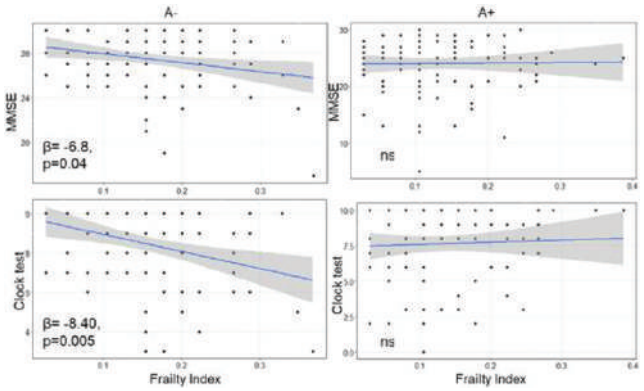
Background and Aims: The relationship between Alzheimer disease neuropathology and its clinical manifestation remains complex and it has been hypothesized that frailty, a measure of biological aging, could modify the association between them. We aimed to investigate the relationship between frailty and biomarkers of beta amyloid (A) and tau (T) pathology in a tertiary memory clinic population.
Methods: Data from 263 patients with dementia, mild cognitive impairment and cognitively unimpaired individuals were collected from the Memory Center of Geneva University Hospital. Frailty was measured using a 36-item frailty index (FI). We assessed A and T positivity through amyloid and tau PET or CSF. FI scores were compared between A- and T- versus A+ and T+ subjects. Linear regression models were used to explore the relationship between FI scores and the demographic and clinical features of participants. Longitudinal linear mixed models examined the impact of FI and biomarkers on cognitive decline.

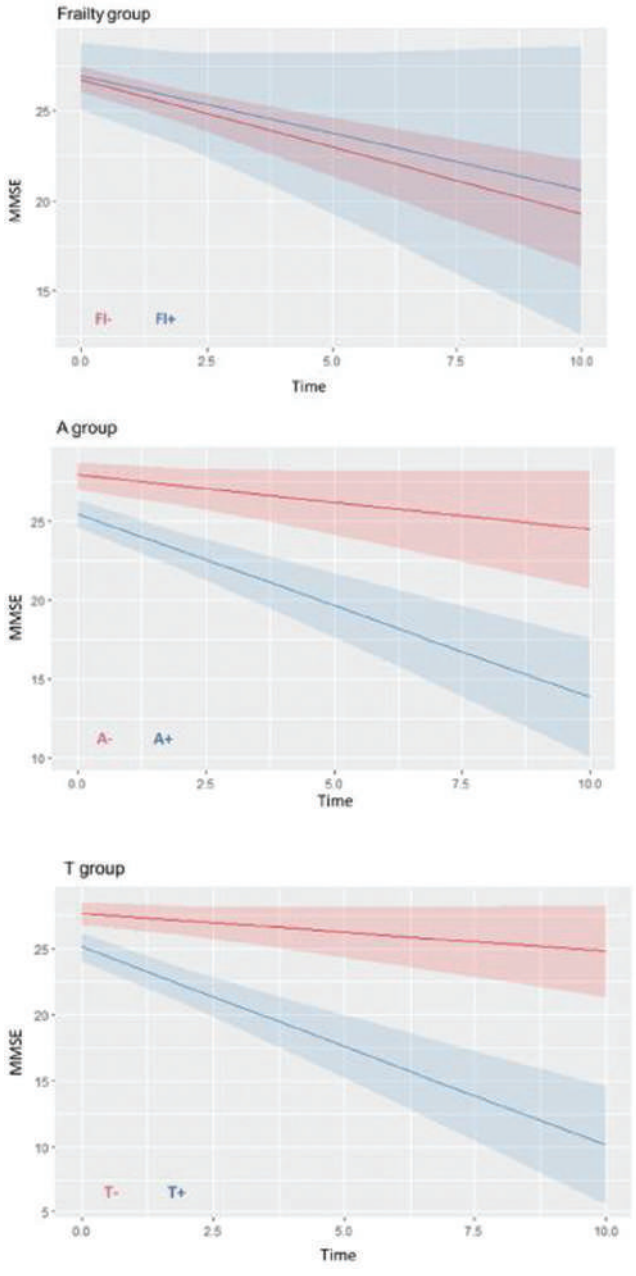
	Variables	Score	Assessment
	Diseases		
1	Cardiovascular diseases	0 absent, 1 present	Medical history
2	Atrial fibrillation		
3	Dermatologic diseases		
4	Respiratory diseases		
5	Head diseases (hear, nose, throat)		
6	Hepatic diseases		
7	Connective tissue diseases		
8	Muscular diseases		
9	Osteoarticular disease		
10	Dysthyroidism		
11	Endocrine diseases (others)		
12	Hematopoietic-lymphatic diseases		
13	Genital diseases		
14	Urinary diseases		
15	Gastrointestinal diseases		
16	Diabetes		
17	Malignancies		
18	Dyslipidaemia		
19	Hypotension		
20	Hypertension		
21	Medication	0 < 5; 1 ≥5	
22	Haemoglobin	0 normal,1 abnormal	Laboratory exams
23	Pacemaker		
	Symptoms		
	Vision loss	0 absent,1 present	Medical history
24	Hearing loss		
25	Urinary incontinence/urgence		
26	Pain		
27	Vertigo		
	Signs		
28	Bradykinesia	0 absent,1present	Medical History Neurological exam
29	Walking Impairment		
30	Balance Impairment		
31	Tremor		Medical History
32	Falls		
33	BP Diastolic	0 <90 mmHg 1 ≥90 mmHg	Redcap
34	BP Systolic	0 <140mmHg 1 ≥140 mmHg	
35	BMI	0 < 25 and >18,5 1 ≥ 25 or < 18,5	
36	Pacemaker	0 no - 1 yes	

Frailty Index.

Results: The mean age was 70 (SD 8.6) years, and 52% were women. FI was positively correlated with age, depression and anxiety. FI was higher in A- and T- versus A+ and T+ ($p < 0.01$) separately; mean MMSE was higher in A-/T- than A+/T+ patients. In A- patients, FI correlated with MMSE ($\beta = -6.8$, $p = 0.04$) and Clock Test ($\beta = -8.40$, $p = 0.005$). Longitudinal models did not reveal statistically significant impact of FI on cognitive decline.



FI and neuropsychological tests in A subgroups.



Longitudinal models.

Conclusion: FI is higher in people with low levels of brain AD pathology. Next steps include to assess the prognostic value of FI in persons with or without AD biomarkers positivity.

Disclosure: Nothing to disclose.

Motor neurone diseases 1

EPR-134 | Cognitive and neuropsychological correlation with brain metabolism in C9Orf72 amyotrophic lateral sclerosis patients

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Background and Aims: C9ORF72 gene mutation accounts for a significant proportion of autosomal dominant ALS/FTD spectrum disorders. ALS patients' carriers of the C9Orf72 mutation (C9+) more commonly have an earlier disease onset, and a high frequency of severe cognitive impairment. In our preliminary report, we compared the 18F-FDG-PET imaging findings in a group of genetic patients, observing an extensive motor and prefrontal hypometabolism in fast progressors C9+ patients. This study aimed to expand the neuropsychological findings in C9+.

Methods: We included ten C9+ patients who underwent a complete neuropsychological evaluation and an 18F-FDG-PET scan at baseline. We obtained hypometabolism maps at a single-subject level following a validated voxel-based SPM procedure. The corresponding 18F-FDG-PET regional hypometabolism was extracted by anatomo-functional ROIs. Patients were divided into ALS-normal (ALS-no, $n=2$), ALS-behavior (ALS-bi, $n=2$), and ALS-cognitive (ALS-ci, $n=6$). The ROIs' hypometabolism was compared with scores in neuropsychological tests. Also, a mean hypometabolism map was derived in each cognitive group to underline brain metabolism differences between ALS-no, ALS-bi and ALS-ci.

Results: We observed several correlations between hypometabolism and anatomo-functional ROIs, such as, prefrontal areas and phonological fluency test (PFT) (r = -0.86, $p=0.03$), Frontal Assessment Battery (FAB) (r = -0.87, $p=0.002$) and Clock Drawing test (CDT) (r = -0.79, $p=0.01$); temporoparietal area and Short Story Test (0.73, $p=0.04$), CDT (r = -0.80, $p=0.001$). The ALS-no

have hypometabolism confined in motor regions; the ALS-bi group showed prominent hypometabolism in temporoparietal and limbic areas, and the ALS-ci group showed extended hypometabolism in motor/prefrontal regions.

Conclusion: The brain metabolism showed specific correlations with neuropsychological impairment in C9+ patients, and different hypometabolism maps based on the cognitive group.

Disclosure: Nothing to disclose.

EPR-135 | Single-center experience with nusinersen and risdiplam in spinal muscular atrophy types 2 and 3 in adults

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Background and Aims: Spinal muscular atrophy (SMA) is an inherited neuromuscular disease with recent available genetic treatments. Risdiplam and nusinersen have shown significant benefits on motor function. We aim to analyze the evolution of our adult SMA cohort.

Methods: Retrospective single-center cohort study of adults with SMA. Demographic information, functional motor assessment scales and respiratory function tests were collected.

Results: We included 18 patients (10 SMA2 and 8 SMA3), 12(67%) men, median age of 32 (IQR = 14) years at the first treatment. The median follow-up time was 23 (IQR = 15) months. The median pre-treatment HFMSE and RULM scores were 4.5 (IQR = 17) and 16 (IQR = 22), respectively. Nusinersen was started in 8 patients (SMA3), 4 changed to risdiplam due to adverse events related to lumbar puncture. The median variation score for the other 4 patients [median age: 36.5 (IQR = 15) years] was 2.5 (IQR = 3.8) in HFMSE and 1 (IQR = 3.5) in RULM. The median change in the 6-minute walk test was −3.5 (IQR = 68) meters. Thirteen patients are treated with risdiplam [median age: 32 (IQR = 13) years], none with gait. The median changes in HFMSE and RULM scores were 0 (IQR = 1) and 0 (IQR = 2), respectively, with no differences between SMA types. The most reported subjective improvement was manual dexterity. The median FEV1/FVC ratio change was 1.5 (IQR = 4.5). One patient showed improved dysphagia.

Conclusion: In our cohort, there is clinical stabilization with those drugs counteracting the negative progression of the natural history of the disease.

Disclosure: Nothing to disclose.

EPR-136 | Prosaccadic alteration is associated with executive dysfunction in a cohort of ALS patients: A cross-sectional study

M. Olivero[1]; F. Verde[2]; A. Maranzano[2]; F. Scheveger[1]; F. Gentile[1]; E. Colombo[2]; C. Gendarini[1]; A. Cocuzza[1]; F. Girotti[2]; C. Morelli[2]; S. Messina[2]; V. Silani[2]; B. Poletti[2]; N. Ticozzi[2]

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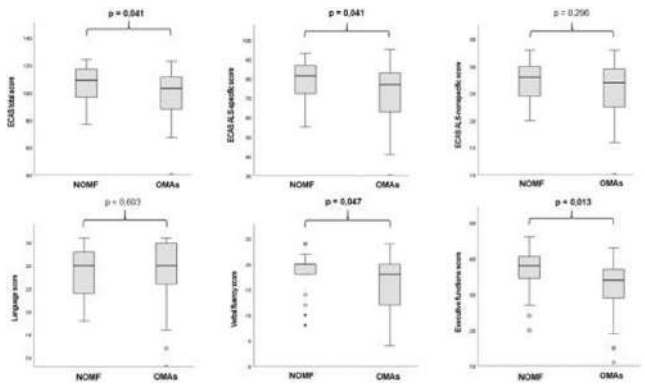
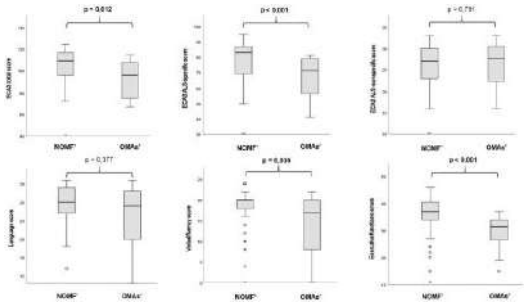
Background and Aims: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease affecting motor neurons, whose phenotype includes extramotor features, such as oculomotor abnormalities (OMAs) and cognitive-behavioral changes. The literature about OMAs, especially antisaccade alteration, detected by bedside neurological examination, is scarce. The aim of our study is to further investigate the characteristics of OMAs and to evaluate associations with clinical features in a cohort of ALS patients.

Methods: We enrolled a cohort of 80 inpatients with ALS. We assessed conjugate gaze, saccades, smooth pursuit and oculomotor praxia, testing for nystagmus. We evaluated cognitive-behavioral phenotype with the Edinburgh Cognitive and Behavioral ALS Screen (ECAS) – Italian version.

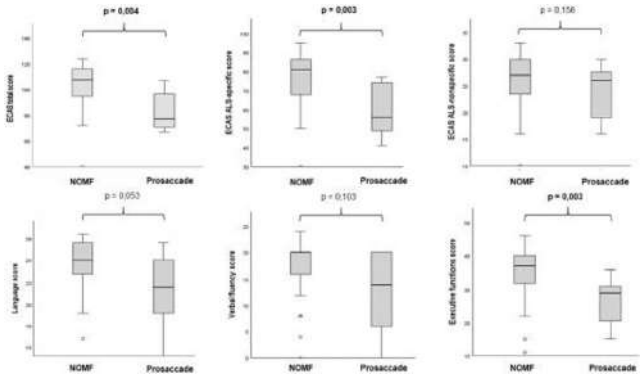
Results: We observed OMAs in 51.3 % and the most frequent was antisaccades dysfunction (82.9 %). We detected lower ECAS total score in ALS patients with OMAs versus normal oculomotor function (NOMF), predominantly in executive function subdomain. Afterwards, we excluded antisaccades variable from the analysis, creating OMAs' and NOMF' cohorts. We found a more significant difference in ECAS total score, mainly driven by executive function subdomain. Whereupon, we compared ECAS total score in patients with specific types of OMAs versus NOMF. We found lower scores in cases with pathologic prosaccades versus NOMF, mainly in executive function subdomain. Furthermore, we did not detect any difference in the frequency of behavioral symptoms in all cohorts analyzed.



Kruskal–Wallis analysis to compare ECAS total, domains and ALS-specific subdomains scores in OMAs versus NOMF ALS groups.



Kruskal–Wallis analysis to compare ECAS total, domains and ALS-specific subdomains scores in OMAs' versus NOMF' ALS groups.



Kruskal–Wallis analysis to compare ECAS total scores, domains and ALS-specific subdomains in prosaccadic alteration versus NOMF ALS groups.

Conclusion: We further confirm the association between cognitive impairment and OMAs in ALS. Prosaccades alteration strongly correlate with executive dysfunction, representing a promising clinical marker of neurodegeneration.

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EPR-137 | Pridopidine for the treatment of ALS – results from the phase 2 Healey ALS platform trial

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Background and Aims: Pridopidine, a S1R agonist, was evaluated in the Phase 2 HEALEY ALS Platform Trial.

Methods: Participants had El Escorial possible, probable, or definite ALS, symptom onset <36mo and vital capacity >50%-predicted. Pridopidine 45 mg bid ($n=121$) was compared to a shared placebo ($n=164$). Primary endpoint was change from baseline through 24 weeks in ALSFRS-R. Secondary and exploratory endpoints included speech, respiration, and quality-of-life measurements. Nominal p-values are reported.

Results: Pridopidine was well tolerated, consistent with prior safety profile. Primary endpoint was not met in all participants. Statistically significant speech improvements were observed, including speaking rate (Δ0.19, $p=0.03$) and articulation rate (Δ0.21, $p=0.01$). Prespecified analysis of definite ALS and early participants showed lessening of decline in ALSFRS-R progression (Δ2.4, $p=0.19$), respiratory domain (Δ1.04, $p=0.18$), and improved dyspnea (Δ1.35, $p=0.014$). Less decline on the ALSAQ-40 quality-of-life scale (Δ-10.83, $p=0.018$), eating & drinking (Δ-19.18, $p=0.015$) and a trend in communication (Δ-13.04, $p=0.12$) were also observed. Post-hoc analysis of definite+probable ALS, early and fast progressors showed slowing of decline in ALSFRS-R (41% vs. placebo; Δ5.2, $p=0.04$), stability of dyspnea (Δ1.41, $p=0.02$) and speech (speaking rate; Δ1.08, $p<0.0001$ and articulation rate; Δ1.03, $p<0.0001$). A Kaplan-Meier survival analysis showed an increase of median survival time (~300 to 600 days) in definite+probable ALS and early participants ($n=37$) versus the delayed-start (168 days) placebo-to-pridopidine participants ($n=12$) (log rank $p=0.069$). The Cox Proportional Hazard Ratio, adjusted for baseline characteristics was 0.429 ($p=0.052$).

Conclusion: The beneficial effects of pridopidine were observed across multiple measures including survival benefits. These observations support conducting a Phase 3 study.

Disclosure: Prilenia Therapeutics is an industry partner of the HEALEY ALS Platform Trial. Full disclosures will be presented.

EPR-138 | Electrophysiological abnormalities in early stages of motor neuron pathology in G93A SOD1 mice

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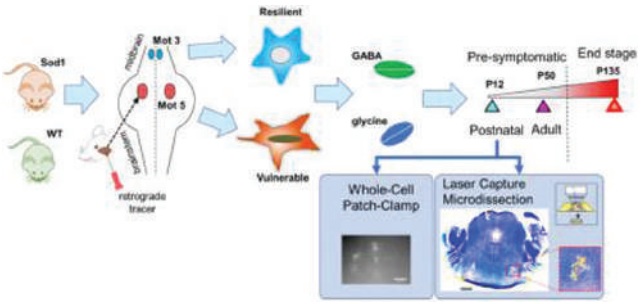
Background and Aims: Motor neuron (MN) degeneration in ALS differs among neurons as MNs controlling extraocular and sphincter muscles remain resilient to degeneration. Efficient intracellular calcium buffering mechanism, enriched neurotrophic factors and genes involved in synaptic transmission including glutamate and GABA receptor subunits can affect neuronal resilience.
Methods: Utilizing transgenic SOD1G93A and wild type (WT) litter control mice at pre-symptomatic, adult and near end-stage, we compare longitudinal changes in pre-synaptic terminal proteins for GABA and glycine neurotransmitters of trigeminal jaw closer (JC) MNs (vulnerable MNs) and midbrain extraocular (EO) MNs (resilient MNs using in-vitro patch-clamp electrophysiology.



Methods Summary.
Results: GAD67 innervation in SOD1G93A trigeminal jaw closer MNs is reduced around age P12, relative to age-matched WT animals without significant difference around P50 and P135. Innate co-expression patterns of GAD67 and GlyT2 with co-dependency in EO MNs compared to JC in both SOD1G93A and WT mice at adult stages (P50 and P135) differ. Around P12 when GAD67 terminals expression was low in the mutant, in vitro patch-clamp electrophysiology showed that SOD1G93A JC MNs have reduced persistent GABA inhibition, relative to WT.
Conclusion: We show different innate co-expression patterns of GAD67 and GlyT2 with co-dependency in EO MNs compared to JC in both SOD1G93A and WT mice at adult stages and low GAD67 terminals expression in the P12 mutant with reduced persistent GABA inhibition in SOD1G93A JC MNs while pharmacological blocking of active GABA conductance disinhibited WT JC MNs and lowered their recruitment threshold, suggest a distinct pattern of intrinsic MN excitability.
Disclosure: Nothing to disclose.

EPR-139 | Risdiplam efficacy in spinal muscular atrophy patients: A single-center experience

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Background and Aims: The study explores the outcomes of Risdiplam treatment in 20 adult Spinal Muscular Atrophy (SMA) patients, initiated between 2020 and 2023, in the Neurology II department, Fundeni Clinical Institute in Bucharest.
Methods: Regular evaluations were conducted every six months using the Hammersmith Functional Motor Scale Expanded (HFMSE), Revised Upper Limb Module (RULM), and 6-Minute Walk Test (6 MWT) assessment scales. Additionally, patients participated in structured interviews to capture subjective benefits reported by the individuals.
Results: Results revealed that 25% of patients improved on the assessment scales, while the remaining patients showed stabilization of motor functions. Notably, all patients reported subjective enhancements and an increased quality of life. Thirty-five percent of participants experienced improved swallowing and chewing, 45% reported increased strength in upper limbs, and 35% noted beneficial respiratory effects. Importantly, no adverse impact necessitating treatment interruption was observed.
Conclusion: The combination of quantitative assessments and patient-reported outcomes offers a comprehensive understanding of the multifaceted benefits associated with Risdiplam therapy.
Disclosure: Nothing to disclose.

EPR-140 | Genetics of amyotrophic lateral sclerosis (ALS): A population-based study in Serbia

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Background and Aims: Although the pathogenesis of ALS is still unknown, the role of several genes in occurrence of this disease is known. Familial amyotrophic lateral sclerosis (FALS) accounts for 10%–20% of all ALS patients. The aim of our study was to examine the clinical characteristics of patients with FALS in Serbia.
Methods: This study included 171 patients with FALS, who were diagnosed between 2000 and 2022. Besides sociodemographic and clinical data, Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-r) was used. Level of significance was $p < 0.05$.
Results: Out of 1061 ALS patients diagnosed during this period, 171 patients had FALS (16%). Most common mutations were in SOD1 gene (63.7%), while 36.3% of patients had C9orf mutation. The average age at the disease onset was 53.94 $\pm$11.94, and FALS more commonly presented in male patients (54.1%). Patients with SOD1 mutation had more frequent spinal onset of the disease (86.1%),

objective sensory loss (46%) and sphincteric disorders (55%) compared to patients with C9orf mutation. While patients with C9orf mutation had a significantly later onset of the disease (59.4 ±8.9), more frequent presence of bulbar symptoms (86%), executive dysfunction (45%) and a higher degree of functional disability with an average value of the ALSFRS-r scale (34.7 ±7.1). Median survival time was significantly shorter in C9orf patients with 30 months, compared to 60 months in SOD1 patients.

Conclusion: Patients with C9orf mutation had significantly more severe clinical presentation, shorter survival time and a higher degree of functional disability compared to SOD1 patients.

Disclosure: Nothing to disclose.

EPR-141 | The relation between disease progression in amyotrophic lateral sclerosis and metabolic biomarkers

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Background and Aims: Amyotrophic lateral sclerosis (ALS), a progressive neurodegenerative disorder, has been extensively studied for its complex pathophysiology. In recent years, the relationship between metabolic biomarkers and the gut-brain axis has emerged as the new potential for therapeutic intervention.

Methods: This study investigates the relationship between metabolic biomarkers and the progression of ALS. We included a number of 44 ALS patients over 3 months followed for another 12 months. During this period, we collected blood samples to analyze various metabolic biomarkers and we also examined them using the ALS Functional Rating Scale (ALFSR). We also used DeltaFS (ΔFS) as a tool to analyze the disease's progression.

Results: The ALSFSR-Respiratory demonstrates positive associations with amylin and insulin while negatively correlating with MCP-1, indicating a potential link between respiratory symptoms and metabolic factors. Similarly, ALSFSR-Bulbar and ALSFSR-Fine motor subscores exhibit positive correlations with amylin, insulin, and leptin, unveiling potential connections between bulbar and fine motor symptoms and metabolic influences. Furthermore, the total ALSFSR score reveals positive correlations with amylin, GLP-1, and insulin, providing insights into the overall impact of these metabolic markers on the severity of ALS symptoms. Additionally, the study identifies GLP-1, glucagon, and MCP-1 as potential predictors for the time of diffusion and generalization of ALS symptoms. ΔFS values, indicative of accelerated disease progression, correlate inversely with amylin, C-peptide, insulin, and leptin.

Conclusion: Our study reveals a significant negative correlation between the progression rate and ALSFSR score in ALS and key metabolic biomarkers. This underscores the potential influence of metabolic dysregulation on the accelerated progression of ALS.

Disclosure: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS – UEFISCDI, project number PN-III-P1-1.1-TE-2021-0960, within PNCDI III.

EPR-142 | Calculated maximal volume ventilation (cMVV) as a marker of early respiratory failure in ALS

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[1]'Rita Levi Montalcini' Department of Neuroscience, University of Turin, Turin, Italy; [2]Academic Neurology Unit, San Luigi Gonzaga University Hospital, Orbassano, Italy; [3]S.C. Pneumologia, S. Croce and Carle Hospital, Cuneo, Italy; [4]S.C. Pneumologia U, AOU Città della Salute e della Scienza di Torino, Turin, Italy

Background and Aims: Among the different pulmonary function tests (PFTs) used in ALS management, maximal voluntary ventilation (MVV) resulted to be able to capture early respiratory modification. In pulmonary disease, a calculated MVV (cMVV) is usually estimated by multiplying forced expiratory flow in first second (FEV1) or peak inspiratory flow (PIF) by a constant value. No study of cMVV in ALS has been performed yet.

Methods: We derived cMVV as prognostic biomarker in a center-based retrospective ALS population belonging to the Piemonte and Valle d'Aosta registry for ALS (PARALS). We collected the pulmonary function tests (PFTs) performed by ALS patients at diagnosis and during pulmonary assessment in the 1995–2015 period. According to current literature we derived cMVV using different methods. Correlation between cMVV other clinical variables were calculated and time-to-event analysis were performed evaluating both overall survival and time to NIV start.

Results: cMVV(40) significantly correlated with FVC% (0.626, $p < 0.001$), FEV1% (0.669, $p < 0.001$), ALSFRS-R total score (0.319, $p < 0.001$), PIF (0.693, $p < 0.001$), peak expiratory flow (PEF) (0.823, $p < 0.001$), pCO2 (-0.278, $p < 0.001$), HCO3- (-0.323, $p < 0.001$), BE (-0.318, $p < 0.001$) and pO2 (0.350, $p < 0.001$). Cox proportional hazard models adjusted confirmed that HRs for both survival and time to NIV decreased significantly with the increase of cMVV, especially in ALS patients with normal FVC% (≥80%).

Conclusion: cMVV is a marker of early respiratory failure in ALS, easily derivable from standard PFTs, especially for its identification in asymptomatic ALS patients with normal FVC measures.

Disclosure: Nothing to disclose.

Neuroepidemiology

EPR-143 | Decreasing number of deaths due to haemorrhagic stroke in Hungary: decreasing incidence or decreasing case fatality?

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Background and Aims: Overall decrease in stroke mortality in the last decades in European countries are mostly explained by less severe strokes despite increasing or stable incidence. We tested if the decreasing annual number of deaths due to intracerebral haemorrhage (ICH) in Hungary is explained by a deceasing number of hospitalized cases or by less severe haemorrhagic strokes resulting in lower case fatality.

Methods: In the framework of the National Brain Research Program we evaluated claim forms submitted by hospitals of the whole country for a 17-year period of 2004–2020 using the NEUROHUN database. Case fatality for all cases with ICH (ICD-10 code of I61) was evaluated at 7 days, 30 days, 180 days and 1 year. As reporting neuroimaging was not always required for DRG reimbursement, in a sensitivity analysis we evaluated those cases where the reporting physician voluntarily declared that neuroimaging was performed.

Results: In the 17-year period, 61.732 patients had a discharge diagnosis of ICH. The annual number of hospitalized cases decreased from 4.520 in 2004 to 2.966 in 2020. Case fatality was 31.6% at 7 days, 45.9% at 30 days, 54.7% at 6 months and 57.6% at one year with only minor changes over the years. Similar case fatality rates were found in the sensitivity analysis of 31.069 cases (26.6%, 41.2%, 50.4% and 53.3% at the 4 time points).

Conclusion: the decreasing number of annual fatal cases due to ICH is explained mostly by decreased incidence and in a much smaller extent by a change in case fatality.

Disclosure: None.

EPR-144 | Epidemiology of late-onset multiple sclerosis: A population based-study

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Background and Aims: Introduction: Multiple Sclerosis (MS) is defined as Late Onset Multiple Sclerosis (LOMS) when the onset occurs after 50 years. Across MS cohorts, the prevalence ranges from 0.6% to 12%, however little is known on the incidence of LOMS in the general population.

Methods: Methods: case ascertainment was conducted using the registries of all the MS centers of the province of Catania. Inclusion criteria for incident cases of LOMS were MS diagnosed according to McDonald criteria; patients older than 50 years at the disease onset; onset between 2005 and 2020; resident in the province of Catania at the time of the onset. Incidence rates (IR) have been calculated for the three quinquennia within the study period. Incidence rate ratios (IRR) have been computed to compare incidence rates.

Results: Results: 171 patients with LOMS were identified (104 women; 60.8%; mean age at onset 56 ±6 years). The average annual crude IR was 2.7/100,000 person-years (pyar) (95% Confidence Intervals, CI 2.31–3.13). Overall incidence risk was quite stable during the entire study period 2005–2020 (2.7/100,000 pyar). Nonetheless we observed an increased risk in the group aged 60–69 from 1.12/100,000 pyar during 2005 and 2010 to 3.12 during 2016–2020. When comparing the last quinquennum 2016–2020 to the first 2005–2010 the IRR was 2.79 (95%CI 1.13–7.81; *p*-value 0.01).

Conclusion: Conclusions: increasing MS incidence in older people may be due to a better accuracy in diagnosis as well as to the aging of the general population. However, possible role of environmental factors cannot be excluded.

Disclosure: Nothing to disclose.

EPR-145 | Incidence and mortality of ALS: A 42-year population-based nationwide study

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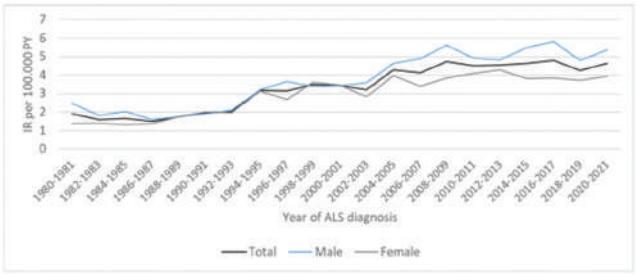
Background and Aims: Recent studies have suggested that the incidence rate (IR) of amyotrophic lateral sclerosis (ALS) and the rate of death (MR) from ALS are increasing. We aimed to examine 42-year trends in the incidence and mortality of ALS in Denmark.

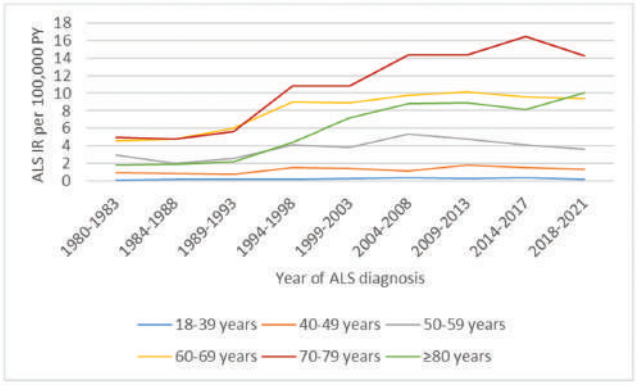
Methods: We retrieved individual-level data of all patients aged 18 and above with a first-time ALS. The IR and MR were calculated based on data from 1980 to 2021.

Results: We identified 5,943 patients with ALS and identified a total of 5,069 deaths among this nationwide population. The overall ALS IR was 3.4 per 100,000 persons per year (PY) (95% CI, 3.4–3.5). ALS incidence gradually rose with year of diagnosis, and the incidence rate ratio (IRR) was clearly higher (IRR, 2.8; 95% CI, 2.4–3.2) when comparing the latest period with the first. The incidence increase was primarily in patients aged ≥70 years. Incidence was associated with male gender compared with females (IRR, 1.3; 95% CI, 1.2–1.3) and rose with age at diagnosis in both genders and peaked in the age-group 70–79 years (IR, 10.9; 95% CI, 10.4–11.4). Parallel to the IR, the MR increased over time and particularly in patients aged

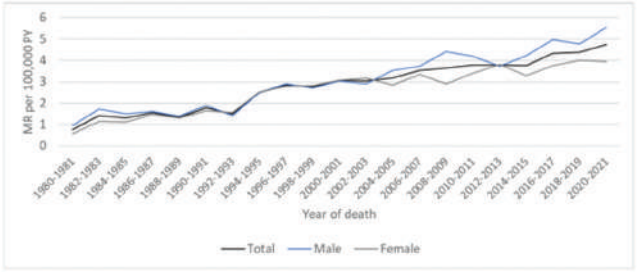
70 years and above. MR rose with age at diagnosis and peaked at the age of 75 years.



ALS incidence rates per 100,000 from 1980 to 2021 in males and females.



ALS incidence rate; age groups and year of diagnosis.



ALS mortality rates per 100,000 from 1980 to 2021 in males and females.

Conclusion: In Denmark the IR and MR of ALS steadily increased over a 42-year period, with important risk increase related to higher age. Thus, the number of elderly patients with ALS can be expected to increase considerably.

Disclosure: Nothing to disclose.

EPR-146 | Validation of the ICD-10 code DG61.8 for chronic inflammatory demyelinating polyneuropathy in Western Denmark

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Background and Aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune disorder leading to muscle weakness and sensory loss. Identification of patients with CIDP for epidemiological studies is challenging. CIDP is diagnosed with ICD-10 code DG618, however the positive predictive value (PPV) is unknown. We aimed to determine the PPV of DG618 for CIDP and thereby calculate the incidence of CIDP in Denmark.

Methods: A complete list of patients diagnosed with DG618 in Denmark from 01.01.1996 to 31.12.2020 ($n=1856$) were obtained from the Danish Healthy Data Authority. Complete medical charts, biochemical workup and reports from imaging and neurophysiology were obtained for 352 patients from hospitals in Western Denmark. Records were validated using EFNS/PNS 2010 diagnostic criteria for CIDP; especially neurophysiology findings were revised meticulously.

Results: Only 91 (median age 60.4 years, 35 females) out of 352 patients fulfilled the criteria for CIDP resulting in a PPV of 25.9% for CIDP. Of confirmed CIDP patients 41 were typical and 50 atypical (20 distal, 16 asymmetrical, 6 pure motor and 3 sensory); 78 definite, 9 probable and 4 possible. The most frequent other diagnoses found were MGUS (Monoclonal Gammopathy of Undetermined Significance) and/or anti-MAG (Myelin Associated Glycoprotein) ($n=43$) and non-MGUS ($n=22$) demyelinating polyneuropathies not fulfilling CIDP criteria, Guillain-Barre syndrome ($n=39$), axonal ($n=21$) and neoplastic ($n=19$) polyneuropathies and spinal stenosis ($n=19$). Based on the PPV the incidence of CIDP is 0.35/100.000 person-years in Denmark.

Conclusion: The PPV of DG618 for CIDP is too low to use this code for epidemiological studies of CIDP using health registries.

Disclosure: This project was sponsored solely from resources from Aarhus University and Aarhus University Hospital. No company or interest organization was part of the study at any level. Helga Haahr-Lillevang, Lars Kjøbsted Markvardsen and Henning Andersen is currently undertaking another study sponsored by CSL Behring. Lars Kjøbsted Markvardsen participates in an advisory- or monitoring board for CSL Behring and furthermore have received payment for either lectures, presentations speaker's bureaus, manuscript writing or educational events from CSL Behring and Takeda Denmark.

EPR-147 | Prevalence, clinical profiles, and prognosis of Isaacs syndrome in Japanese nationwide survey

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Background and Aims: To elucidate current epidemiological, clinical, and immunological profiles and treatments of Isaacs syndrome in Japan.
Methods: A nationwide mail survey was conducted using an established method. Data processing sheets were sent to neurology in hospitals and clinics throughout Japan to identify Isaacs patients who were seen between April 2018 and March 2021.
Results: The total estimated number of patients with Isaacs syndrome was 114 [95% confidence interval (CI): 89.63–138.92], and the estimated prevalence was 0.091 per 100,000 population. Detailed clinical profiles were available for 44 patients. The median age at onset was 40 years (range, 17–78 years), and 24 (55%) were female. The median time from symptom onset to diagnosis was 24 months (range, 1–372 months). Forty patients (91%) showed electrophysiological findings supporting peripheral nerve hyperexcitability. Antibodies to LGI-1 and CASPR2 in serum and/or CSF were examined for 28 patients by cell-based assay (CBA). Of these, 3 patients (11%) had both LGI-1 and CASPR2 antibodies and 3 patients (11%) had only LGI-1 antibodies. Thirty-six of 38 patients (95%) responded to immunotherapy. The median modified Rankin Scale (mRS) at baseline was 2, and median mRS at last follow-up was 1.5. The symptom severity was independent risk factors for poor outcome (mRS ≥3) in the Isaacs syndrome patients (Odds ratio, 10.33; 95% CI, 1.7–63.99).
Conclusion: This study provides the current epidemiological and clinical status of Isaacs syndrome in Japan. The outcome of Isaacs patients was similar to the previous studies, but more early diagnosis is needed.
Disclosure: Nothing to disclosure.

EPR-148 | Epidemiology of Aquaporin-4-IgG-positive NMOSD in Sardinia, Italy

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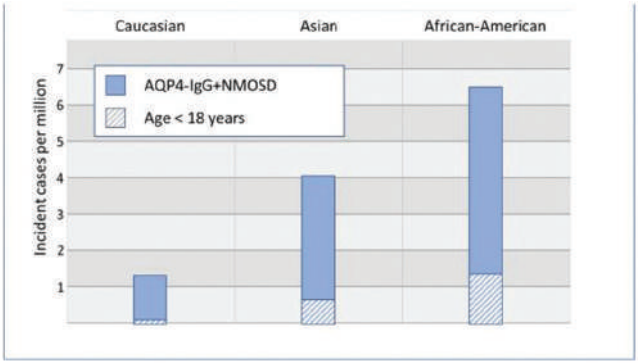
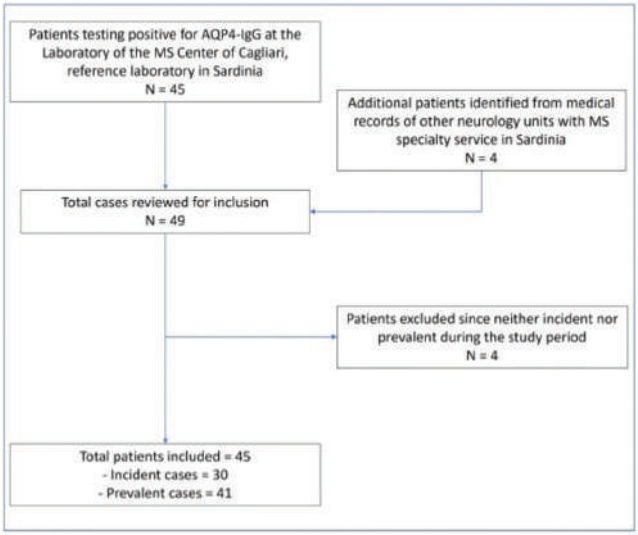
Background and Aims: The Italian Island of Sardinia (population, 1,587,413) is well recognized as a high-risk area for multiple sclerosis (MS). It is unclear, however, whether other less common demyelinating diseases of the central nervous system (CNS) such as aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG+NMOSD) are similarly over-represented. We determined the incidence and prevalence of AQP4-IgG+NMOSD in Sardinia.



The bar graph shows the average reported incidence of AQP4-IgG+NMOSD per million person-years among Caucasians, Asians and African-Americans. Within each bar, the relative frequency of patients with pediatric onset (<18 years of age) is highlighted by diagonal lines.

Methods: Incidence was calculated between January 1, 2013 and December 31, 2022; while the prevalence day was December 31, 2022. Patients with AQP4-IgG+NMOSD were retrospectively identified using two sources: (1) Laboratory archives of the MS Center in Cagliari (reference and only laboratory for AQP4-IgG testing in Sardinia); and (2) medical records of the four Sardinian Units specialized in the treatment of MS and other CNS demyelinating disorders. Serum positivity for AQP4-IgG was assessed by cell-based assay.



The flow chart summarizes the steps towards identification of patients with AQP4-IgG+NMOSD.

Results: A total of 45 cases were included (incident, 30; prevalent, 41). The median age at disease onset was 51 (range, 6–78) years; 96% were Caucasian. The female to male ratio was 9:1. The crude incidence and prevalence were 1.9 (95% CI; 1.3-2.6)/million person-years and 2.6 (95% CI; 1.9-3.5)/100,000, respectively. After age-standardization to the World population, these estimates decreased to 1.3 (95% CI: 0.8-1.9)/million and 1.8 (95% CI: 1.2-2.5)/100,000, respectively.

Table 1 – Demographics and clinical characteristics for the full cohort of included cases with AQP4-IgG+NMOSD and for incident cases only; continuous and categorical variables are reported as median (range) and numbers (%)

	Full cohort (N=45)	Incident cases (N=30)
Age at disease onset	51 (6-78)	54 (17-78)
Onset age <18 years	3 (7%)	1 (4%)
Onset age 18-39 years	9 (20%)	4 (13%)
Onset age 40-64 years	21 (46%)	13 (43%)
Onset age 65+ years	12 (27%)	12 (40%)
Female sex	40 (89%)	28 (93%)
Ethnicity		
White	43 (96%)	29 (97%)
Black	1 (2%)	0 (0%)
Asian	1 (2%)	1 (3%)
Coexisting autoimmunity	23 (51%)	15 (50%)
Number of relapses	2 (1-15)	2 (1-6)
Presenting attack		
LETM	26 (57%)	21 (70%)
ON	13 (29%)	4 (13%)
Brain/brainstem attack	3 (7%)	3 (10%)
Combinations of the above	3 (7%)	2 (7%)
CSF-restricted OCB (≥2)	4/27 (15%)	3/19 (16%)
EDSS at last follow-up	4 (0-8.5)	3 (0-8.5)
Follow-up duration, years	6 (1-27)	3 (1-9)

Abbreviations – CSF = cerebrospinal fluid; EDSS n= expanded disability status scale-score; LETM = longitudinally extensive transverse myelitis; OCB = oligoclonal bands; ON = optic neuritis.

Demographics and clinical characteristics for the full cohort of included cases with AQP4-IgG+NMOSD and for incident cases only; continuous and categorical variables are reported as median (range) and numbers (%).

Conclusion: The incidence and prevalence of AQP4-IgG+NMOSD in Sardinia are comparable to those reported in other predominantly Caucasian countries (≈1/million and 0.8-3.3/100,000, respectively). The higher MS risk in the Island seems to be disease-specific and not paralleled by a higher risk for other CNS demyelinating diseases.

Disclosure: Nothing to disclose.

EPR-149 | The impact of patient factors on long-term institutionalization in Alzheimer disease

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Background and Aims: Our goal is to identify patient factors associated with institutionalization in Alzheimer disease (AD) in order to design interventions from which delay this step and reduce costs.

Methods: A descriptive study that prospectively recorded data of 479 consecutive patients who met NIA-AA criteria for AD (mean age 79.5 ±7.1 years, mean duration of dementia 4.1 ±3.9 years, 30.9% men) followed-up in a Dementia Unit.

Results: Overall, institutionalization occurred in 19.3% of participants. This was significantly more prevalent in housewives ($p=0.031$), patients with an older age ($p=0.02$) or a single or widowed status ($p<0.001$). Other factors associated with institutionalization were not only higher scores in Clinical Dementia Rating ($p<0.001$), Mini Mental State Examination ($p<0.001$), Barthel Index ($p<0.001$) and disease duration ($p=0.007$), but also the presence of delusions [OR=2.0-IC (1.3-3.1)-$p=0.003$], agitation [OR=3.1-IC (1.9–5.1)-$p<0.001$], epilepsy [OR=3.9-IC (1.5–10.4)-$p=0.004$], rapid progression [OR=1.9-IC (1.1–3.2)-$p=0.023$], antipsychotics [OR=3.7-IC (2.3–5.8)-$p<0.001$], anxiolytics [OR=1.8-IC (1.1–2.8)-$p=0.014$], no acetylcholinesterase inhibitors (AChEI) and/or memantine use [$p=0.022$] and multiple drug therapy ($p<0.001$). No differences were found in other neuropsychiatric symptoms, vascular risk factors, living in a rural or urban area, gender or education level.

Conclusion: A smaller family support network or being older than 80 years, the severity of disability, those symptoms related to dementia that cause more caregiver burden (psychosis) and no AChEI and/or memantine use predict institutionalization in AD. Identifying modifiable risk factors for institutionalization and, consequently, implementing appropriate measures can be an important step in AD care management.

Disclosure: Nothing to disclose.

EPR-150 | New-onset psychogenic nonepileptic seizures after intracranial neurosurgery: A meta-analysis

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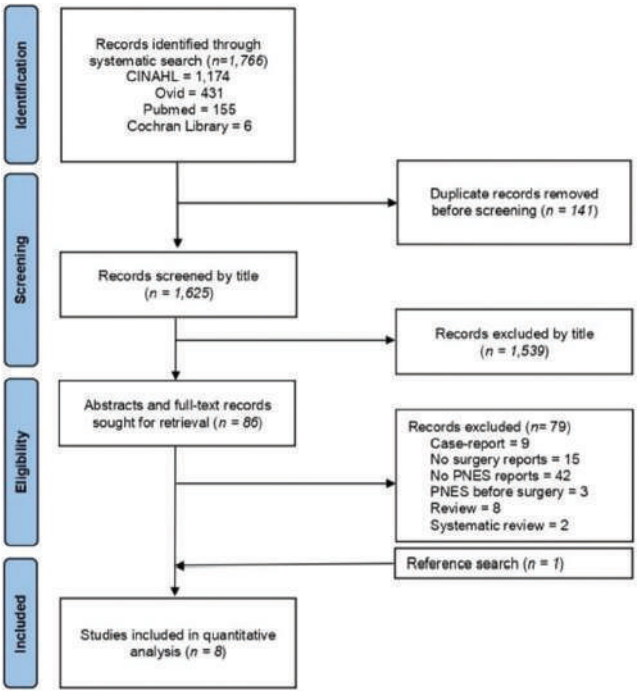
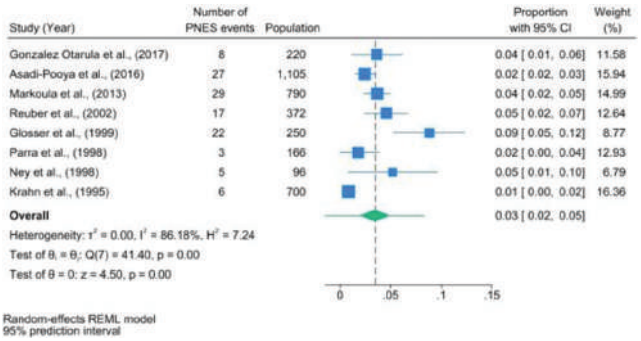
Background and Aims: PNES are among the most prevalent neurological conditions, its epidemiology and neurobiology remain unclear. Although approximately 14 million people need neurosurgical care annually, there is a dearth of thorough analysis on the PNES occurrence following surgery.

Methods: We conducted a comprehensive literature search of the PubMed, Ovid, CINAHL, and Cochrane Library databases until December 2023. We identified studies on the occurrence of PNES in patients underwent intracranial surgery, and confirmed diagnosis using video-EEG. Estimates are reported as both Freeman–Tukey transformed proportions and raw proportions using random effects models. We reported both 95% CIs and prediction intervals (PI). We assessed the risk of bias and identified the pooled odds ratio (OR) for mutually exclusive groups. The heterogeneity investigated using the I^2 statistic and significance determined using Cochran's Q-test p-value. Post-hoc Egger's regression test, and series of sensitivity analyses performed. This study was registered in PROSPERO.

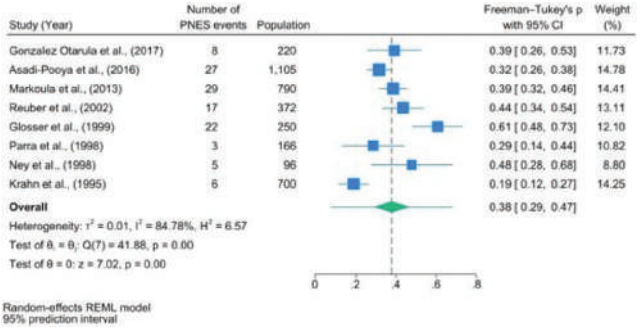


PRISMA.

Results: Of the 1766 studies identified, 86 were selected for the review. Eight studies ($n = 3,699$) were eligible for inclusion. Studies, spanning from 1995 to 2017, primarily focused on epilepsy surgeries. The pooled raw proportion was 3% (95% CI 2%-5%; 95% PI 0%-11%), Freeman-Tukey proportions were 0.38 (95% CI 0.29–0.47; 95% PI 0.08–0.68). Meta-analysis on surgery areas indicated two-fold increase in PNES following temporal resections (OR 2.05, 95%CI 0.81–5.19). Publication year and approximated reference population were associated with heterogeneity in estimates



Forest plot of raw proportions with prediction interval (inverse Freeman-Tukey's proportions).



Forest plot (Freeman-Tukey's transformed proportions).

Conclusion: These findings emphasize the importance of sustained video-EEG monitoring and psychiatric assessments. Careful assessments should become an essential component of care and integrated into clinical practice

Disclosure: Nothing to disclose.

EPR-151 | The prognosis of mild cognitive impairment: A systematic review and meta-analysis

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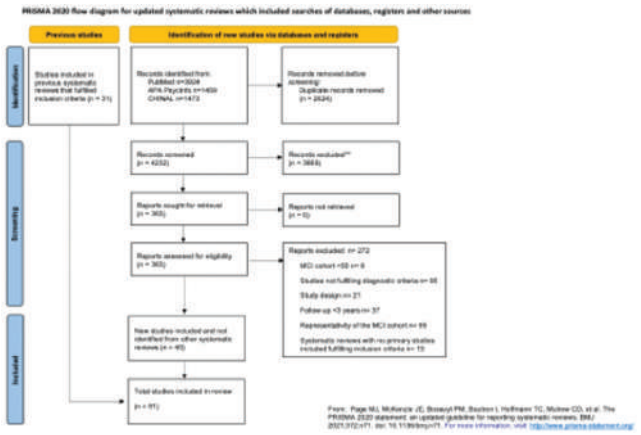
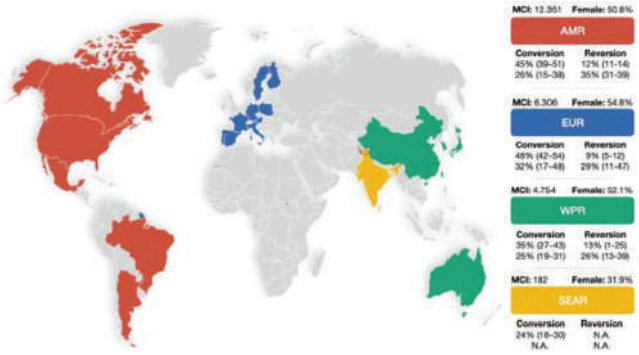
Background and Aims: Controversies persist on the prognosis of MCI: highly variable conversion rates have been described and reversion to normal cognition has only recently been analyzed. We updated the evidence on the risk of conversion to dementia integrating it with the recent data on reversion and stability rates. To our knowledge, this is the first systematic review that comprehensively evaluates the different cognitive trajectories of MCI.

Methods: All studies published up to June 2023 were retrieved by searching databases. We included studies evaluating the prognosis of MCI, with at least a 3-year follow-up. MCI and dementia diagnoses should align with established international criteria.

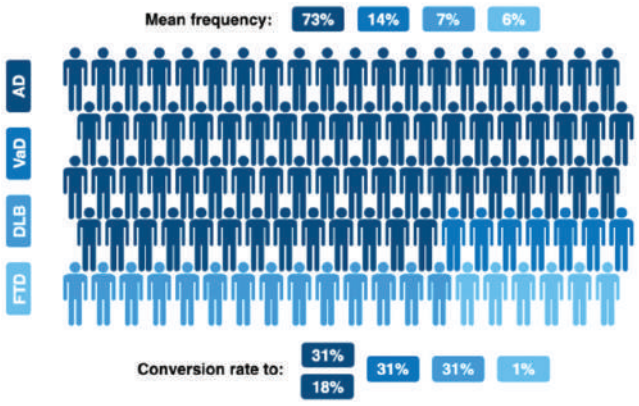


Prisma flow diagram

Results: We included 91 studies evaluating a total of 33.198 participants. Conversion and reversion rates were 43% (95%CI: 39%-46%) and 12% (95%CI: 7%-16%) in clinical-based studies and 28% (95%CI: 22%-35%) and 28% (95%CI: 17%-39%) in population-based studies. AD dementia was the most frequent diagnosis (72.0%) followed by VaD. FTD and DLB diagnoses showed higher mean frequencies in the clinical- compared with the population-based setting (7.0% vs. 4.9% and 6.1% vs. 3.4%, respectively).



World map of included studies by WHO regions.



Distribution of dementia subtypes.

Conclusion: We observed a probability of reverting to normal cognition three times higher in the population-based setting. Up to 50% of patients with MCI did not convert to dementia even in the studies with the longest follow-up (≥5 years) and annual conversion rates decreased with longer follow-ups. Our data might be helpful to improve clinical practice, provide context to ongoing and future studies on prognostic factors, and support the organization of sustainable and accessible dedicated care pathways.

Disclosure: Nothing to disclose.

Neurocritical care

EPR-152 | Periodic discharges and status epilepticus: A critical reappraisal

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Background and Aims: Periodic Discharges (PDs) in Status Epilepticus (SE) are historically related to negative outcome, and the Epidemiology-based Mortality Score in SE (EMSE) identifies PDs as

an EEG feature associated with unfavorable prognosis. However, supportive evidence is conflicting. This study aims to evaluate the prognostic significance of interictal PDs during and following SE.

Methods: All 2020–2023 non-hypoxic-ischemic SE patients with available EEG during SE were retrospectively assessed. Interictal PDs during SE (SE-PDs) and PDs occurring 24–72 h after SE resolution (post-SE-PDs) were examined. In-hospital death was defined as the primary outcome.

Results: 189 SE patients were finally included. SE-PDs were not related to outcome, while post-SE-PDs were related to poor prognosis confirmed after multiple regression analysis. EMSE global AUC was 0.751 (95%CI: 0.680–0.823) and for EMSE-64 cutoff sensitivity was 0.85, specificity 0.52, accuracy 63%. We recalculated EMSE score including only post-SE-PDs. Modified EMSE (mEMSE) global AUC was 0.803 (95%CI: 0.734–0.872) and for mEMSE-64 cutoff sensitivity was 0.84, specificity 0.68, accuracy 73%.

Conclusion: Interictal PDs during SE were not related to outcome whereas PDs persisting or appearing >24h after SE resolution were strongly associated to unfavorable prognosis. EMSE performed well in our cohort but considering only post-SE-PDs raised specificity and accuracy for mEMSE64 cutoff. This study supports the utility of differentiating between interictal PDs during and after SE for prognostic assessment.

Disclosure: Nothing to disclose.

EPR-153 | Prognostic value of signal abnormalities on brain MRI in post-anoxic super-refractory status epilepticus

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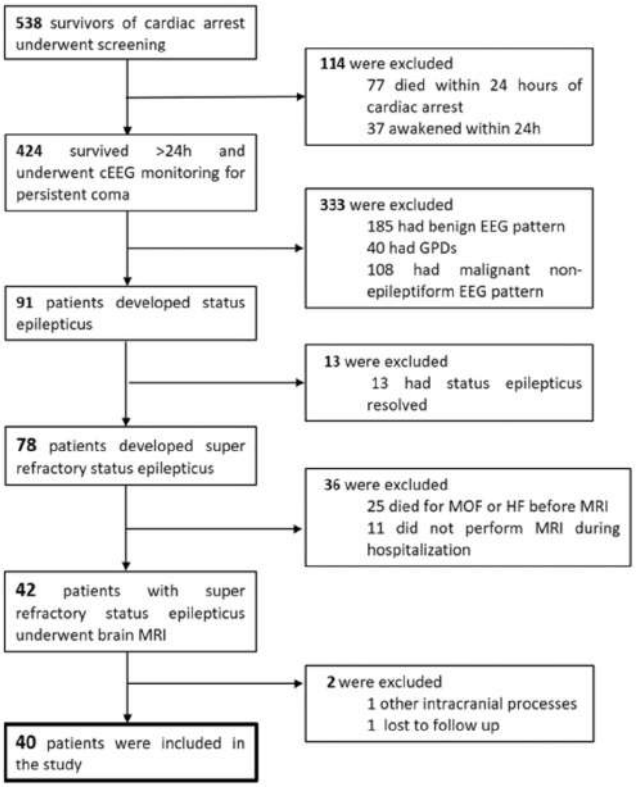
Background and Aims: Comatose patients following cardiac arrest experience refractory status epilepticus (SE) in about one-third of cases, potentially signaling an adverse prognosis. Nevertheless, the association between SE and hypoxic-ischemic brain injury (HIBI) radiological signs remains uncertain.

Methods: In this single-center retrospective study, we investigated the distribution of HIBI in post-anoxic super-refractory SE using brain MRI. Patients were classified into two groups based on cortical gray matter involvement. The study examined associations between these two patterns and outcomes, including neurological status at six months, SE resolution, consciousness recovery before discharge, and six-month mortality.

Results: From November 2012 to March 2023, 40 patients were included. HIBI distribution: basal ganglia (55%), cerebellum (46.2%), cerebral cortex (45%), hippocampus (28.7%), and thalamus (22.5%). HIBI was non-severe in 22 patients (55%, Group I) and severe in 18 (45%, Group II). Poor neurological outcome at 6 months was 27% in Group I and 83% in Group II (OR 13.3, CI 95% [2.81–63.11], $p < 0.001$). Consciousness recovery before discharge occurred in 73% of cases in Group I versus 22% in Group II (OR 9.3, CI 95% [2.1–39.9], $p = 0.003$). SE resolved in 95% of patients in Group I versus 67% in Group II (OR 10.5, CI 95% [1.1–97.9], $p = 0.032$). Mortality at 6 months was 40% in Group I versus 55% in Group II (OR 1.81, CI 95% [0.5–6.3], $p = 0.356$).



Study population.

	CPC 1-2	CPC 3-5	OR‡ (95% CI)	p value
Patient group				
Group I: non-severe radiological pattern* (reference)	16/22 (73%)	6/22 (27%)	13.33 (2.81 – 63.11)	p < 0.001
Group II: severe radiological pattern**	3/18 (17%)	15/18 (83%)		
Brain MRI pattern				
Type 1:absent brain injury	12/16 (75%)	4/16 (25%)	1.00 (reference)	
Type2: mild to moderate brain injury	4/6 (67%)	2/6 (33%)	1.5 (0.2 – 11.54)	p=0.69
Type 3: severe brain injury	3/18 (17%)	15/18 (83%)	15 (2.8 – 80.35)	p<0.001

*Non-severe radiological pattern includes both the Type 1 and Type 2 MRI patterns
**Severe radiological pattern refers to Type 3 MRI pattern
‡ OR, Odds ratio was calculated as the ratio of the odds of poor neurological outcome (CPC 3-5) between groups

Cerebral Performance Category at 6 months according to the severity of post-anoxic brain injury.

	Awakening				Resolution of status epilepticus				Mortality at 6 months			
	Yes N(%)	No N(%)	OR [CI 95%]	p value	Yes N(%)	No N(%)	OR [CI 95%]	p value	Yes N(%)	No N(%)	OR [CI 95%]	p value
Patient group												
Group I: non-severe radiological pattern* (reference)	16/22 (73%)	6/22 (27%)	9.3 [2.1 – 39.9]	0.003	21/22 (95%)	1/22 (5%)	10.5 [1.1-97.9]	0.032	9/22 (40%)	13/22 (60%)	1.81 [0.5-6.3]	0.356
Group II: severe radiological pattern**	4/18 (22%)	14/18 (78%)			12/18 (67%)	6/18 (33%)			10/18 (55%)	8/18 (45%)		
MRI Pattern												
Type 1	12/16 (75%)	4/16 (25%)	1 (reference)		16/16 (100%)	0/16 (0%)	1 (reference)		4/16 (25%)	12/16 (75%)		
Type2	4/6 (66%)	2/6 (33%)	1.5 [0.2-11.5]	0.69	5/6 (83%)	1/6 (17%)	9 [0.3-254]	0.13	5/6 (83%)	1/6 (17%)	-	-
Type 3	4/18 (22%)	14/18 (78%)	10.5 [2.1-51.2]	0.002	12/18 (67%)	6/18 (33%)	17 [0.6-304]	0.018	10/18 (55%)	6/18 (45%)	-	-

*Non-severe radiological pattern includes both the Type 1 and Type 2 MRI patterns
**Severe radiological pattern refers to Type 3 MRI pattern

Secondary outcomes according to the severity of post-anoxic brain injury.

Conclusion: Severe HIBI was associated with increased chances of poor outcomes, reduced probabilities of consciousness recovery and SE resolution. Six-month mortality showed no significant difference between severe and non-severe HIBI patients.

Disclosure: Nothing to disclose.

EPR-154 | Mapping burst suppression and structural brain injury post-cardiac arrest

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[1]Department of Neurology, University of California, San Francisco; [2]Department of Radiology, Duke University Medical Center; [3]Department of Radiology & Biomedical Imaging, University of California, San Francisco; [4]Department of Neurology Massachusetts General Hospital; [5]Department of Neurology, Brigham and Women's Hospital

Background and Aims: Burst suppression is a neurophysiological marker of severe hypoxic-ischemic brain injury post-cardiac arrest. This study's goal was to identify the neuroanatomical sources of burst suppression post-cardiac arrest.

Methods: MRI and EEG data from 86 comatose patients following cardiac arrest in two academic hospitals were retrospectively obtained. For EEG epochs with burst suppression detected, individual bursts were segmented and underwent whole brain source localization using the Champagne algorithm and mapped onto the Desikan-Killiany atlas. The eight regions with the highest EEG burst power (>90th percentile) were determined for each patient. Structural brain injury severity on MRI was measured using percent volume per ROI with apparent diffusion coefficient (ADC) $<650 \times 10^{-6}$ mm^2/s. The presence of brain injury on MRI was defined based on qualitative review of ADC maps.

Results: 39 (45%) patients had burst suppression and 23 (59%) had injury on MRI. Burst sources on EEG originated from bilateral lateral occipital lobes, pars triangularis, superior frontal regions, rostral middle frontal gyrus, and left middle temporal gyrus. Higher burst power was correlated with greater brain injury volume in bilateral lateral occipital lobes (Left: $r=0.209$, $p<0.01$; Right: $r=0.547$, $p<0.001$), bilateral pars triagularis (Left: $r=0.174$, $p=0.026$; Right: $r=0.413$, $p<0.001$), left superior frontal gyrus ($r=0.354$, $p<0.001$), and left middle temporal gyrus ($r=0.304$, $p<0.001$).

Table 1. Frequency of Regions Found in the Top 90th Percentile of EEG Burst Power

Hemisphere	Region	Frequency (Max n=39)	Mean Power Percentile (%)
Right	Inferiorparietal	20	96.27
Left	Lateraloccipital	19	96.40
Right	Lateraloccipital	16	96.84
Left	Middletemporal	20	95.76
Left	Parstriangularis	16	97.55
Right	Parstriangularis	15	97.81
Left	Rostralmiddlefrontal	14	95.66
Right	Rostralmiddlefrontal	12	96.94
Left	Superiorfrontal	13	95.81
Right	Superiorfrontal	19	94.20
Left	Superiorparietal	16	94.62

Figure 1. Correlation between EEG Burst Power & Percent Volume with ADC < 650

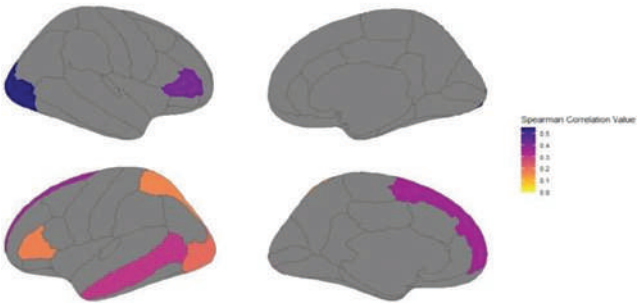

Table 2. Correlation between EEG Burst Power & Percent Volume with ADC < 650

Hemisphere	Region	Spearman Correlation	p-value
Left	Lateraloccipital	0.209	0.007
Right	Lateraloccipital	0.547	<.001
Left	Middletemporal	0.304	<.001
Left	Parstriangularis	0.174	0.026
Right	Parstriangularis	0.413	<.001
Left	Superiorfrontal	0.354	<.001
Left	Superiorparietal	0.167	0.033

Conclusion: Burst suppression post-cardiac arrest preferentially involves the lateral occipital lobes, pars triangularis, and superior frontal regions. Higher regional EEG burst power was associated with greater injury severity on MRI.

Disclosure: This study was supported by the American Heart Association (20CDA35310297), CURE Epilepsy Foundation (Taking Flight Award), Neurocritical Care Society (NCS research training fellowship), Weil-Society of Critical Care Medicine Research Grant, the NIH (1K23NS090900, 1R01NS102190, 1R01NS102574, 1R01NS107291, 1K23NS119794). M.B.W. is a co-founder of Beacon

Biosignals. Beacon Biosignals did not contribute funding nor played any role in the study.

EPR-155 | Management of oral secretions following tracheostomy: A longitudinal prospective study from a Neurocritical Care Unit

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Background and Aims: Patients in Neurocritical Care Units (NCCU) who undergo tracheostomy may require interventions to manage oral secretions. This study reviewed the management of oral secretions and outcomes following tracheostomy among patients admitted to NCCU.

Methods: Longitudinal prospective study of patients requiring tracheostomy in NCCU.

Results: 54 (5.4%) of 999 patients admitted to NCCU required tracheostomy during the study period. The mortality among these patients was 11.1% ($n=6$). The tracheostomy tube could be removed in 59.3% ($n=32$). Tracheostomies were more common in males, low GCS at admission and those with cerebrovascular pathologies. 55.6% ($n=30$) of patients had oral secretion issues. 6 different types of drugs were used for secretion management; hyoscine hydrobromide was the most common among them, followed by glycopyrronium bromide and botulinum neurotoxin type-A. Presence of oral secretion management issues demonstrated significant associations with the total length of stay in NCCU, time taken for decannulation and need for recannulation, admission GCS, fibreoptic endoscopic evaluation of swallowing (FEES) referrals, pulmonary infections and oral candidiasis ($p<0.05$). Secretion issues were not significantly associated with seizures, delirium, hydrocephalus interventions, neurosurgical interventions and spasticity interventions ($p>0.05$). Incidence of chest infections was higher before the institution of secretion pharmacotherapies. Prevalence of oral candidiasis was higher among people who had oral secretion management.

Conclusion: This study highlights the impact of oral secretion management on outcomes following tracheostomy among patients in NCCU. It presents a case for early initiation of pharmacotherapy in managing oral secretions.

Disclosure: The study was supported by a grant from Merz, manufacturers of Xeomin. Amin Mohamed Abu Baker: Nothing to disclose Sachin Watve: Nothing to disclose Vikrant Devgire: Nothing to disclose Sabrina Eltringham: Nothing to disclose Amanda Forrester: Nothing to disclose Krishnan Padmakumari Sivaraman Nair was supported by the NIHR Sheffield Biomedical Research Centre (BRC)/ NIHR Sheffield Clinical Research Facility (CRF). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care (DHSC).

EPR-156 | Abstract withdrawn

EPR-157 | Behavior of refractory status epilepticus in the Intensive Care Unit in Mexico: Case series

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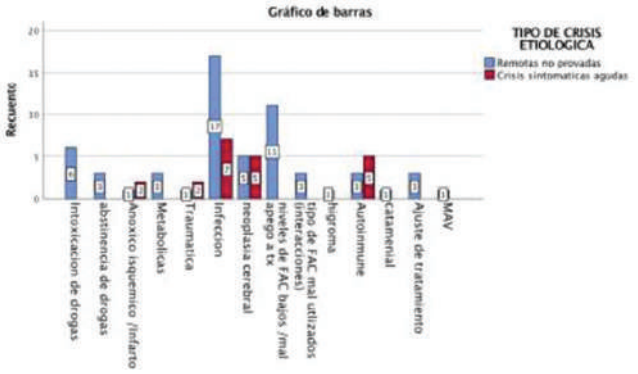
National Institute of Neurology and Neurosurgery

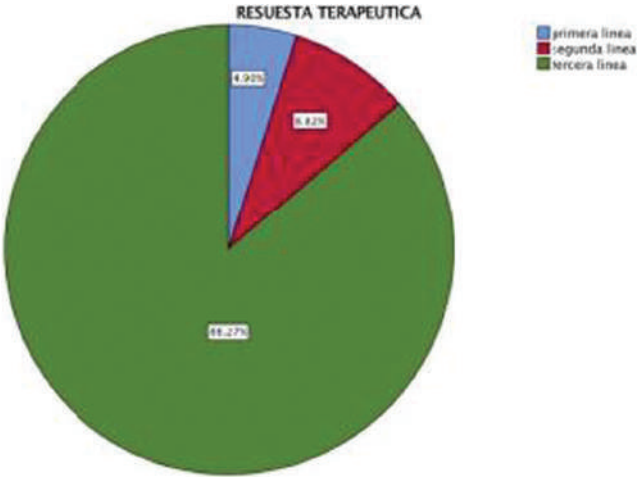
Background and Aims: Refractory status epilepticus has different characteristics with respect to established status epilepticus (SE).

Methods: A descriptive case series study. A total of 102 patients with SE in the ICU of the National Institute of Neurology and Neurosurgery (2010–2024) were evaluated. IBM SPSS statics was used for the descriptive statistical analysis.

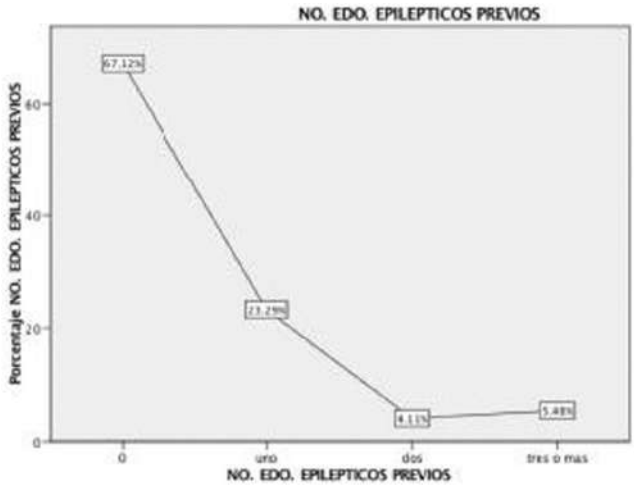
Results: The characteristics were female (53%), age 36.4+13.9 years with a diagnosis of epilepsy at 16.3+14.0 years in 73 patients of focal type (20/21) without severity (18/21) and of structural cause (51%), with encephalopathy (42/73), drug resistance (78%) and lack of control in the last month (44%), of which 24 had had at least one previous SE. Fifty-seven percent were admitted with stupor/coma (Glasgow 8.8+4.5 points) with infections identified as the major cause of exacerbation (30%) and serum levels of anti-seizures drugs decreased in 6%. EEG monitoring lasted 2.7+9.0 h, localizing severe (22%) frontal lobe activity (21%) and dysfunction (60%), identifying 21% of non-convulsive SE. Levetiracetam and valproate were the most used together with the use of IV anesthetics in 46% (midazolam 0.35+0.2 mg/kg/h or propofol 1.9+1.3 mg/kg/h) for 8.4+11.3 days (max 64); being that the use of mechanical ventilation was 12.8+15.2 days (max 91) with a final hospital days of 32.1+31.6(max 146). The 10.8% with extraordinary therapies including 11 patients who underwent surgery (partial callosotomy 3/11). The STESS scale of 2.4+0.8 points, leaving with major disability 35.3% (RANKIN 2.7+1.9) and a mortality of 13%.



Cause of status epilepticus.



Therapeutic response.



Number of previous status epilepticus.

Conclusion: SE in the UTI have demographic, clinical, neurophysiological, therapeutic and prognostic characteristics in the Mexican population.

Disclosure: Nothing to disclose.

EPR-158 | Efficacy of lumbar drains in reducing intracranial blood volume in patients with aneurysmal subarachnoid hemorrhage

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[1]*Department of Neurosurgery, Charité – Universitätsmedizin Berlin, Berlin, Germany;* [2]*Berlin Institute of Health at Charité – Universitätsmedizin Berlin, BIH Charité Junior Clinician Scientist Program*

Background and Aims: The utility of lumbar drainage (LD) in reducing unfavorable outcomes following aneurysmal subarachnoid hemorrhage (aSAH) has been established by the EARLYDRAIN trial(1). The underlying mechanism remains unelucidated. Here, we investigated the effect of LD on intracranial blood volume (IBV) in aSAH patients in comparison to no drainage or drainage via an external ventricular drain.

Methods: Different types of intracranial hemorrhage (basal SAH, cortical SAH, subdural hematoma, intracerebral and intraventricular hemorrhage) were manually segmented on longitudinal non-contrast enhanced CT scans of 68 patients treated at a single institution in the EARLYDRAIN trial using ITK-SNAP. Changes in IBV were analyzed and compared between patients treated with and without LD using generalized additive models.

Results: Twenty-eight patients were treated with and 40 without LD. No significant differences in demographic characteristics were observed. Total hemorrhage volume on admission was unevenly distributed among patients, with a median of 29.1 mL (range: 4.4-100.0 mL). No significant difference regarding initial hemorrhage volume was noted between the groups ($p=0.14$). LD was associated with a faster reduction of total IBV in the first 14 days following aSAH ($p=0.0003$), with a maximum difference observed between day 3 and 5. The reduction was most pronounced in the cortical SAH volume ($p=0.0027$), followed by the intraventricular ($p=0.069$) and basal SAH ($p=0.073$) components.

Conclusion: LD appears to contribute to a more rapid reduction of IBV measured by CT. This may indicate a potential mechanism serving as an explanation for the improved outcome by early application of LD in patients with aSAH. Further analysis is warranted.

Disclosure: Nothing to disclose.

Neuroimmunology 2

EPR-159 | Deep peripheral blood mononuclear cell phenotyping aiming to separate early- and late-onset myasthenia gravis

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Background and Aims: Myasthenia gravis (MG) is an autoimmune disorder of neuromuscular transmission, most commonly caused by autoantibodies towards the acetylcholine receptor (AChR+). The major MG subtypes without thymoma-association are early- and late onset MG (EOMG and LOMG). Divergences in age, sex ratio, HLA associations, autoantibodies and thymic hyperplasia suggest

different pathogeneses and potentially treatment needs for EOMG and LOMG patients. However, in clinical practice, the primary factor used for subgrouping is age. The main aim of the current project is to identify biomarkers by deep peripheral blood mononuclear cell (PBMC) phenotyping that could help to complement the separation of EOMG from LOMG by pathophysiologically sound criteria.

Methods: 1. Identification of cell populations and markers distinguishing EOMG from LOMG by single-cell trascriptomic, surface proteomic and B- and T-cell receptor analyses, in PBMC from 16 symptomatic patients, 8 each with EOMG or LOMG, all immunologically untreated, AChR+, plus a matched control set. 2. Checking the above screening hits by spectral cytometry in an independent replication cohort from Oxford of untreated AChR+ patients (13 with EOMG, 17 with LOMG) and 20 healthy controls.

Results: Initial screening identified populations of innate lymphoid/natural killer cells and CD4 T cells as most promising for separation of EOMG and LOMG. The replication analyses are ongoing and will be included in the presentation.

Conclusion: We have identified possible, biologically plausible, cell-surface biomarker candidates separating the two myasthenia patient subgroups, now being validated in an independent cohort. If confirmed, this may enable flow cytometry-based techniques to facilitate separation of the two MG subforms.

Disclosure: Funding for this study was received from the Swedish Wenner-Gren foundation, FT2021-0005, the Swedish MRC (grant no. 2020-02700) and EJPRD23-104 (OptiMyG) Jakob Theorell has received a fee for presenting at a Lundbeck-financed conference, not relating to this work. Susanna Brauner has received in non-restricted research grants from UCB Pharma and Janssen, not related to this study. Fredrik Piehl has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

EPR-160 | The short chain fatty acid sodium butyrate protects for oxidative stress in the peripheral nervous system

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Background and Aims: Butyrate is one of the short-chain fatty acids produced in the gut by bacteria during the anaerobic fermentation of indigestible fibers and is known for its immunomodulatory properties on T cells and macrophages through its binding to G-protein coupled receptors, free fatty acid receptors 2 and 3. This study describes for the first time the effects of butyrate in the peripheral nervous system via cultures of Schwann cells and dorsal root ganglia.

Methods: Survival of Schwann cells and outgrowth of dorsal root ganglia were evaluated after inducing oxidative stress with S-nitroso-N-acetyl-D-L-penicillamine treatment after pre-treatment with sodium butyrate. Furthermore, we performed an investigation of gene expression of the cell cultures after oxidative stress induction and sodium butyrate treatment as well as of the myelination of the nerve fibers under the influence of sodium butyrate in embryonic dorsal root ganglia and Schwann cell co-cultures.

Results: Coincubation of the Schwann cells with sodium butyrate 24 hours before induction of oxidative stress was able to protect the cells and reduce cellular death, visualized by microscopy and measured by propidium iodide staining. Furthermore, it modulated the gene expression of histone deacetylase 1 and 2, as well as the expression of the nuclear factor kB (NF-kB) and the protein kinase mammalian target of rapamycin (mTor).

Conclusion: We were able to demonstrate an anti-oxidative effect of sodium butyrate on Schwann cells through modulation of the expression of histone deacetylases. These effects might have therapeutical implications for patients with inflammatory and degenerative diseases of the peripheral nervous system.

Disclosure: Nothing to disclose.

EPR-161 | Evobrutinib ameliorates pathologies in a mouse model of neuromyelitis optica spectrum disorder

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Background and Aims: Neuromyelitis optica spectrum disorders (NMOSD) are autoimmune inflammatory demyelinating disorders of the central nervous system (CNS). Most NMOSD patients exhibit seropositivity for the pathogenic autoantibodies aquaporin-4-immunoglobulin G (AQP4-IgG). B cells play a crucial role in the mechanism underlying AQP4 autoimmunity. Bruton's tyrosine kinase (BTK) contributes to B-cell activation upon antigen recognition by B-cell receptor. The therapeutic potential of inhibiting BTK in NMOSD is unclear. We aim to study whether the BTK inhibitor evobrutinib ameliorates NMOSD-like pathologies in a mouse model of NMOSD with AQP4 autoimmunity [1].

Methods: Mice were immunized against AQP4 using in vivo electroporation [1]. Then mice received evobrutinib (oral gavage) or vehicle for 42 days. All mice were euthanized at day 42 for tissue harvesting. [1] Yick LW et al. JCI Insight 2023;e161003.

Results: AQP4 immunization triggered AQP4 autoimmunity and NMOSD-like spinal cord pathologies in mice. Immunofluorescence revealed prominent loss of AQP4 and GFAP, as well as patchy demyelination and axonal loss, in the spinal cord of AQP4 immunized mice compared to sham controls. Flow cytometry analysis demonstrated that AQP4 immunization caused the expansion of splenic memory B cells and plasma cells. Importantly, evobrutinib treatment improved

motor impairments, reduced AQP4 and GFAP loss, and decreased demyelination and axonal loss in AQP4 immunized mice. These were associated with reduction in the frequency of splenic antigen-presenting B cells. These results indicate that evobrutinib ameliorated NMOSD-like pathologies in mice with AQP4 autoimmunity.

Conclusion: Our findings suggest evobrutinib exerts therapeutic effect in NMOSD by modulating the function of B cells.

Disclosure: Nothing to disclose.

EPR-162 | CSF plasma cells produce highly specific autoantibodies in patients with LGI1/CASPR2 autoimmune encephalitis

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Background and Aims: Autoimmune encephalitis (AE) are inflammatory diseases characterized by adaptive autoimmunity against synaptic proteins and receptors of the central nervous system (CNS). Autoantibodies targeting the neuronal proteins leucine-rich-glioma-inactivated-1 (LGI1) and contactin-associated protein-like 2 (CASPR2) define common subtypes of AE associated with cognitive dysfunction, epileptic seizures, and psychiatric syndromes. Although inflammatory changes of cerebrospinal fluid (CSF) are mostly absent and serologic findings have suggested primarily systemic autoantibody production, plasma cells in CSF and a strong HLAII restriction are hallmarks of these diseases.

Methods: To evaluate the role of clonally expanded plasma cells in the CSF of patients with LGI1 and CASPR2-AE, we analyzed the CSF of 5 untreated patients with AE (3 LGI1 and 2 CASPR2), using scRNA (10x, 5' and VDJ), and performed a comprehensive in silico analysis of their B cell repertoire. We synthesized recombinant antibodies (rHumAB) of the top 5-7 clonally expanded antibody-producing cells per patient and analyzed these rHumAbs for specificity, epitopes, affinity, and somatic hypermutation (SHM).

Results: Cell and tissue-based assays, and flow cytometry analysis, demonstrated that 10/10 rHumAbs from CASPR2 and 17/17 rHumAbs from LGI1 patients' CSF were indeed autoantigen reactive, with high avidity and affinity. These results were in line with an increased number of SHM and epitope complexity.

Conclusion: We conclude that patients with LGI1/CASPR2-AE harbor a high rate of intrathecally expanded, autoantigen-specific plasma cells in their CSF compartment, which suggests prominent local T-cells help driving the disease development. This finding needs to be considered for monitoring response to therapy and future therapy development.

Disclosure: "Nothing to disclose."

EPR-163 | Dysautonomia in anti-Hu paraneoplastic neurological syndromes

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Background and Aims: Dysautonomia has been associated with paraneoplastic neurological syndrome (PNS)-related mortality in anti-Hu PNS, but its frequency and spectrum remain ill-defined. We describe anti-Hu patients with dysautonomia, estimate its frequency, and compare them to patients without dysautonomia.

Methods: Patients with anti-Hu antibodies diagnosed in the study centre (1990–2022) were retrospectively reviewed; those with autonomic signs and symptoms were identified.

Results: Among 477 anti-Hu patients, 126 (26%) had dysautonomia (the only PNS manifestation in 7/126, 6%); gastrointestinal (82/126, 65%), cardiovascular (64/126, 51%), urogenital (24/126, 19%), pupillomotor/secretomotor (each, 11/126, 9%), and central hypoventilation (10/126, 8%). Patients with isolated CNS involvement less frequently had gastrointestinal dysautonomia than those with peripheral (alone or combined with CNS) involvement (7/23, 30% vs. 31/44, 70% vs. 37/52, 71%; $p=0.002$); while more frequently central hypoventilation (7/23, 30% vs. 1/44, 2.3% vs. 2/52, 4%; $p<0.001$) and/or cardiovascular alterations (18/23, 78% vs. 20/44, 45% vs. 26/52, 50%; $p=0.055$). Median [95%CI] overall survival was not significantly different between patients with (37[17;91] months) or without dysautonomia (28[22;39] months; $p=0.78$). Cardiovascular dysautonomia (HR:1.57, 95%CI[1.05;2.36]; $p=0.030$) and central hypoventilation (HR:3.51, 95%CI[1.54;8.01]; $p=0.003$) were associated with a higher risk of death, and secretomotor dysautonomia a lower risk (HR:0.28, 95%CI[0.09;0.89]; $p=0.032$). Patients with cardiovascular dysautonomia dying ≤1 year from clinical onset had severe CNS (21/27, 78%), frequently brainstem (13/27, 48%), involvement.

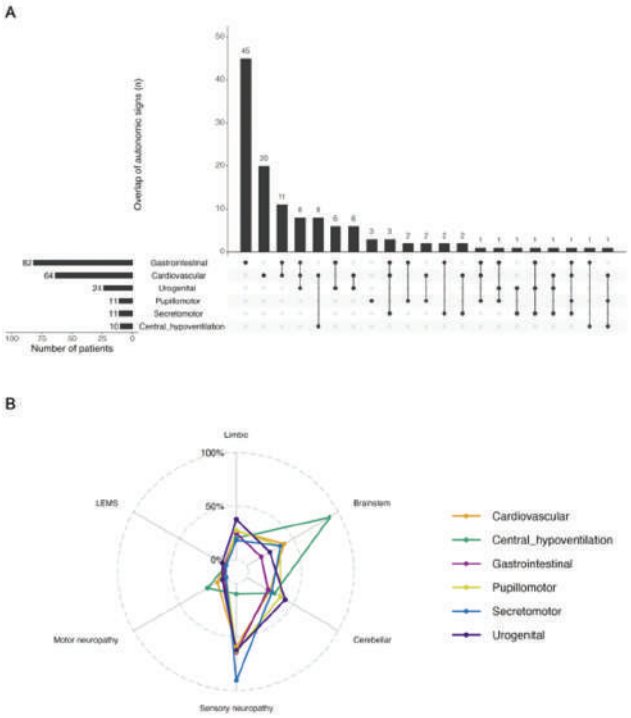

FIGURE 1. Characterisation of autonomic and extra-autonomic neurological involvement. (A) Upset plot presenting the numbers and different combinations of autonomic involvement in $n = 126$ patients with anti-Hu PNS. Each row represents an autonomic domain, th.

TABLE 1. Autonomic symptoms and signs in anti-Hu patients.

Table 1. Autonomic symptoms and signs in anti-Hu patients.

	n = 126
Gastrointestinal, n (%)	82 (65)
Constipation/diarrhoea	61 (74)
Deglutition problems	45 (55)
Nausea	45 (55)
Obstructive syndrome	40 (49)
Achalasia	24 (29)
Early satiety	11 (13)
Cardiovascular, n (%)	64 (51)
Orthostatic intolerance	45 (70)
Hypotension	15 (23)
Labile blood pressure	13 (20)
Bradycardia[a]	6 (9)
Cardiac arrest	6 (9)
Hypertension	5 (8)
Labile heart rate	4 (6)
Tachycardia	3 (5)
Takotsubo cardiomyopathy	1 (2)
Urogenital, n (%)	24 (19)
Urinary retention	20 (83)
Overflow incontinence	5 (21)
Erectile dysfunction	2 (8)
Pupillomotor, n (%)	11 (9)
Adie's pupil	11 (100)
Secretomotor, n (%)	11 (9)
Inadequate sweating[b]	6 (55)
Sicca syndrome	3 (27)
Hypersalivation	2 (18)
Skin flushing	1 (9)
Central hypoventilation, n (%)	10 (8)

[a]Third degree atrioventricular block in n=1 patient.
[b]Manifested as thermal dysregulation in n=1 patient.
Abbreviations: n, number.

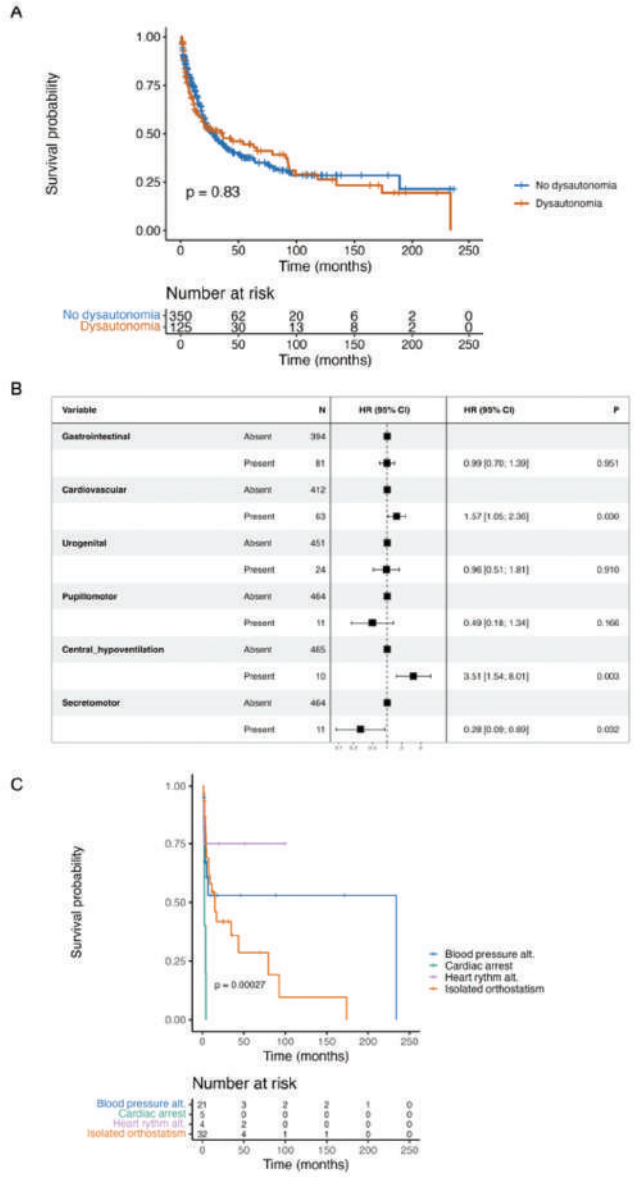

FIGURE 2. Survival analyses. (A) Kaplan-Meier curves according to the presence or absence of dysautonomia. Tick marks indicate censored patients, and the comparison was made using the Log-rank test. Two patients had to be excluded due to missing date of P.

Conclusion: Anti-Hu PNS dysautonomia is rarely isolated, frequently gastrointestinal, cardiovascular and urogenital. CNS dysfunction, particularly brainstem, associates with lethal cardiovascular alterations and central hypoventilation, while peripheral involvement preferentially associates with gastrointestinal or secretomotor dysautonomia, being the latest more indolent.

Disclosure: This study was developed within the BETPSY project, which is supported by a public grant overseen by the Agence Nationale de la Recherche (ANR) as part of the second Investissements d'Avenir program (ANR-18-RHUS-0012). The study is supported by the European Reference Network RITA, M.V-G. is supported by a research grant from Fundación Alfonso Martín Escudero (Spain), and A.F was granted a research fellowship by the European Academy of Neurology.

EPR-164 | Plasma and CSF leiomodin-1 antibodies in patients with long standing Nodding Syndrome

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Background and Aims: Nodding syndrome (NS) is a complex neurological disorder of unknown aetiology. Here we investigated the role of autoimmunity to neuronal antigens in NS patients.

Methods: We screened for the presence of leiomodin-1 and neuronal antibodies in plasma and CSF of 240 NS patients enrolled in a phase II trial of doxycycline for the treatment of NS. Plasma was tested for antibodies to Onchocerca volvulus (Ov16 and Ov3261) and leioimodin-1. Filarial worm infection was defined as a positive antibody test to any of the two Onchocerca volvulus antigens. CSF was tested by immunohistochemistry (IHC) on rodent brain sections and by antigen specific cell-based assays for neuronal proteins and leiomodin-1.

Results: A total of 232/240 (96.7%) plasma samples tested positive for Onchocerca volvulus. Leiomodin-1 antibodies were detected in 77/240 (32.1%) plasma samples and in 26/240 (10.8%) CSF samples. Circulating leioimodin-1 antibodies (76/232 [32.8%] Ov16/Ov3261 positive vs. 1/8 [12.5%] Ov16/Ov3261 negative, $p=0.044$) but not CSF leioimodin-1 antibodies (25/232 [10.8%] Ov16/Ov3261-positive vs. 1/8 [12.5%] Ov16/Ov3261-negative, $p=1.0$) was associated with Onchocerca volvulus infection. However, CSF leiomodin-1 antibodies were more likely to be present in patients with myoclonic seizures or drop attacks. Neuropilar staining by IHC was found in 28/240 (11.7%) NS CSFs. Among them, 2 had GABAbR antibodies and one had CASPR2 antibodies. Only 8/28 (28.6%) patients had both leiomodin-1 and neuropilar antibodies.

Conclusion: NS is associated with infection by Onchocerca volvulus and circulating antibodies to leioimodin-1. In addition, patients with CSF leioimodin-1 antibodies present with myoclonic seizures and drop attacks.

Disclosure: None

EPR-165 | Improvements in pain and quality of life after inebilizumab in attack-free NMOSD participants

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Background and Aims: Chronic pain and disability contribute to decreased quality of life (QoL) in NMOSD. Previous analyses showed year-over-year improvements in pain and QoL with inebilizumab. Here we further evaluated Pain and QoL improvement in attack-free, inebilizumab participants over 3-years to determine improvements in non-attack-related pain and QoL.

Methods: N-MOmentum (NCT02200770) had 6-month-randomized-control-period (RCP) with an open-label-extension-period (OLP) of ≥2 years. Year-over-year changes in pain (SF-36-Bodily-Pain-Score [BPS]), QoL (SF-36-physical-component-summary[PCS]), and disability (Expanded-Disability-Status-Scale[EDSS]) were assessed for significance using mixed linear models in 95 participants who were attack-free with ≥3-years of inebilizumab. Sensitivity analysis was conducted in 72/95 participants who were attack-free for ≥6 months prior to inebilizumab treatment to control for acute attack-related recovery.

Results: At Baseline, 38% (36/95) participants reported an abnormal QoL score (SF36-PCS <40), 89% (32/36) of these reported increased pain (SF36-Bp <40) and 50% (18/36) reported significant disability (EDSS ≥5). After 3-years of inebilizumab, QoL scores improved in 89% (32/36) of attack-free participants with an abnormal baseline QoL score. 39% (37/95) of participants had abnormal pain scores (SF36-BPS <40) at baseline and improvements were reported in 78% (29/37) $p < 0.001$ after 3-years of inebilizumab. SF36-PCS and BPS scores also improved in participants with normal (≥40) baseline scores after 3-years of inebilizumab. Improvements in EDSS from baseline to 3-years of inebilizumab were observed in 44% (40/91) of participants including 36% (25/69) with less disability (<5 EDSS) and 68% (15/22) with greater disability (≥5 EDSS) at baseline. These results were consistent with the sensitivity analysis.

Conclusion: Year-over-year Improvements in Pain, QoL, and EDSS were observed in attack-free participants on inebilizumab. Interestingly, these improvements were independent of acute attack-related recovery.

Disclosure: O Aktas: DFG, BMBF, Alexion, Almirall, Bayer HealthCare, Biogen, Horizon, Merck Serono, Novartis, Roche, Sanofi, Teva, Guthy-Jackson Charitable Foundation. F Paul: Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi Genzyme, Teva, DFG Exc 257), Guthy-Jackson Charitable Foundation, and Novartis. HP Hartung: Bayer HealthCare, Biogen Idec, Celgene Receptos, CSL Behring, GeNeuro, Genzyme, Horizon, MedDay, MedImmune, Merck Serono, Novartis, Roche, Sanofi,TG Therapeutics. J Graves: TG Therapeutics and Novartis. DK Sato: CNPq, FAPERGS, Teva, Merck, Biogen, Merck, Roche, Horizon and Alexion. JM Burton: Roche, Alexion, Novartis, Biogen, CADTH, U of Calgary, and MS Canada MA Smith, WA Rees and KR Patterson: Amgen BAC Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Hexal/Sandoz, Horizon, Immunic AG, Kyverna, Neuron23, Novartis, Sanofi, Siemens,TG Therapeutics and Genentech.

EPR-166 | Bone marrow granulopoiesis instructs B cell-mediated neuroinflammation and autoimmunity

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Background and Aims: B cells are active participants in autoimmune etiology. Bone marrow hematopoietic stem and progenitor cells (HSPCs) are integrative hubs to sense immune activation and orchestrate inflammation. Yet the alterations of bone marrow HSPCs in B cell-mediated autoimmunity and their potential impact on disease progression remain unknown. Neuromyelitis optica spectrum disorder (NMOSD) is a B cell-mediated autoimmune neurological disease with autoantibodies to aquaporin-4 (AQP4-IgG) in 75% of patients.

Methods: We assessed bone marrow HSPC activity and B cell development using combined approaches of single cell sequencing and flow cytometry. We examined the safety and efficacy of belimumab in 14 patients with NMOSD and followed up for at least 52 weeks.

Results: In patients with NMOSD, we found remarkably augmented granulopoiesis in bone marrow, accompanied by expansion of B cell clones. This aberrant granulopoiesis is mediated by hyperactive JAK-STAT signaling, leading to a significant increase of neutrophils that produce BAFF to drive the generation of antibody-secreting cells and AQP4-IgG. Augmented neutropoiesis is also observed in NMOSD patients receiving rituximab who experienced a relapse. In an open-label, single-arm trial of belimumab, an anti-BAFF monoclonal antibody, in 14 NMOSD patients, belimumab prevented relapse and reduced the production of antibody-secreting cells and AQP4-IgG.

Conclusion: Thus, targeting bone marrow niche presents a new avenue to treat patients with NMOSD and perhaps other immune-mediated central nervous system diseases.

Disclosure: Nothing to disclose.

Neuro-oncology

EPR-167 | Primary meningeal melanocytic tumors (PMMT): A review from the Ultra Rare Brain Tumors domain of the EURACAN

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Background and Aims: PMMT are ultra rare entities with distinct histological and molecular features as compared with other melanocytic or pigmented intracranial lesions.

Methods: The EUropean Network for RAre CANcers (EURACAN) Task Force on Ultrarare Brain Tumors (domain 10) has perfomed a literature revision from January 1985 to December 2023 regarding the evidence of epidemiologic and clinical characteristics, histological and molecular features, radiological findings, and activity of local and systemic therapies.

Results: Molecular analysis can detect specific mutations, including SF3B1, EIF1AX, BAP1, NRAS and BRAF, that are found in PMMT and not in other melanocytic lesions. Neuroimaging shows the leptomeningeal involvement with or without parenchymal lesions with meningeal base implant, delineate the extension with respect to adjacent structures, but cannot reveal the aggressiveness of the disease. Gross-total resection is the first choice in case of circumscribed meningeal melanocytoma and melanoma; conversely, meningeal biopsy may be reserved for patients with diffuse and multinodular leptomeningeal spread to achieve a definitive diagnosis. High-dose radiotherapy is rarely indicated in diffuse melanocytic tumors except as palliative treatment to alleviate symptoms. A definitive advantage of a specific systemic treatment over other could not be concluded, as most of the data available derive from case reports or small cohorts.

Conclusion: As PMMT are extremely rare, weak correlations between clinical characteristics, molecular profile, radiological findings at diagnosis and progression, and poor evidence on the best therapeutic approach are available thus far. There is the need to develop shared platforms and registries to capture more knowledge regarding these ultra rare entities.

Disclosure: The authors declare no conflict of interest.

EPR-168 | Severe myasthenia gravis and myositis overlap syndrome following CAR T cell therapy for B cell non-Hodgkin lymphoma

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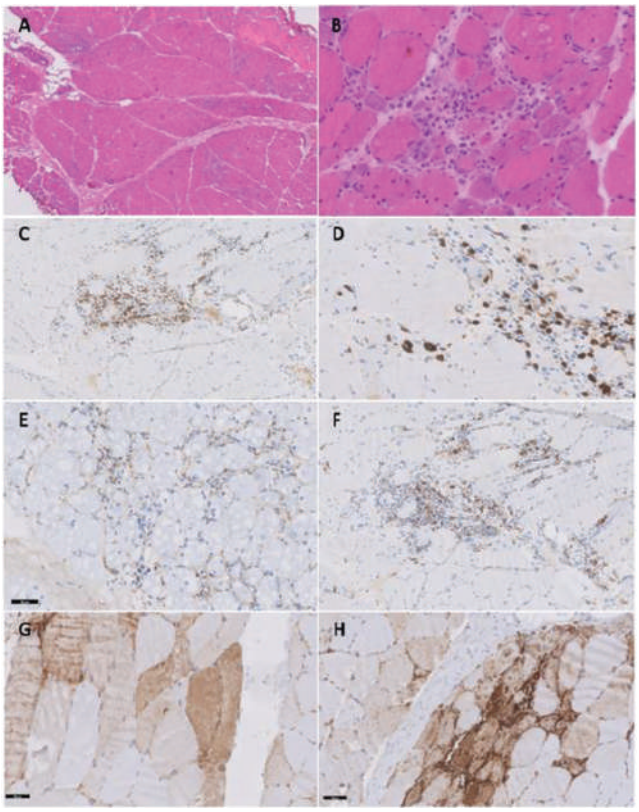
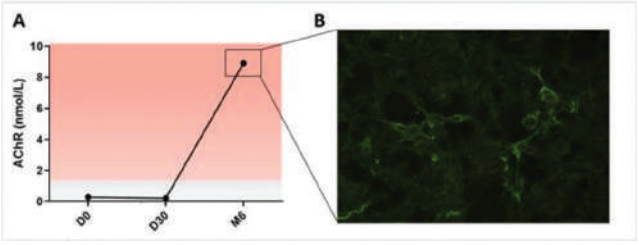
Background and Aims: Chimeric antigen receptor (CAR) T-cell therapy has significantly improved prognosis of relapsed/refractory B-cell lymphomas (DLBL). However, it can generate potential life-threatening complications. Reports of delayed immune-related adverse events (irAEs) are extremely rare. Here we describe the first case of neurological irAE following CAR-T therapy.

Methods: Case report.

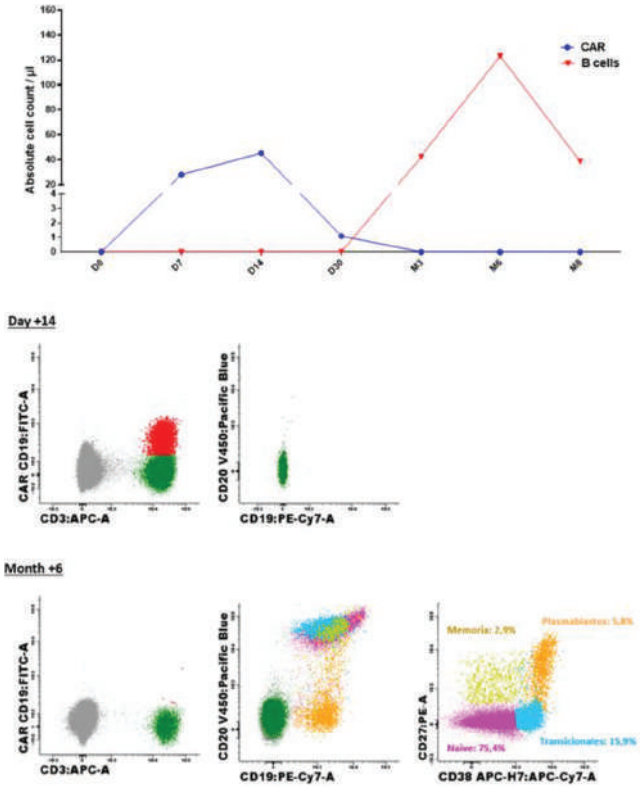
Results: A 68-year-old man with history of relapsed DLBL received CAR-T therapy (axicabtagene-ciloleucel), with complete metabolic response. Six months later he developed progressive proximal muscle weakness, dysphagia, and respiratory failure requiring invasive mechanical ventilation. DLBL relapse was ruled out by CT-scan and core-needle biopsy. Diagnostic workup showed elevated creatine kinase concentrations [1685 U/L (normal range 38-174)], myopathic signs on EMG, inflammatory TCD8+ infiltrates on muscle biopsy (Figure 1), pathological single-fibre EMG, and positive anti-acetylcholine-receptor (anti-AChR) antibodies. Anti-AChR antibodies were tested in two historical sera of the patient with negative results (Figure 2). Flow cytometry analysis showed undetectable circulating CAR-T cells, with complete reconstitution of B compartment (Figure 3). He was finally diagnosed with a severe myasthenia gravis (MG) and polymyositis overlap syndrome. Treatment with high-dose corticosteroids, intravenous immunoglobulins, support therapies, and prolonged physiotherapy were required for significant clinical improvement at one-month follow-up [modified Rankin Scale: 1; MG-Activities of Daily Living: 3/24 (12 points improvement)].



Deltoid muscle biopsy compatible with polymyositis: necrotic fibres (A-B), inflammatory aggregates of TCD8+ lymphocytes (C-D), scarce complement deposits (E), frequent macrophages CD68+ (F), and intense immunoreactivity in anti-HLA-1 staining (G-H).



(A) Evolution of anti-AChR antibodies titles, analysed with ELISA: immediately before CAR-T infusion (D0), on first month (D30), and on sixth month (M6) coinciding with symptom-onset. (B) shows cell-based assay (Euroimmun) positivity confirmation.



Expansion kinetics of anti-CD19 CAR-T cells and B-cell counts in peripheral blood, analysed by flow cytometry (A). Peak expansion of CAR-T cells (in red) on day 14 (B). Undetectable CAR-T cells with reconstitution of B compartment on month 6 (C).

Conclusion: To our knowledge, this is the first late-onset neurological irAE described with CAR-T. The cause of immune tolerance-breakdown is not yet identified. In our case, it occurred after CAR-T cells ceased to be detectable, coinciding with complete reconstitution of the B compartment. Further investigation of the mechanisms involved is warranted.

Disclosure: None.

EPR-169 | Neuronal injury and neurofilaments abnormalities in patients treated with anti-CD19 CAR-T cells

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Background and Aims: Patients receiving anti-CD19 Chimeric Antigen Receptor (CAR) T-cell therapy may develop Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) after infusion. Information regarding the occurrence of neuronal injury during ICANS is scarce. Our goal was to describe serum neurofilament light chain (NfLs) dynamics after anti-CD19 CAR T-cell therapy, comparing patients who developed ICANS with a control cohort who did not.

Methods: This was a nested case–control study within a prospective cohort that included all anti-CD19 CAR-T-treated patients at a single center. Cases manifested ICANS, with matched controls lacking ICANS. We assessed NfLs levels (normalized Z-scores) at baseline, Day 7, and Day 14 post CAR-T administration. Comparative risk analyses, linear mixed analysis with a split-plot design, and ROC analysis for optimal NfLs cut-off to differentiate ICANs presence and grade ≥2 were performed.

Results: We identified 32 cases and 24 controls. Yescarta use (OR6.6; 95%CI 2.0–21.7) and CRS occurrence (OR4.8; 95%CI 1.1–20.8) increased ICANS risk. Baseline NfL concentrations were elevated in both cases and controls versus normal expected values ($p=0.025$, $p=0.032$, respectively; Figure 1). In the Split-plot design, day 7 NfLs were significantly higher in ICANS grade ≥2 (means Z-score 2.19 and 1.60, respectively; $p=0.022$), with no differences at baseline and Day 14 (Figure 1). Patients lacking ICANS on Day 7, with NfLs exceeding Z-score >2.197, exhibited a higher incidence of ICANS grade ≥2 (38.5%vs. 4.6%, $p=0.01$).

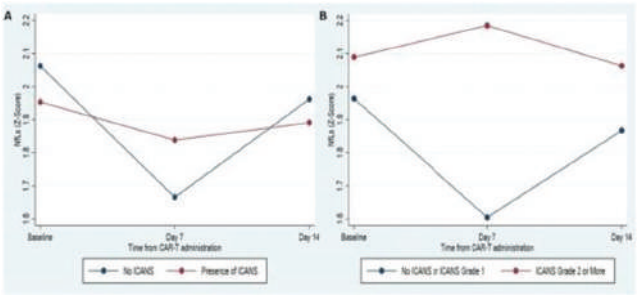

FIGURE 1. Linear Mixed Analysis by ICANS Presence (A) and ICANS Grade 2 or more (B).

Conclusion: Patients with ICANS grade 2 or higher exhibit an increase in NfLs compared to patients without ICANS or who only develop ICANS grade 1, being a Z-score ≥ 2.197 the best cut-off value to differentiate them.

Disclosure: Grant (CM22/00247).

EPR-170 | Neuroimaging and neuropsychological features of hypothalamic syndrome after craniopharyngioma

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Background and Aims: Hypothalamic obesity (HO) and neuropsychological deficits are common in craniopharyngioma (CP) patients, significantly impacting their quality of life. The study aimed to uncover shared pathogenetic pathways between obesity and psychological disturbances in individuals with HO following CP.

Methods: Fourteen CP patients (7 with HO, 7 without) underwent comprehensive assessments, including neuropsychological evaluations, functional magnetic resonance imaging (fMRI) tasks related to eating behavior and emotional recognition, and cortical thickness analysis. Correlations between cortical thickness and the expression of oxytocinergic pathway genes were explored.

Results: CP HO patients exhibited reduced bilateral insula cortical thickness correlating with eating behavior questionnaire scores. Increased insula activity, along with other hedonic network regions, was observed. CP patients showed greater anterior cingulate cortex activation during fMRI tasks. In emotional recognition tasks, CP HO subjects displayed increased prefrontal region activation. No correlation was found with oxytocin gene expression, but a significant correlation with oxytocin receptor gene expression was observed.

Conclusion: These findings align with obesity studies, indicating altered brain activation in CP HO resembling patterns associated with pleasurable food processing and lacking inhibitory control seen in CP. Oxytocin may offer therapeutic potential for reinstating physiological emotional processing in CP HO subjects post-CP, as suggested by gene expression correlations indicating conservation of areas expressing oxytocin receptors.

Disclosure: Nothing to disclose.

EPR-171 | IL6 blockade: An effective approach in steroid-refractory immune checkpoint inhibitor-related neuropathies

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Background and Aims: Immune checkpoint inhibitor-related neuropathies (irAE-np) are generally responding to steroids and

intravenous immunoglobulin (IVIG), however little is known regarding the management of refractory cases. The use of tocilizumab (anti-receptor for interleukin 6R) in steroid-refractory immune-related adverse event (irAE) has already been documented as safe form oncological standpoint and efficient in tissue agnostic irAE. Our aim is to describe the clinical response of steroid-refractory irAE-np to Tocilizumab with or without synchronous ICI rechallenge.

Methods: We retrospectively collected the cases of steroid-refractory irAE-np referred to the French OncoNeuroTox network from 2021 to 2023. The inclusion criteria were (i) subacute onset of neuropathy less than three months after the last ICI infusion, (ii) after exclusion of alternative diagnoses, and (iii) refractory to corticosteroid therapy at 1 mg/kg or 3 boli of 1g + IVIG.

Results: Four cases of polyradiculoneuropathy under ICIs for melanoma were identified (anti-PD1 2/4; anti-PD1 + anti-CTLA4 2/4). The median time to irAE-np onset was 47 (10-300) days. All patients presented with a demyelinating electrophysiological phenotype and ¾ fulfilled the EFNS 2021 criteria. The CSF analysis showed an albumin-cytological dissociation with a proteins at 0.68 (0.42-2.4) g/L and 6 (2-13) cells/mm^3 and a subnormal IL6 level at 5 (3-9) pg/mL. Monthly Tocilizumab allowed a neurological improvement ($\Delta mRS = 1$) maintained even after ICIs rechallenge.

Conclusion: Little is known on the management and the ICI rechallenge in steroid-refractory irAE-np. Our series points to Tocilizumab to be an effective and secure treatment for steroid-refractory irAE-np in monotherapy or in combination with an anti-PD1.

Disclosure: Nothing to disclose.

EPR-172 | Management of glioblastoma (GBM) at recurrence: treatment modalities and predictors of response.

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Background and Aims: The choice of treatments at recurrence for glioblastoma (GBM) patients is challenging. We explored which factors affected the response to treatments at recurrence of an institutional real-life cohort.

Methods: We retrospectively included IDH-wildtype GBM patients treated from 2010 and 2023. We defined first progression-free survival (1st-PFS) from diagnosis to first recurrence, 2nd-PFS from first to second recurrence, overall survival (OS) from second recurrence to death/censoring.

Results: We included 109 GBM patients at recurrence. Treatments modalities were re-resection (16/109, 14.7%), re-RT (11/109, 10.1%), and 2nd-line CHT/antiangiogenic agents (98/109, 89.9%) – of those, 40/98 (40.8%) received regorafenib, 20/98 (20.4%) bevacizumab, 19/98 (19.4%) TMZ rechallenge, and 19/98 (19.4%) nitrosoureas. 2nd-PFS an OS were 6.0 and 11.0 months. Patients receiving TMZ had a longer median 2nd-PFS (17 months, vs. 5.0 for regorafenib, 5.0 for bevacizumab, and 5.0 for nitrosoureas, $p = 0.004$), and OS (32.0 months, versus 13.0 for bevacizumab, 9.0 for nitrosoureas, and 10.0 for regorafenib, $p < 0.027$). TMZ was predominantly given to MGMTp-methylated patients (16/17, 94.1%, vs. 50.0%, 68.4% and 52.6% for bevacizumab, nitrosoureas and regorafenib, $p = 0.016$), with longer 1st-PFS (35.0 months vs. 11.5, 11.0 and 11.0 for bevacizumab, nitrosoureas and regorafenib, $p < 0.001$). In a multivariate analysis on 2nd-PFS, age and use of regorafenib correlated with shorter 2nd-PFS. In a multivariate analysis on OS, MGMTp methylation was the only positive factor.

Conclusion: Selected GBM patients with favourable baseline characteristics (MGMTp methylation; prolonged 1st-PFS) benefited from TMZ rechallenge at recurrence. Except for those, we could not identify subgroups who took advantage from other strategies.

Disclosure: Nothing to disclose.

EPR-173 | Neurotoxicity using academic and commercial anti-cd19 cart therapy in patients with refractory hematologic diseases

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Background and Aims: CART therapy can associate cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). We aim to describe the incidence of CRS/ICANS and outcome of patients treated with two different anti-CD19 CART products.

Methods: Single-center retrospective study of consecutive patients treated with commercial Axicabtagene Ciloleucel or ARI-0001 (produced in-house) between 2019 and 2023. ARI-0001 was split into 3 fractions (10%, 30%, 60%) with full administration depending on the absence of CRS. We assessed demographic and clinical features, and toxicity-related complications.

Results: 84 patients (59.5% males), median age 60 years (interquartile range 47.5–67), 72.6% with ECOG = 0 were included. 44 patients received ARI-0001 (36.4% transformed follicular lymphoma). In 10 patients (22.7%) administration of ARI-0001 was partial, 9 due to CRS grade 1-2 and 1 by macrophage activation syndrome. Three cases developed ICANS grade 1-2. Of the 34 who completed

3 doses, CRS was observed in 25 (73.5%) patients, grade >3 in 3, and none developed ICANS. 40 patients received Axicabtagene Ciloleucel (65% diffuse large B-cell lymphoma). CRS was observed in 33 (82.5%) patients, achieving grade >3 in 1, and 23 (57.5%) patients developed ICANS, grade >3 in 6 (15%). No deaths were attributed to CRS or ICANS for any product.

Conclusion: Despite a similar frequency of CRS, the academic CART showed a lower incidence of ICANS than the commercial product, probably explained by different indications and fractionated administration.

Disclosure: Nothing to disclose.

EPR-174 | Zotiraciclib for newly diagnosed or recurrent glioblastoma: updated outcome and biomarker analysis

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Background and Aims: Standards of care for recurrent glioblastoma are poorly defined. The multi-cyclin dependent kinase inhibitor Zotiraciclib depletes short-lived survival proteins such as c-MYC and MCL-1 which are overexpressed in glioblastoma.

Methods: EORTC 1608 was a three parallel group phase Ib, non-randomized, multicenter study in IDH wildtype newly diagnosed glioblastoma or anaplastic astrocytoma. In groups A and B, the maximum tolerated dose (MTD) of Zotiraciclib in elderly patients, in combination with radiotherapy alone (group A) or temozolomide alone (group B), by O6-methylguanine DNA methyltransferase promoter methylation status, were determined. In group C, we explored single agent activity of TG02 at first relapse with a primary endpoint of progression-free survival at 6 months (PFS-6). Tumor expression of CDK-9, c-MYC and MCL-1 was determined by immunohistochemistry. Tumor-related extracellular vesicles were quantified according to the minimal information for studies of extracellular vesicles 2018 (MISEV2018) guidelines.

Results: Main toxicities of zotiraciclib were neutropenia, gastrointestinal disorders and hepatotoxicity. The MTD was 150 mg twice weekly in group A or bi-weekly in group B. PFS-6 in group C was 6.7%. The tumor expression of c-MYC and MCL-1 was moderately cross-correlated. High protein levels of MCL-1 were associated with inferior survival. The levels of tumor-related extracellular vesicles in the blood correlated with tumor volumes determined by MRI and increased from baseline to recurrence.

Conclusion: Zotiraciclib exhibits overlapping toxicity with alkylators and low single agent clinical activity. The role of c-MYC and MCL-1 as therapeutic targets and the diagnostic value of extracellular vesicles in peripheral blood in glioblastoma warrant further study.

Disclosure: This study was supported by an unrestricted research grant from Adastra Pharmaceuticals (San Diego, CA) to the European Organisation for Research and Treatment of Cancer (EORTC).

EPR-175 | High-grade gliomas with pleomorphic and pseudopapillary features (HPAP) are circumscribed tumors with long-term survival

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Background and Aims: The taxonomy of primary CNS tumors is evolving. Recently, DNA methylation profiling has contributed to the identification of HPAP (high-grade glioma with pleomorphic and pseudopapillary features), a potential new tumor entity that harbors variable morphology, recurrent MAP kinase pathway activating events, and a significantly longer survival compared to glioblastoma. Our goal is to independently validate and further characterize this entity.

Methods: We retrieved prospective and retrospective cases with histological (pleomorphic xanthoastrocytoma, astroblastoma) or molecular (chromosome 13 loss) features compatible with the diagnosis of HPAP and performed tSNE dimensionality reduction on their methylome profile.

Results: We identified nine cases that clustered with previously reported HPAP cases. Median age was 42 years (range 23–66), and there was a female predominance (male/female ratio 0.5). Presenting symptoms included intracranial hypertension (44%), focal deficits (33%), and seizures (33%). The most common localization was the temporal lobe (50%). All cases were IDH1/2 wildtype. Recurrently mutated genes included TP53, ATRX, and RB1. Two cases (22%)

had activating BRAF V600E mutations. Upfront management was heterogeneous (Figure), and included surgery alone (22%), adjuvant radiotherapy (33%), or radiotherapy plus temozolomide (44%). After a median follow-up of 7.0 years (range 0.4–15.3, Figure), all patients but one were alive. The only observed death was due to intratumoral hemorrhage in a patient treated with bevacizumab. CDKN2A loss seemed to identify more aggressive tumor course.

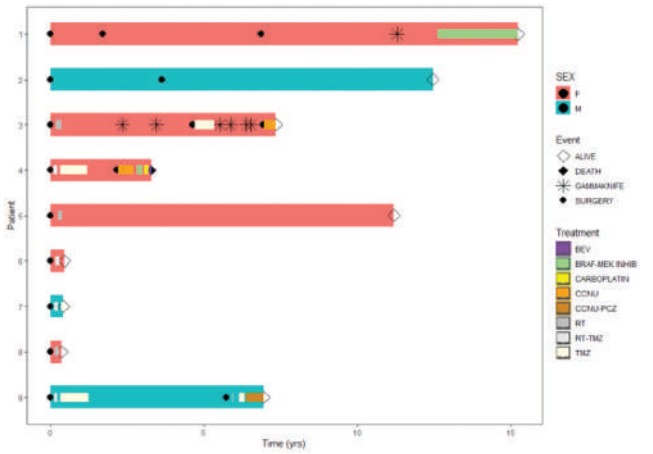

FIGURE 1. Swimmer plot of the nine cases indicating the received treatments.

Conclusion: HPAP is a novel entity of circumscribed gliomas with frequent high-grade histological presentation but excellent long-term survival. A proper identification could guide neuro-oncologist in appropriate treatment choices.
Disclosure: Nothing to disclose.

Neurogenetics 2

EPR-176 | Clinical and genetic characterization of a Hereditary spastic paraplegias cohort: Experience from the University of Pisa

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Background and Aims: Hereditary spastic paraparesis or paraplegias (HSPs) are a heterogeneous group of inherited neurodegenerative disorders caused by the degeneration of the pyramidal tracts. The present study aims to characterize the clinical features and molecular data of a cohort of patients diagnosed with HSP analyzing the baseline data from a continuous, prospective cohort.
Methods: Phenotype and genotype data of patients with clinical signs and symptoms indicative of pure or complicated HSP were collected from the TreatHSP Consortium's register. Disease severity was assessed using the Spastic Paraplegia Rating Scale (SPRS) at baseline, 6- and 12-months follow-up.
Results: A cohort of 40 patients was studied. Family history indicated dominant (40%), recessive (5%), and simplex (55%) inheritance. SPG4 was the major cause of HSP (22.5%). SPG7 and SPG10 were the second genetic cause (12.5%). Other genotypes were rarer (SPG3A, SPG11, SPG12, SPG17, SPG31, SPG84, CCDC88C, ANO5). Disease severity correlated with disease duration. The average duration of illness was 19.5 ± 16.3 years. The average disease duration before loss of the ability to walk independently was of 18.9 ± 18.3 years. Earlier onset (<25 years) was associate with longer diagnostic delay. SPRS baseline was available for 28 patients and reliably reflected disease severity. Follow-up (25) not showing minimal changes in an average follow-up of 6.1 months.
Conclusion: HSP has slowly progressive course. SPRS reliably reflects disease severity although it is unable to detect small differences within a short follow-up period. A future prospective study will confirm this baseline data on disease course over a long period.
Disclosure: The authors declare no conflicts of interest.

EPR-177 | Neurological manifestation and genetics of phacomatoses: A retrospective study from University of Pisa

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Background and Aims: This study aimed to assess neurological presentations and genetic characterization in patients with phacomatoses at our adult neurological center.
Methods: This retrospective study examined a cohort of 40 patients (40% male, mean age 46, 3 years) clinically suspected or with a molecular diagnosis of Tuberous Sclerosis Complex (TSC) or Neurofibromatosis (NF). Genetic testing was performed using single gene or panel next-generation sequencing and Multiplex ligation-dependent probe amplification from DNA extracted from blood. Clinical and neuroradiological data were collected from the patient's medical records.
Results: Neurological symptoms were present in 50% of patients, with epilepsy (35%), pediatric intellectual/learning disability (25%), headache (20%), and adult mood disorders (10%) being the most common ones. A neuroradiological central nervous system involvement was present in 19/32 confirmed or suspected NF/Schwannomatosis and 7/7 confirmed or suspected TSC. Molecular diagnosis was established in 29 cases. Mutations in NF1, NF2, TSC1, TSC2, and LZTR1 led to molecular diagnosis of NFI (20), NFII (3), TSC1 (3), TSC2 (2) and Schwannomatosis (1). For NF1 mutations, single nucleotide variants were most common (70%).

Conclusion: Phacomatoses, complex genetic diseases with common neurological involvement, require a profound understanding for timely diagnosis and optimized management, especially considering the prevalence of NFI and the recent approval of drugs for TSC-associated manifestations. To enhance our initial findings next steps might include, in addition to expanding the cohort size and thoroughly examining non-neurological aspects, investigating correlations such as genotype-phenotype and phenotype-diagnostic yield.
Disclosure: No conflict of interests to declare.

EPR-178 | The prevalence of pathogenic and likely pathogenic CSF1R variants in the UK Biobank

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Background and Aims: CSF1R-related adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) is an autosomal dominant inherited white matter disorder, leading to a variable combination of dementia, movement disorders, upper motor neuron signs and ataxia. Though increasingly recognized, the true prevalence of CSF1R-related ALSP is unknown.
Methods: Pathogenic and likely pathogenic CSF1R variants (as classified by American College of Medical Genetics criteria) were identified in UK Biobank whole-exome sequencing data ($N = 470{,}000$). Available demographic and phenotypic data were also extracted and analysed to identify clinical manifestation of a disease state.
Results: We identified 18 unique CSF1R pathogenic variants present across 25 subjects (giving a prevalence of ~1 in 18,800), and 44 unique likely pathogenic mutations across 107 subjects (~1 in 4,400) – with a combined prevalence is 132 (~1 in 3,500). Individuals carrying a pathogenic CSF1R variant were significantly more likely to have a psychiatric diagnosis or a diagnosis of Parkinson's disease.
Conclusion: Pathogenic and likely pathogenic CSF1R variants are more common in the UK Biobank population than previously anticipated. Available clinical data points to possible clinical manifestation of the disease in those carrying pathogenic variants, and suggests that ALSP may be significantly underrecognized as a disease entity.
Disclosure: Nothing to disclose.

EPR-179 | Whole Exome Sequencing of 126 patients highlights variants in candidate genes associated with FSHD

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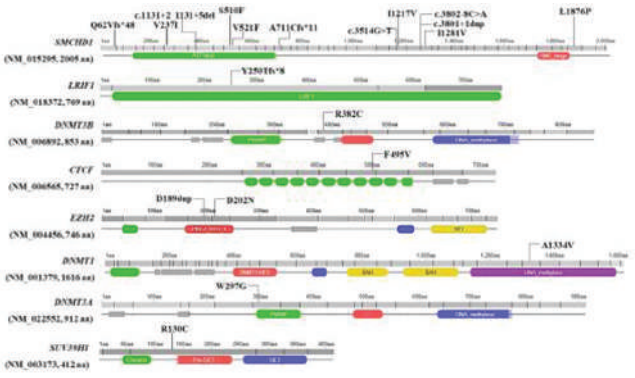
Background and Aims: Despite the progress made in the study of FSHD, the wide heterogeneity of disease complicates its diagnosis and the genotype-phenotype correlation. The present work employed Whole Exome Sequencing (WES) to investigate known and unknown genetic contributors that may be involved in FSHD and represent potential disease modifiers, even in presence of a D4Z4 Reduced Allele (DRA).
Methods: The study involved 126 patients with clinical signs of FSHD, which were characterized by D4Z4 sizing, methylation analysis, WES and segregation analysis. In-house protocols were employed for D4Z4 sizing and methylation analysis, whereas the Illumina® Next-Seq 550 system was utilized for WES.
Results: The WES data analysis highlighted 20 relevant variants (Figure 1), among which 14 were located in known genetic modifiers (SMCHD1, DNMT3B and LRIF1) and 6 in novel genes (CTCF, DNMT1, DNMT3A, EZH2 and SUV39H1) implicated in the DUX4-repressive machinery (Figure 2). Most of them were found together with a permissive short (4-7 RU) or borderline/long DRA (8–20 RU). The segregation and methylation analysis among family members, together with clinical findings, provided a more comprehensive picture of patients.



The variants identified in genes known to cause FSHD (SMCHD1, DNMT3B and LRIFI1) and candidate genes (CTCF, DNMT1, DNMT3A, EZH2 and SUV39H1).

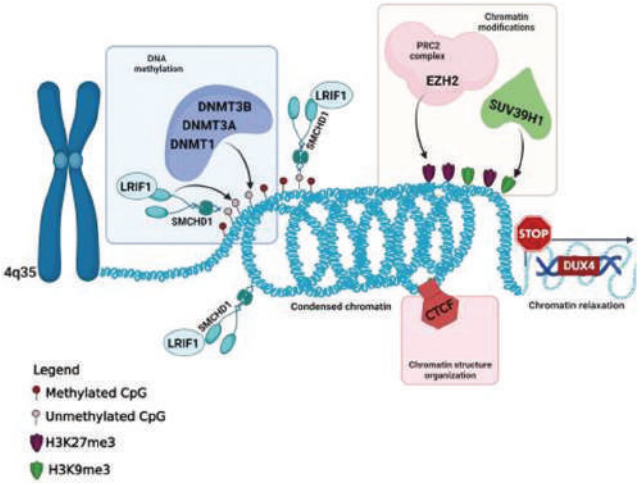


Illustration of the genes harboring the variants identified in FSHD patients and their role in the DUX4-repressive machinery.

Conclusion: Our results support FSHD as a genetically complex disease, in which variations in known and candidate genes could influence the phenotype, penetrance and severity of disease among patients as well as within the same family. Our results further emphasize the importance of extending the analysis of molecular findings within the proband's family, with the purpose of providing a broader framework for understanding single cases and allowing finer genotype-phenotype correlations in FSHD-affected families.

Disclosure: None.

EPR-180 | Validation of a machine learning tool for identifying FSHD patients: A one-year follow-up study

D. Megalizzi[1]; R. Cascella[2]; G. Trastulli[1]; L. Colantoni[3]; E. Proietti Piorgo[3]; M. Monforte[4]; G. Tasca[5]; E. Ricci[6]; C. Caltagirone[7]; C. Strafella[3]; E. Giardina[1]

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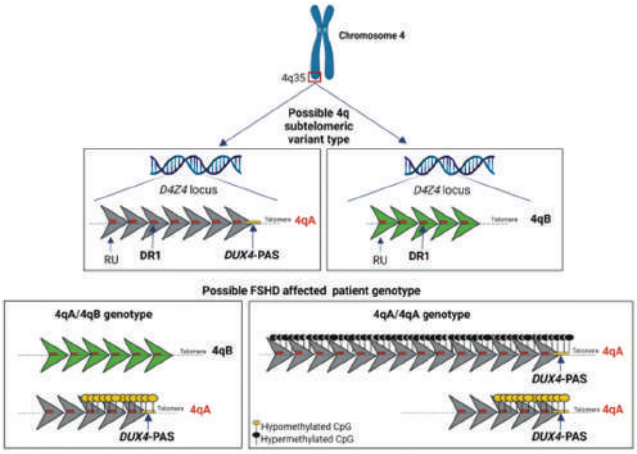
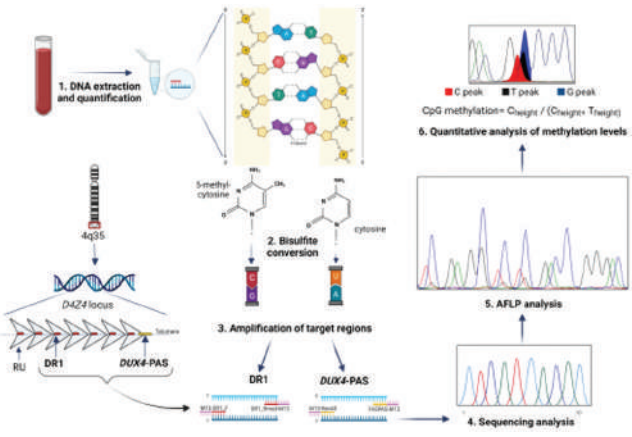
Background and Aims: Facio-Scapulo-Humeral Dystrophy (FSHD) is a myopathy characterized by the loss of repressive epigenetic features affecting the D4Z4 locus (4q35) (Figure 1). The study aimed at validating a machine learning (ML) pipeline for discriminating FSHD subjects according to the DNA methylation profile of D4Z4.



4q35 D4Z4 locus, permissive 4qA allele and epigenetic landscape of FSHD.

Methods: 251 subjects with clinical signs of FSHD sent to our center during 2022–2023 were analyzed. The recruited subjects were tested for the 4q subtelomeric variant by means of specific PCR. Subjects carrying at least a 4qA allele underwent methylation levels analysis of two D4Z4 regions (Figure 2). The identification of methylation profiles compatible with FSHD was performed by running a ML algorithm based on methylation levels. The presence of a short D4Z4 allele and/or of pathogenic variants in FSHD genes was simultaneously evaluated.



D4Z4 methylation analysis workflow.

Results: Among the 251 subjects, the 4q variant type distribution was 41% 4qA/4qA, 51% 4qA/4qB and 8% 4qB/4qB. Of the 232 carriers of at least a 4qA allele, the ML model predicted 122 subjects as FSHD in line with the reduced methylation levels compatible with the disease. The remaining 110 subjects were predicted as non-FSHD and showed high methylation levels. By comparing the results of D4Z4 allele sizing, for 122 hypomethylated subjects the FSHD prediction was fully concordant with the presence of FSHD genetic signatures. Among the 110 subjects classified as non-FSHD, 85 were concordant with the absence of FSHD genetic alterations and 25 subjects displayed borderline methylation levels.

Conclusion: The present method emerges as a powerful tool to be implemented into the FSHD diagnostic practice.

Disclosure: Nothing to disclose.

EPR-181 | Predictors of survival in Friedreich's Ataxia: A prospective cohort study

E. Indelicato[1]; K. Reetz[2]; W. Nachbauer[1]; M. Amprosi[1]; P. Giunti[3]; C. Mariotti[4]; L. Nanetti[4]; A. Durr[5]; F. de Rivera Garrido[6]; T. Klopstock[7]; L. Schöls[8]; T. Klockgether[9]; K. Bürk[10]; M. Pandolfo[11]; J. Schulz[2]; H. Ulmer[12]; W. Dichtl[13]; S. Boesch[1]

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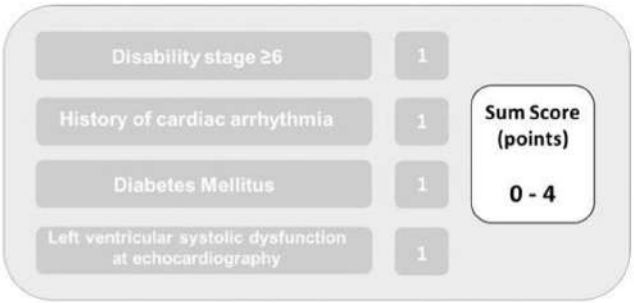
Background and Aims: Friedreich's ataxia (FA) is a rare multisystemic disorder which can cause premature death. We investigated predictors of survival in FA within a prospective registry established by the EFACTS (European Friedreich's Ataxia Consortium for Translational Studies, ClinicalTrials.gov Identifier NCT02069509).

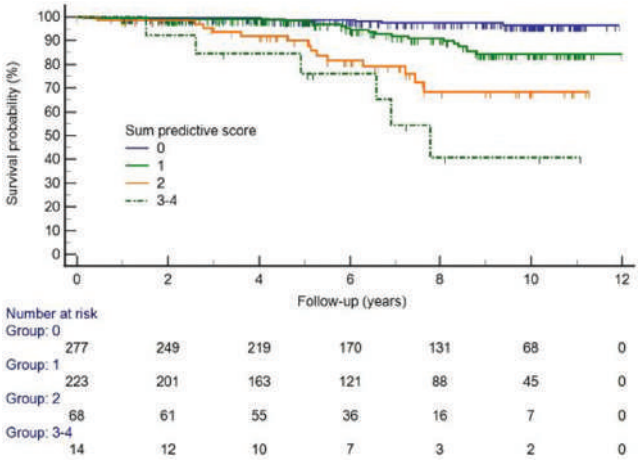
Methods: We enrolled genetically confirmed FA patients at 11 tertiary centres and followed them in yearly intervals. We investigated overall survival applying the Kaplan-Meier method, life-tables and log-rank test. We explored prognostic factors applying Cox proportional hazards regression and subsequently built a risk score which was assessed for discrimination and calibration performance.

Results: Between September 2010 and March 2017, we enrolled 631 FA patients. Median age at inclusion was 31 years (range 6–76). Until December 2022, 44 patients died and 119 terminated the study for other reasons. The 10-year cumulative survival rate was 87%. In a multivariable analysis, the disability stage (hazard ratio [HR] 1.51; 95% CI 1.08–2.12, $p=0.02$), history of arrhythmic disorder (HR 2.93; 95% CI 1.34–6.39, $p=0.007$) and diabetes mellitus (HR 2.31; 95% CI 1.05–5.10, $p=0.04$) were independent predictors of survival. GAA-repeat lengths did not improve the survival model. A risk score built on the previously described factors plus the presence of left ventricular systolic dysfunction at echocardiography enabled to distinguish four trajectories to prognosticate up to 10-year survival (log-rank test $p<0.001$).



Sum score	10-years cumulative survival rate	95% CI
0	96·4%	93·4%-99·4%
1	84·3%	77·4%-91·3%
2	69·6%	55·4%-83·8%
≥3	42·4%	10·7%-74·1%

EFACTS Survival Predictive Score (EFACTS-SPS).



Survival rates in the EFACTS cohort according to the developed prognostic score.

Conclusion: Arrhythmias, progressive neurological disability, and diabetes mellitus influence the overall survival in Friedreich's Ataxia. We built a survival prognostic score which identifies patients deserving closer surveillance and who may benefit from early invasive cardiac monitoring and therapy.

Disclosure: Nothing to disclose.

EPR-182 | Identifying p.P102L-associated Gerstmann-Sträussler-Scheinker syndrome phenotypes using machine learning clustering

E. Minerva[1]; A. Canosa[1]; S. Callegaro[1]; L. Tavaglione[1]; R. Vasta[1]; U. Manera[1]; M. Grassano[1]; F. Palumbo[1]; S. Cabras[1]; E. Matteoni[1]; F. De Mattei[1]; F. Di Pede[1]; G. Zocco[1]; G. Pellegrino[1]; C. Moglia[1]; A. Calvo[1]; A. Brusco[2]; D. Imperiale[3]; S. Gallone[4]; A. Chiò[1]

[1]*ALS Centre, "Rita Levi Montalcini" Department of Neuroscience, University of Turin, Turin, Italy*; [2]*Medical Genetics Unit, "Rita Levi Montalcini" Department of Neuroscience, University of Turin, Turin, Italy*; [3]*Neurology Unit, Prion Disease Regional Center, Maria Vittoria Hospital, Turin, Italy*; [4]*Neurogenetic Unit, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Turin, Italy*

Background and Aims: Gerstmann-Sträussler-Scheinker disease (GSS) is the second most common inherited prion disease, often associated with the PRNP variant p.P102L. Addressing its significant clinical heterogeneity, we proposed a new onset-based phenotypic classification, aiming at supporting diagnostic and prognostic assessments.

Methods: Clinical data from patients with confirmed p.P102L GSS, spanning 1987–2022, were collected from two Neurology Centres in Turin (Italy). Then we reviewed the literature for cases with p.P102L GSS. Original and literature cases were merged and a k-means clustering based on age and symptoms at onset was performed to define phenotypic groups, which were analysed for significant differences in clinical features and codon 129 polymorphism (Met/Val).

Results: We collected 253 patients (10 original cases + 243 literature cases), uncovering ataxia as the predominant onset symptom, followed by cognitive impairment. Codon 129 polymorphism (Met/Val) exhibited significant associations with age of onset and disease duration. K-means clustering resulted in four distinct groups: "Early onset and long survival", "Cognitive impairment and rapid progression" mimicking classic Creutzfeldt–Jakob disease, "Late onset with classic phenotype", and "Sensory/Motor onset".

Conclusion: Our findings confirm the phenotypic heterogeneity of p.P102L GSS, even within the same pedigree. This study, encompassing the largest cohort of Italian patients and the most extensive literature review assessed so far, identified four distinct clinical phenotypes that appear meaningful for the diagnostic approach and the prognostic evaluation of GSS. Preliminary data hint at a potential role of sex and codon 129 polymorphism in GSS phenotypic variability.

Disclosure: Nothing to disclosure.

EPR-183 | Neurological features of Gaucher's disease: A multicenter longitudinal study

M. Percetti[1]; E. Monfrini[2]; G. Franco[3]; I. Trezzi[3]; M. Malaguti[4]; F. Cavalieri[5]; F. Valzania[5]; G. Cossu[6]; S. Ramat[7]; A. Govoni[7]; C. Comi[8]; A. Tessitore[9]; R. De Micco[9]; A. Barbato[10]; P. Tirelli[11]; F. Spagnolo[12]; M. Cappellini[13]; E. Cassinerio[13]; I. Motta[13]; N. Scaramellini[13]; F. Carubbi[14]; F. Nascimbeni[15]; L. Borin[16]; F. Giona[17]; A. Di Fonzo[3]

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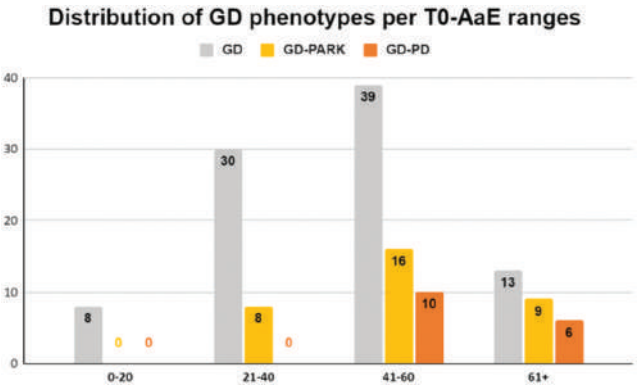
Hospital, Monza, Italy; [17]Department of Translational and Precision Medicine, Sapienza University, Rome, Italy

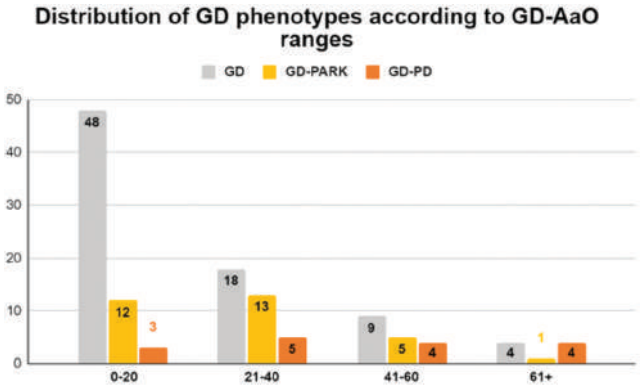
Background and Aims: Gaucher's disease (GD) is a lysosomal storage disorder caused by biallelic GBA1 mutations. GBA1 mutations are the major genetic risk factor for Parkinson's disease (PD) and dementia with Lewy bodies (DLB). The aim of the study was to investigate the prevalence of motor and non-motor clinical features of PD in a cohort of GD patients, and to identify possible predictors of phenoconversion to PD or DLB.

Methods: GD patients consecutively underwent neurological examination at baseline (T0) and after five years (T1) by movement disorders specialists. Patients with at least two non-motor symptoms or one motor and non-motor symptom were classified as patients with parkinsonian syndrome (GD-PARK).

Results: 147 GD patients were evaluated with a mean T0 age-at-examination (T0-AaE) was 47.3 ±15.9 y. 16 patients (10.9%) were diagnosed with PD with a mean age-at-onset (AaO) of 55.6 ±12.5 y. The occurrence of PD was higher according to AaE ($p=0.026$) and AaO of GD ($p=0.006$). The PD-AaO positively correlated with T0-AaE ($p=0.002$), GD-AaO ($p=0.001$), and age-at-GD therapy ($p=0.005$). 33 patients (22.4%) were classified as GD-PARK, displaying a higher burden of non-motor symptoms than GD patients ($p=0.006$). A subgroup of 32 patients (21.8%) underwent a second evaluation, where three patients phenoconverted to PD, six to DLB. Only urinary urgency resulted more frequent in phenoconverted patients ($p=0.049$).



Distribution of Gaucher's disease (GD) phenotypes according to ranges of age-at-examination at baseline (T0-AaE). GD-PARK = GD patients with parkinsonian syndrome; GD-PD = GD patients with diagnosis of Parkinson's disease (PD).



Distribution of Gaucher's disease (GD) phenotypes according to ranges of age-at-onset of GD (GD-AaO). GD-PARK = GD patients with parkinsonian syndrome; GD-PD = GD patients with diagnosis of Parkinson's disease (PD).

Conclusion: A high portion of GD patients display motor and, more frequently, non-motor symptoms of PD. This study highlights the potentialities of studying the GD population to identify specific biomarkers defining the prodromal phase and risk of conversion to PD.

Disclosure: Nothing to disclose.

Epilepsy 2

EPR-184 | Relation between SEEG parameters and tau pathology in patients with pharmacoresistant TLE

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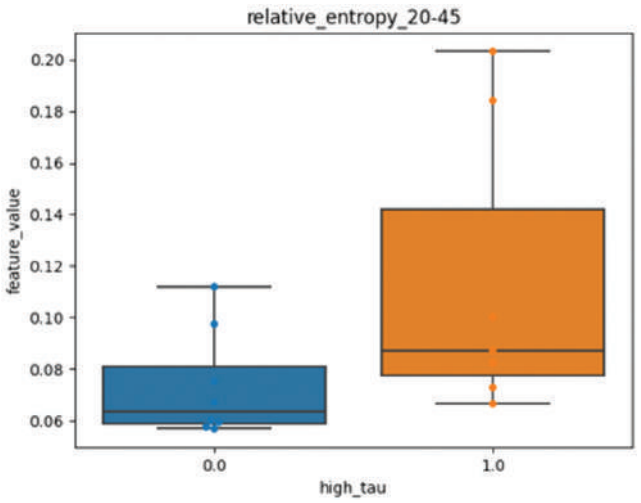
Background and Aims: This study explores the association between hyperphosphorylated tau, commonly linked with neurodegenerative disorders like Alzheimer's, and temporal lobe epilepsy (TLE). TLE is the most prevalent form of pharmacoresistant epilepsy that profoundly affects patients' daily lives. The burden of tau pathology observed in the temporal lobe of young TLE patients is much bigger in comparison with the general population (Thom et al., 2011).

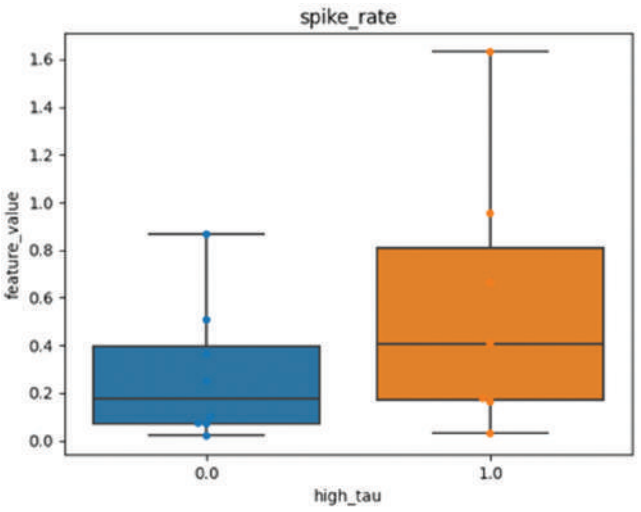
Methods: This study is focused on 15 patients who underwent anterior-mesial temporal resection between 2005 and 2022 for pharmacoresistant TLE with hippocampal sclerosis. It investigates the correlation between tau pathology and electrophysiological parameters in preoperative stereoelectroencephalography (SEEG) recordings. According to the immunohistochemically analysed resection samples were patients categorized into high ($n=8$) and low ($n=7$) tau burden groups.

Results: Although not statistically significant due to the sample size, patients with high tau burden displayed trends of increased spike count ($p=0.29$, medium effect size) and decreased functional

connectivity (higher relative entropy, $p = 0.07$, large effect size) compared to the low tau burden group.



Relative entropy



Spike rate

Conclusion: This study suggests a potential link between tau pathology and electrophysiological parameters in pharmacoresistant epilepsy, offering insights into epileptogenic mechanisms. Further validation on a larger sample size could aid in identifying patients at a higher risk of relapse post-epilepsy surgery and those prone to post-operative cognitive dysfunction. Additionally, it raises the prospect of targeting neurodegenerative proteins as therapeutic interventions and identifying novel prognostic biomarkers for personalized epilepsy care.

Disclosure: This work was supported by the project nr. LX22NPO5107 (MEYS): Financed by EU – Next Generation EU, and by the Ministry of Health of the Czechia, grant nr. NU22-04-00366.

EPR-185 | Poststroke epilepsy after mechanical thrombectomy: Voxel-based lesion symptom mapping

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Background and Aims: Poststroke epilepsy (PSE) is an important complication of stroke. Data regarding the predictors of PSE in patients with large-vessel occlusion stroke receiving mechanical thrombectomy (MT) are scarce. Voxel-based lesion symptom mapping on MRI might be a valuable tool in risk prediction of PSE. This study aims to assess PSE risk after acute stroke treated with MT via voxel- and volumetric-based analyses.

Methods: In this bi-center study from two large tertiary stroke centers, we included stroke patients who had received MT between 2011 and 2017 and available post-interventional brain MRI as well as long-term-follow-up data. Lesion symptom mapping was done with FLAIR (Fluid Attenuated Inversion Recovery) scans. All lesion masks were registered to a FLAIR group template using FLIRT (FMRIB's Linear Image Registration Tool). Lesion symptom mapping was applied using the NiiStat software, with MATLAB. The analysis was confined to voxels showing a lesion overlap in at least 10 patients. Statistical significance was set at $p < 0.05$ corrected for familywise error.

Results: We analyzed 348 patients (median age: 67 years, 45% women) with follow-up of median 76 months. 32 patients (9.2%) developed PSE. Finally, lesion maps from 281 patients were considered for lesion symptom mapping including 28 patients with PSE. Analyses identified the area tempestas, the temporal pole and the precentral area independently related to PSE risk.

Conclusion: In our study, patients with large vessel occlusion stroke receiving MT showed an increased risk of developing PSE with infarction in the area tempestas, the temporal pole and the precentral area.

Disclosure: None related to this study.

EPR-186 | Efficacy of adjunctive cenobamate for patients with different epilepsy aetiologies: Results of an open-label study

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[1]Fundación Jiménez Díaz University Hospital, Madrid, Spain; [2]Epilepsy Diagnostic and Therapeutic Centre, Foundation of Epileptology, Warsaw, Poland; [3]Angelini Pharma España, Madrid, Spain; [4]Global Medical Department, Angelini Pharma S.p.A, Rome, Italy; [5]MeDaStats LLC, Tampa, FL, USA; [6]Bethel Epilepsy Centre, Mara Hospital, Bielefeld, Germany

Background and Aims: The aetiology of epilepsy can be a prognostic predictor for seizure recurrence. An open-label extension (OLE) of the international, double-blind, placebo-controlled clinical trial C017 (NCT01866111) evaluated long-term efficacy and safety of adjunctive cenobamate. This post-hoc analysis assessed cenobamate efficacy in different types of epilepsies.

Methods: The modified intent-to-treat population included 354 adults who completed the double-blind phase and entered the OLE. They were grouped according to 1 or more of the following definite or possible specific epilepsy aetiologies: viral/bacterial/parasitic infection; traumatic brain injury; stroke/intraventricular haemorrhage; hypoxic-ischemic encephalopathy; genetic/chromosomal developmental encephalopathies; cortical malformations; mesial temporal sclerosis; and other aetiologies (metabolic/toxic insults, neurocutaneous syndromes, inborn errors of metabolism, neoplasia, dementia, and other degenerative neurologic disease). Comparison of baseline and post-baseline seizure frequency (percentage reduction) in each group was conducted.

Results: The median baseline seizure frequency per 28 days ranged from 6 (traumatic brain injury) to 11.5 (cortical malformation/brain development). Median disease duration ranged from 17.3 years (viral/bacterial/parasitic infection) to 27 years (intraventricular haemorrhage/stroke). Long-term responders (≥50% seizure reduction) for the 5-year analyses were: viral/bacterial/parasitic infection, 60.7% (17/28); traumatic brain injury, 58.5% (24/41); stroke/intraventricular haemorrhage, 60.0% (9/15); hypoxic-ischemic encephalopathy, 73.3% (11/15); mesial temporal sclerosis, 64.7% (22/34); other aetiologies 59.1% (13/22); cortical malformation/brain development, 42.3% (30/71); and 69.7% of patients who had an unknown classification (122/175).

Conclusion: This post-hoc analysis further supports the efficacy of cenobamate by demonstrating a sustained response in patients with different epilepsy aetiologies.

Disclosure: The original study C017 (NCT01866111) was supported by SK Life Science, Inc. (Paramus, NJ, USA) and these analyses were supported by Angelini Pharma S.p.A. (Rome, Italy). JMS: Consultant/advisor: Angelini, BIAL, Eisai, GW Pharmaceuticals, Jazz, UCB Pharma; Speaker: Angelini, BIAL, Eisai, Krka, UCB Pharma. BMZ: Consultant/advisor: Angelini, UCB Pharma; Speaker: Adamed, Sanofi, Angelini, UCB Pharma. EAB: Employee of Angelini Pharma S.p.A. JPL: Employee of Angelini Pharma S.p.A. KT: Consultant: Angelini Pharma S.p.A. CB: Consultant/advisor: Angelini, Eisai, GW Pharmaceuticals, Jazz, Johnson & Johnson, Marinus, UCB Pharma, Xenon; Speaker: Angelini, Eisai, UCB Pharma.

EPR-187 | EEG signal analysis as a clinical trajectory biomarker in brain glioma patients: Preliminary data

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Background and Aims: Gliomas are the most common primary tumor of the CNS parenchyma in adults, often with a poor prognosis. Brain-tumor-related epilepsy (BTRE) is a cause of high morbility and mortality in these patients. The aim of the study is to explore the prognostic power of EEG's qualitative and quantitative features.

Methods: Patients affected by brain glioma that underwent brain surgery (gross tumor resection) and at least one EEG after the surgery were enrolled at the IRCSS Ospedale Policlinico San Martino. Qualitative (slow and epileptiform abnormalities) and quantitative (spectra power and mean frequencies, at lesional and lobar level) EEG features in the lesionectomy zone were compared between patients with and without seizures after surgery, and between patients with and without tumor recurrence.

Results: 81 patients (52 males, mean age 54.40 yo, 53 glioblastoma multiforme, 19 astrocytoma, 9 oligodendroglioma) were enrolled. At qualitative analysis, slow abnormalities in post-surgical EEG were more frequent in patients having seizures after surgery ($p = 0.045$).

Quantitative analysis showed that in post-surgical EEGs, the alpha power spectrum at lesionectomy was lower in patients having seizures after surgery ($p=0.046$). Moreover, in pre-surgical EEGs, the delta spectrum at lesion level was lower in patients with tumor recurrence ($p=0.019$).

Conclusion: EEG may be a predictive-prognostic tool for seizure recurrence and for progression free survival, proving clues about the clinical trajectory in glioma patients. In particular, focal slowing and alpha power reduction was associated with seizures. Larger data are needed to confirm these preliminary results.

Disclosure: Nothing to disclose.

EPR-188 | Interim European outcomes for patients enrolled in the CORE-VNS registry

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Background and Aims: The Comprehensive Outcomes Registry in Subjects with Epilepsy Treated with Vagus Nerve Stimulation (VNS) Therapy (CORE-VNS) is an ongoing prospective study in patients with drug-resistant epilepsy (DRE) in a real-world setting.

Methods: DRE patients receiving implantable VNS (new or replacement) were eligible for participation in the CORE-VNS. Seizure frequency (SF), maximum SF free periods, seizure severity, post-ictal severity, changes in quality of life and sleep, anti-epileptic drug and rescue drug use, and seizure-related hospital and emergency department visits were evaluated at baseline and at 3, 6, 12, 24 and 36 months. Interim results for the European cohort are presented.

Results: Across Europe, a total of 341 subjects signed informed consent with 327 included in the modified safety population across 6 different countries. The mean age at consent was 24.9 years and epilepsy types include combined (30.1%), focal (54%), and generalized (14.2%). Sixty-seven percent of subjects were naïve to VNS Therapy (43% < 18 years of age and 53.1% female). The responder rate (percent of subjects with >50% reduction in seizures) for subjects reporting at 24 months was 74.1% (all seizures). A median percent reduction in SF was 79.2% with a median seizure count of 9 (all seizures).

Age at Informed Consent (Years)	First Implant N=226	Re-Implant N=100	Total (N=338)
Mean (SD)	24.9 (17.2)	33.7 (16.1)	27.6 (17.3)
Median	21	31	25.5
Min, Max	1, 71	11, 73	1, 73
< 4 years (%)	15 (6.6%)	0 (0.0%)	15 (4.4%)
4 - 11 years (%)	46 (20.4%)	4 (4%)	52 (15.4%)
12 - <18 years (%)	37 (16.4%)	12 (12%)	50 (14.8%)
≥ 18 years (%)	128 (56.6%)	84 (84%)	221 (65.4%)
Female	120 (53.1%)	43 (43%)	170 (50.3%)
Male	106 (46.9%)	57 (57%)	168 (49.7%)

Demographics

Conclusion: At the 24-month visit, 74.1% of subjects reporting had experienced more than 50% SF reduction and nearly 60% had experienced >80% SF reduction.

Disclosure: AS is a primary investigator in the CORE-VNS prospective registry. MD is an employee of LivaNova PLC.

EPR-189 | Risk of post-stroke epilepsy following revascularization therapies: A 7-years single-center observational study

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Background and Aims: To date, the incidence and risk factors for Post-Stroke Epilepsy (PSE) in patients receiving revascularization therapies have not yet been completely assessed.

Methods: Observational, single-center, retrospective study of prospectively acquired data in consecutive patients admitted to the Stroke Unit of Modena Academic Hospital (Italy) who received revascularization therapies (intravenous thrombolysis [IVT] and/or endovascular thrombectomy [EVT]) for first ever acute ischemic stroke from January 1st 2014 to December 31st 2021. Early (ES) and late (LS) post-stroke seizures were classified according to the ILAE definitions. The incidence of LS was assessed through a survival analysis, while a Cox regression model was used to identify outcome predictors.

Results: 1094 patients were included, 665 (61%) and 169 (15%) of whom were treated with IVT or EVT, respectively. In 260 cases, both treatments were performed. Overall, 28 patients (3%) developed ES, whereas LS occurred in 66 patients (6%). The highest risk of LS was observed within 12 months after stroke (3.1%) (mean follow-up: 53 months). Cortical involvement (HR 3.2 95% CI 1.6–6.6; $p = <0.01$) and NIHSS values at discharge suggestive of moderate (NIHSS 4–10)

(HR 3.2 95% CI 1.6–6.6; $p = <0.01$) or severe stroke (NIHSS ≥ 11) (HR 5.4, 95% CI 1.02–18.6; $p < 0.01$) were independently associated to the development of LS.

Conclusion: In our cohort of stroke patients receiving revascularization therapies the risk of LS was low. Cortical involvement and stroke severity (NIHSS score after treatment) were independently associated with the onset of LS.

Disclosure: Nothing to disclose.

EPR-190 | Theta burst transcranial magnetic stimulation in patients with generalized epilepsy: A TBS-hdEEG paradigm approach

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Background and Aims: Transcranial theta burst magnetic stimulation (TBS) coupled with high-density electroencephalography (hd-EEG) is a continuously developing area of research with promising clinical application in the management of epilepsy patients. It aims to explore how targeted magnetic stimulation impacts neural networks and potential mechanisms of seizure control.

Methods: We hypothesized that multifocal cTBS could improve clinical outcomes compared to baseline by reducing seizure frequency/days, severity of seizures; improve quality of life with few adverse events. Patients received six cTBS stimulation sessions on consecutive days. Each session consisted of 3 cTBS trains with 10 min intertrain-interval. One cTBS train included 600 pulses delivered in bursts at theta frequency during 40s at 80% of RMT over Cz (covering bilateral motor cortices). Patients underwent follow-up assessments at 4, 8, and 12 weeks, spanning a 12-week period.

Results: Among fourteen enrolled generalized epilepsy patients, twelve completed the trial (age 33.1 ± 7.5; 10 females). Over 12 weeks, reduction of ≥50% compared to baseline in seizure frequency was achieved in 75% at 4 and 12 weeks ($p < 0.05$); seizure days 75% and 83.3% respectively ($p < 0.05$); seizure severity 66.6% and 75% ($p < 0.05$). Compared to baseline, changes in all clinical outcomes parameters were statistically significant during each follow-up visit ($p < 0.05$), nevertheless, inter-visit changes were not. A tendency towards the reduction of interictal EEG discharges and cortical excitability was observed. No significant adverse events were recorded.

Conclusion: Our research provides compelling evidence that novel cTBS-EEG approaches hold value in identifying meaningful biomarkers while simultaneously facilitating therapeutic improvements in generalized epilepsy patients.

Disclosure: Nothing to disclose.

EPR-191 | Abstract withdrawn

EPR-192 | Spikes, fast ripples and SEEG stimulated seizures: A common hyperexcitability mechanism?

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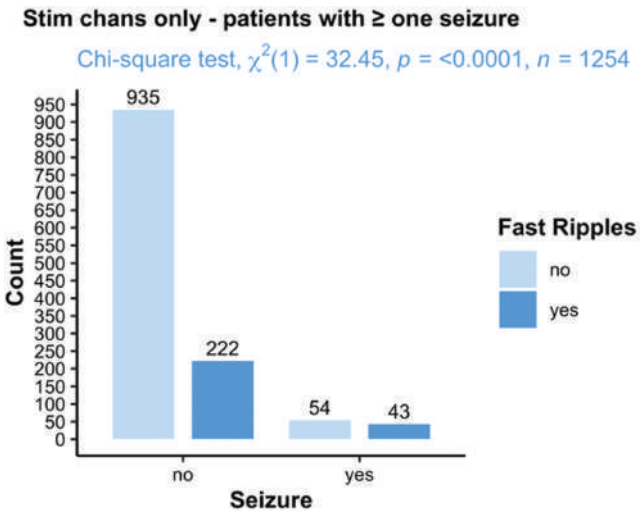
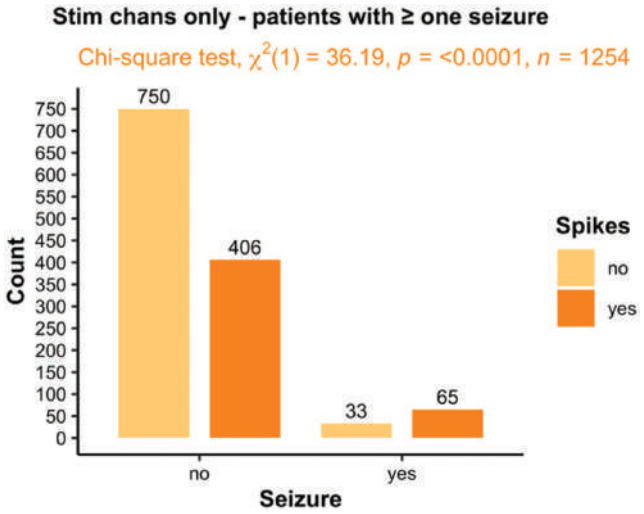
Background and Aims: Interictal spikes and High Frequency Oscillations are being studied as epileptogenicity/hyperexcitability biomarkers. We investigated the association between the presence of spikes and Fast Ripples (FR) during the interictal period and the probability of generating a seizure by stimulating a channel during the SEEG procedure.

Methods: We analyzed non-REM sleep SEEG recordings, sampled at 2048 Hz, of 49 patients, of whom 38 had at least one seizure during the SEEG stimulation procedure. We considered both stimulations by choc (1 Hz) and by train (50 Hz). FR (250–500 Hz) and spikes were automatically detected (Delphos detector). Channels were considered "spiky" or with a high rate of FR when above the 75° percentile after normalization. The statistical tests used are Chi-square and Wilcoxon test.

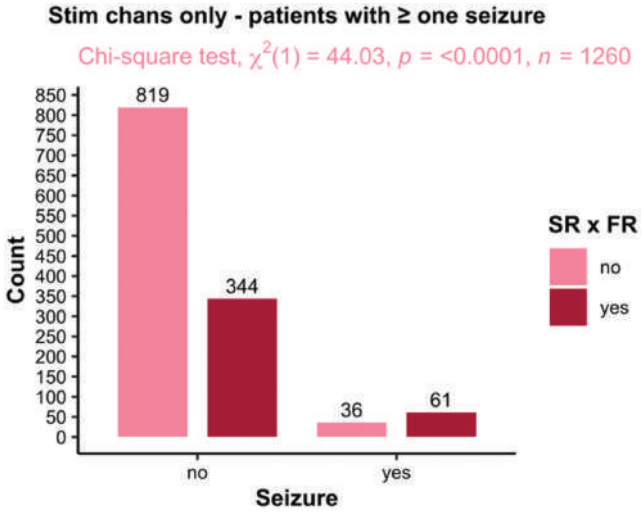
Results: In patients that experienced one or more seizures by stimulation, among the stimulated channels that generated a seizure: - 65% of channels were spiky, 33% were not (sensitivity 66.3%, specificity 64.9%). - 43% had FR, 54% did not (sensitivity 44.3%, specificity 80.8%). - 61% had spikes × FR, 35% did not (sensitivity 62.9%, specificity 70.4%). There is a statistically significant difference ($p = <0.0001$) in proportion of channels with spikes and with spikes × FR between the stimulations that generated a seizure and the ones that did not.



Seizures in stimulated channels with a high number of Fast Ripples.



Seizures in stimulated channels with a high number of spikes.



Seizures in stimulated channels with a high number of spikes × Fast Ripples.

Conclusion: Channels with a high rate of spikes and spikes × FR are more likely to generate a seizure if stimulated. These results can have a clinical utility: when trying to generate a seizure by stimulation (Trebuchon et al., 2020), it would be better to directly stimulate those channels.

Disclosure: Nothing to disclose.

Headache 2

EPR-193 | **Efficacy of atogepant in trial completers: A post hoc analysis of the 12-week ADVANCE and 52-week open-label trials**

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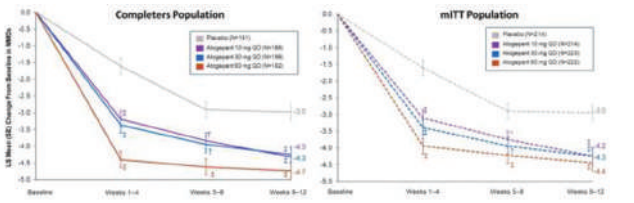
Background and Aims: Atogepant is an oral calcitonin gene–related peptide receptor antagonist approved for the preventive treatment of migraine in adults. This analysis evaluated efficacy of atogepant in participants who completed the ADVANCE or 52-week open-label trials.

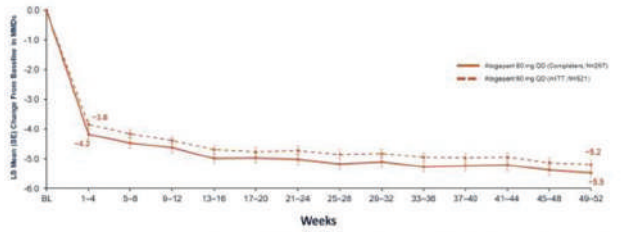
Methods: ADVANCE was a 12-week, double-blind, placebo-controlled trial that evaluated safety and efficacy of atogepant for preventive treatment of episodic migraine. A separate 52-week, open-label trial evaluated long-term safety and efficacy of atogepant. This analysis evaluated efficacy in participants who completed the trial with non-missing monthly migraine day (MMD) data for all visits. Change from baseline in MMDs and proportions of participants achieving ≥50% MMD decrease were evaluated.

Results: In ADVANCE, 765 participants completed the trial with non-missing MMD data (placebo: $n = 191$; atogepant 10 mg: $n = 186$; atogepant 30 mg: $n = 196$; atogepant 60 mg: $n = 192$). Among completers, similar decreases in MMDs compared with the mITT population were observed (Figure 1). A ≥50% decrease in MMDs was reported by 65.6% and 71.4% of atogepant 60 mg-treated completers at weeks 1–4 and 9–12, respectively. In the 52-week trial, 297 of 546 (54.4%) randomized atogepant 60 mg participants met completer criteria. LS mean changes in MMDs for completers were −4.2 during weeks 1–4 and −5.5 during weeks 49–52 (Figure 2). The proportions of completers who achieved ≥50% decrease in MMDs were 65.0% during weeks 1–4 and 84.5% during weeks 49–52 (Figure 3).



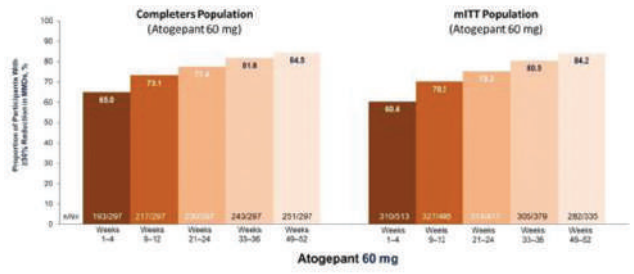
*P<0.05; †P<0.01; ‡P<0.001. Nominal P values were not tested in hierarchical order or adjusted for multiplicity.
LS = least squares; mITT = modified intent-to-treat; MMDs = monthly migraine days; QD = once daily; SE = standard error.

FIGURE 1. Changes in baseline in MMDs during the ADVANCE trial.



BL = baseline; LS = least squares; mITT = modified intent-to-treat; MMDs = monthly migraine day; QD = once daily; SE = standard error.

FIGURE 2. Changes in baseline in MMDs over time in the 52-week open-label trial.



mITT = modified intent-to-treat; MMDs = monthly migraine day.

FIGURE 3. Proportions of participants achieving ≥50% reduction in MMDs from baseline over time in the 52-week open-label trial.

Conclusion: Similar reductions in MMDs were observed with the 12- and 52-week trial completers and mITT populations, with the completer population demonstrating a trend towards greater reduction with atogepant over time.

Disclosure: This study was supported by AbbVie.

EPR-194 | Real-world effectiveness of switching to fremanezumab from other CGRP pathway mAbs: PEARL study 4th interim analysis

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Background and Aims: According to the European Headache Federation guidelines for preventive migraine therapy use, switching from one monoclonal antibody (mAb) targeting the calcitonin gene-related peptide (CGRP) pathway to another may be beneficial in patients who experience adverse events or inadequate response; however, long-term, prospective effectiveness data supporting this approach are limited.

Methods: PEARL (EUPAS35111) is an observational, Phase 4 study evaluating the effectiveness of fremanezumab in adults with episodic or chronic migraine (EM, CM). The fourth interim analysis was conducted when all enrolled participants had completed ≥12 months of treatment. This sub-analysis explored reductions in monthly migraine days (MMD) in participants who switched to fremanezumab from another CGRP pathway mAb.

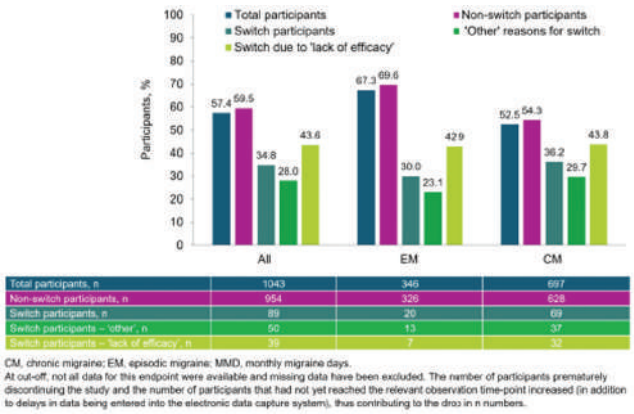
Results: Of 96 switch participants enrolled at baseline, 89 had data for full analysis (Table 1). During the first 6 months of treatment, 31 switch participants (34.8%) achieved ≥50% MMD reduction from baseline. Responses were numerically higher in participants who switched due to lack of efficacy than for 'other' reasons, while responses were similar for participants with EM and CM (Figure 1).

Over the same time period, 40 switch participants with CM (58.0%) achieved ≥30% MMD reduction. Mean change from baseline in MMD remained consistent through months 1 to 15 (Figure 2) in the switch cohort.

TABLE 1. Previous CGRP pathway mAb use.

	Total participants (N = 89)	EM participants (n = 20)	CM participants (n = 69)
Reasons for switch*, n (%)			
Switch due to lack of efficacy	39 (43.8)	7 (35.0)	32 (46.4)
Switch due to reasons other than 'lack of efficacy'	50 (56.2)	13 (65.0)	37 (53.6)
Previous CGRP pathway mAb treatment, n (%)			
Galcanezumab only	1 (1.1)	0	1 (1.4)
Erenumab only	84 (94.4)	19 (95.0)	65 (94.2)
Galcanezumab and erenumab†	4 (4.5)	1 (5.0)	3 (4.3)
Mean duration of preventive therapy, months (SD)			
Galcanezumab	4.0 (1.8)	–	–
Erenumab	12.1 (11.4)	–	–

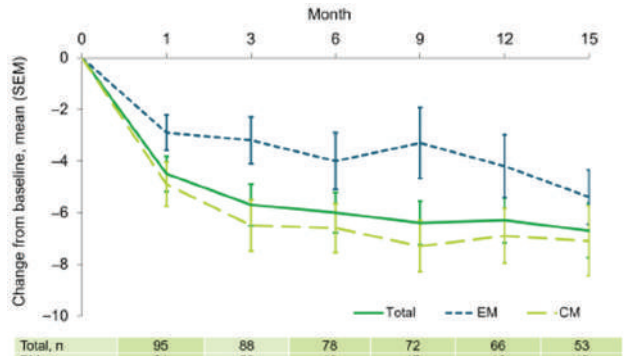
*As reported by the participant; †On separate occasions.
CGRP, calcitonin gene-related peptide; CM, chronic migraine; EM, episodic migraine; mAb, monoclonal antibody.



	All	EM	CM
Total participants, n	1043	346	697
Non-switch participants, n	954	326	628
Switch participants, n	89	20	69
Switch participants – 'other', n	50	13	37
Switch participants – 'lack of efficacy', n	39	7	32

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of participants prematurely discontinuing the study and the number of participants that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers.

FIGURE 1: Proportion of participants with ≥50% reduction from baseline in MMD during the 6 months after fremanezumab initiation, by migraine type.



Total, n	95	88	78	72	66	53
EM, n	21	20	18	17	16	13
CM, n	74	68	60	55	50	40

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days; SEM, standard error of the mean.
Not all participants had data available for each time point and missing data have been excluded. The number of participants prematurely discontinuing the study and the number of participants that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers.

FIGURE 2: Mean change from baseline in MMD in switch participants from Month 1 to Month 15, by migraine type.

Conclusion: This analysis demonstrates the long-term effectiveness of fremanezumab in participants who have not responded to, or tolerated, another CGRP pathway mAb for preventive migraine treatment. Switching to fremanezumab may therefore be a beneficial treatment option in this patient population.

Disclosure: Funded by Teva Pharmaceuticals.

EPR-195 | Real-world effectiveness of anti-CGRP monoclonal antibodies compared to OnabotulinumtoxinA (RAMO) in chronic migraine

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Background and Aims: Anti-CGRP mAbs and BoNT-A are the only treatment specifically approved for CM prophylaxis. Direct comparisons between the two treatments are not available, so far.

Methods: We performed an observational, retrospective, multicenter study to compare the real-world effectiveness of anti-CGRP mAbs and BoNT-A. Patients with CM having received either treatment according to Italian prescribing regulations were extracted form available clinical databases. Efficacy outcomes included the change from baseline in monthly headache days (MHD), Migraine disability assessment test (MIDAS), and migraine acute medications (MAM) evaluated at 6 and 12 months of follow- up. The primary outcome was MHD change from baseline at 12 months. Safety outcomes included serious adverse events (SAE) and treatment discontinuation.

Results: 216 potentially eligible patients were screened and 183 (86 anti-CGRP mAbs; 97 BoNT-A) were included. Anti-CGRP mAbs resulted in a significant reduction in MHD compared to BoNT-A at 12 months of follow-up. Anti-CGRP mAbs showed a significant MIDAS and MAM reduction compared to BoNT-A at 6 and 12 months. No SAE were reported. Treatment discontinuations, mainly for inefficacy, were comparable between the two treatments.

Conclusion: Anti-CGRP mAbs seemed more effective than BoNT-A with comparable safety.

Disclosure: Nothing to disclose.

EPR-196 | Impact of fremanezumab cessation and reinitiation in migraine management: PEARL study 4th interim analysis

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Background and Aims: Despite recent updates to the guidelines, some reimbursement authorities still mandate a pause in preventive treatment with calcitonin gene-related peptide (CGRP) pathway monoclonal antibodies (mAbs) after 1 year of continuous use. However, migraine symptoms frequently return following treatment cessation and treatment effectiveness can be reduced upon reinitiation.

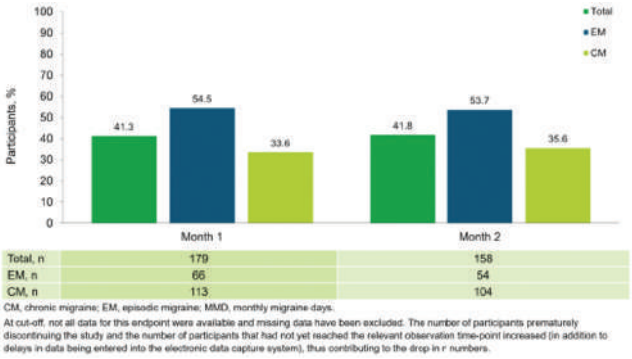
Methods: PEARL (EUPAS35111) is a Phase 4 study evaluating the real-world effectiveness of fremanezumab in adults with episodic or chronic migraine. The fourth interim analysis was conducted when all participants completed ≥12 months of treatment; this subanalysis explored the impact of fremanezumab cessation and reinitiation on monthly migraine days (MMD).

Results: Of 220 participants with documented cessation of fremanezumab, 98 stopped treatment for reimbursement, and 192 reinitiated after a mean (SD) period of 2.6 (2.0) months (Table 1). Over 40% of participants experienced worsening of migraine (≥50% increase in MMD) at Months 1 and 2 post-cessation (Figure 1). Mean MMD decreased after reinitiation but remained higher than before cessation (Figure 2). The proportion of participants achieving ≥50% reduction in MMD at Month 1 and Month 3, respectively, was 49.0% and 58.9% in the first treatment period (before cessation) versus 35.7% and 45.5% in the second treatment period (after reinitiation).

TABLE 1: Participants with documented cessation and reinitiation of fremanezumab.

	Total	EM participants	CM participants
Participants with documented cessations	n = 220	n = 83	n = 137
Time from first dose to cessation, months (SD)	11.2 (3.6)	11.6 (2.6)	10.9 (4.1)
Reason for cessation, n (%)			
Reimbursement	98 (44.5)	47 (56.6)	51 (37.2)
Improvement of migraine	18 (8.2)	5 (6.0)	13 (9.5)
Other	80 (36.4)	26 (31.3)	54 (39.4)
Participants with documented reinitiation	n = 192	n = 72	n = 120
Time from cessation to reinitiation, months (SD)	2.6 (2.0)	2.6 (1.9)	2.6 (2.1)
Reason for reinitiation of fremanezumab, n (%)			
Worsening of migraine	77 (40.1)	40 (55.6)	37 (30.8)
Improvement of AE	3 (1.6)	–	3 (2.5)
Other	112 (58.3)	32 (44.4)	80 (66.7)

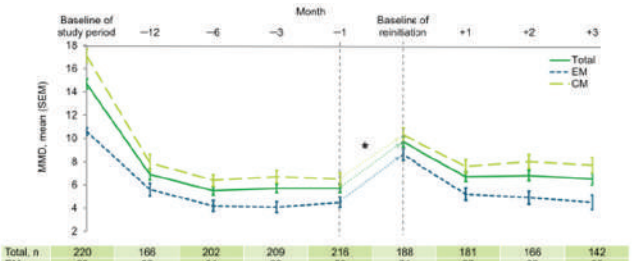
AE, adverse event; CM, chronic migraine; EM, episodic migraine; SD, standard deviation.



	Month 1	Month 2
Total, n	179	158
EM, n	66	54
CM, n	113	104

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
At cut-off, not all data for this endpoint were available and missing data have been excluded. The number of participants prematurely discontinuing the study and the number of participants that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n' numbers.

FIGURE 1: The proportion of participants with a ≥50% increase in MMD from the time of cessation to Month 1 and 2 after cessation.



Total, n	220	166	202	209	216	188	181	166	142
EM, n	83	67	81	82	83	71	67	63	55
CM, n	137	99	121	127	133	117	114	103	87

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days; SEM, standard error of the mean.
*Data for MMD during the cessation period are not captured in the graph. MMD at Month 1 following cessation of fremanezumab were 7.6, 6.8 and 8.0 for Total, EM and CM participants, respectively.
Not all participants had data available for each time point and missing data have been excluded. The number of participants prematurely discontinuing the study and the number of participants that had not yet reached the relevant observation time-point increased (in addition to delays in data being entered into the electronic data capture system), thus contributing to the drop in n numbers.

FIGURE 2: Mean MMD through the first treatment period up to 1 month prior to cessation and through the second treatment period from the baseline of reinitiation.

Conclusion: Post-fremanezumab cessation, a notable rise in MMD was observed, with reduced effectiveness upon reinitiation. This challenges the rationale behind mandated treatment pauses, underscoring the need for individualized patient management strategies.
Disclosure: This study was funded by Teva Pharmaceuticals.

EPR-197 | Number needed to treat and cost per responder analysis of anti-CGRP monoclonal antibodies for migraine prevention

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Background and Aims: Four monoclonal antibodies (mAbs) targeting calcitonin gene-related peptide (CGRP) are approved for migraine prevention, and they are commonly prescribed/reimbursed after failure of traditional oral medications. Patients achieving clinical response (e.g., ≥50% monthly migraine day [MMD] reduction) during an anti-CGRP mAb trial are likely to continue treatment. We compared number needed to treat (NNT) and quarterly cost per responder (CPR) across anti-CGRP mAbs.
Methods: Data were from randomized, double-blind, placebo-controlled phase 3b clinical trials that evaluated an anti-CGRP mAb (eptinezumab, erenumab, fremanezumab, or galcanezumab) for migraine prevention in adults with episodic or chronic migraine and 2–4 prior preventive treatment failures. NNT was calculated as 1 divided by absolute risk reduction (difference between active and placebo in proportion of patients with ≥50% MMD reduction over Weeks 1–12). CPR was calculated by multiplying NNT by the quarterly (3-month) drug acquisition cost per drug (2023 UK £).
Results: All anti-CGRP mAbs demonstrated higher rates of ≥50% MMD reduction over Weeks 1–12 than their respective placebos ($p < 0.05$; Figure 1). Corresponding NNTs were 3.4 with eptinezumab 100 mg, 6.3 with erenumab 140 mg, 4.0 for both fremanezumab 225 mg and 675 mg, and 4.0 with galcanezumab 120 mg. CPRs were £4,655 with eptinezumab 100 mg, £7247 with erenumab 140 mg, £5,400 for both fremanezumab 225 mg and 675 mg, and £5400 with galcanezumab 120 mg.

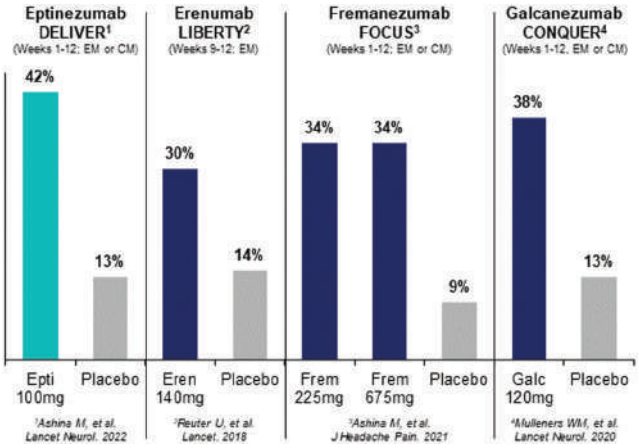

FIGURE 1: Percentage of patients with ≥50% reduction in MMDs from analyzed studies. Please note methodological differences between studies may preclude reliable comparison. CM, chronic migraine; EM, episodic migraine.

Conclusion: These results show a low number of patients with migraine need to be treated with an anti-GCRP mAb to achieve one patient with a ≥50% reduction in pre-treatment MMDs over Weeks 1–12, with eptinezumab showing the lowest NNT and CPR.
Disclosure: DDM-Consulting fees-Novartis, Eli Lilly, Teva, and Lundbeck. Honoraria and Lectures-Allergan, Eli Lilly, Novartis, Lundbeck, and Teva. Support for attending meetings/travel-Allergan, Genesis, Eli Lilly, Novartis, Lundbeck, and Teva. Leadership or fiduciary role-Pres. Hellenic Headache Society, Co-chair Headache Panel at European Academy of Neurology. RK- LPB-Lundbeck employee. XYL -Lundbeck employee. RP-Lundbeck employee. SS-Grants or contracts-Novartis, Uriach. Consulting fees-Novartis, Allergan-Abbvie, Teva, Lilly, Lundbeck, Pfizer, NovoNordisk, Abbott, and AtraZenica. Payment or honoraria-Novartis, Allergan-Abbvie, Teva, Lilly, Lundbeck, Pfizer, NovoNordisk, Abbott, AstraZenica. Support for meetings/travel- Lilly, Novartis, Teva, Lundbeck. Leadership or fiduciary role- Pres. elect European Stroke Organization, Second VP European Headache Federation. Receipt of equipment, materials, drugs, medical writing, gifts, or other services-Allergan-Abbvie, NovoNordisk.

EPR-198 | Inflammatory profile and monocytes differentiation in migraine: Association with disease severity

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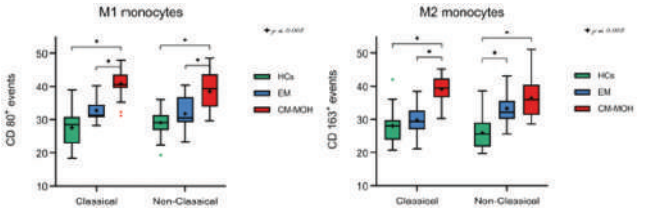
Background and Aims: Neuroinflammation has been considered in the pathogenesis of migraine. There is growing evidence of

aberrant cytokine production in migraine patients. The objective of the present study is to evaluate the expression levels of pro- and anti-inflammatory cytokines and the differentiation of monocytes in patients suffering episodic migraine (EM), chronic migraine with medication overuse headache (CM-MOH), and healthy controls (HCs).

Methods: In this cross-sectional study we assessed the gene expression of IL-1β, TNF-α and IL-10 (Relative Quantification – RQ) in peripheral blood monocytes. Monocyte differentiation was assessed by the number of events recorded using fluorescence-activated cell sorting. Pro-inflammatory M1 monocytes are defined as CD80+ whereas anti-inflammatory M2 monocytes are identified as CD163+. Monocytic subpopulations were differentiated in classical (CD14++/CD16−) and non-classical (CD14+/CD16++). All patients were studied in the interictal migraine phase.

Results: Demographic features were similar among 52 EM, 44 CM-MOH and 30 HCs. IL-1β and TNF-α expression levels were higher in CM-MOH patients compared to EM and HCs subjects ($p=0.001$ for all intergroup comparisons). IL-10 gene expression was lower in EM and CM-MOH when compared to HCs ($p=0.001$). Regarding monocyte profile, CM-MOH patients showed increased number of both M1 and M2 phenotypes when compared to EM and HCs (all $p \leq 0.005$).



Number of events recorded for the different monocytic subtypes among the three study groups.

Conclusion: Migraine patients exhibit a pro-inflammatory status with higher gene expression of IL-1β and TNF-α and reduced expression of IL-10. Monocyte phenotype distribution in migraine patients shows an overlap of increased pro-inflammatory and anti-inflammatory profiles. These alterations appear to be associated with the disease severity, being especially noticeable in patients with CM-MOH.

Disclosure: GS received honoraria for the participation in advisory boards or for oral presentations from Eli-Lilly and Novartis. CT received honoraria for the participation in advisory boards or for oral presentations from: Allergan, ElectroCore, Eli-Lilly, Novartis, and Teva. CT has no ownership interest and does not own stocks of any pharmaceutical company. CT serves as Chief Section Editor of Frontiers in Neurology—Section Headache Medicine and Facial Pain and on the editorial board of The Journal of Headache and Pain. RDI received honoraria for oral presentations from Eli-Lilly. Other authors have nothing to disclose.

EPR-199 | Hypersensitivity to PACAP-38 in post-traumatic headache: A randomized clinical trial

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Background and Aims: Pituitary adenylate cyclase-activating polypeptide-38 (PACAP-38), known for its role in migraine pathogenesis, has been identified as a novel drug target. Given the clinical parallels between post-traumatic headache (PTH) and migraine, we explored the possible role of PACAP-38 in the pathogenesis of PTH.

Methods: We conducted a randomized, double-blind, placebo-controlled, 2-way crossover trial involving participants diagnosed with persistent PTH resulting from mild traumatic brain injury. Participants were randomly assigned to receive a 20-min continuous intravenous infusion of either PACAP-38 (10 pmol/kg/min) or placebo (isotonic saline) on two separate experimental days, with a 1-week wash-out period in between. The primary outcome was the difference in incidence of migraine-like headache between PACAP-38 and placebo during a 12-h observational period post-infusion. The secondary outcome was the difference in the area under the curve (AUC) for baseline-corrected median headache intensity scores during the same 12-h observational period.

Results: During the 12-h observational period, 20 (95%) of 21 participants developed migraine-like headache after intravenous infusion of PACAP-38, compared with 2 (10%) participants after placebo ($p<0.001$). Furthermore, the baseline-corrected AUC values for median headache intensity scores during the 12-h observational period was higher after PACAP-38 than placebo ($p<0.001$).

Conclusion: These compelling results demonstrate that PACAP-38 is potent inducer of migraine-like headache in people with persistent PTH. Thus, targeting PACAP-38 signalling might be a promising avenue for the treatment of PTH.

Disclosure: F.M.A. reports personal fees from Eli Lilly, Lundbeck, Pfizer, and Teva, outside of the submitted work. R.B. reports research support received from Allergan, Dr. Reddy's Laboratories, Eli Lilly, and Teva, outside of the submitted work. In addition, R.B. has received honoraria, acted as a consultant or advisory board member for Alder, Allergan, Amgen, Autonomic Technologies, Avanir, Biohaven, CGRP Diagnostics, Dr. Reddy's Laboratories, ElectroCore, Eli Lilly, GlaxoSmithKline, Merck, Pernix, Teva, and Trigemina. R.B. also reports receiving CME fees from Healthlogix, Medlogix, and WebMD/Medscape, and holds patents for several products, including (9061025, 11732265.1, 10806890, US2021-0015908, WO21007165, US2021-0128724, WO21005497). R.B. is a reviewer for the National Institute of Neurological Disorders and Stroke (NINDS) and holds stock options in Allay Lamp and Percept, outside of the submitted work. H.A. reports personal fees from Teva, outside of the submitted work. The remaining authors declare no competing interests.

EPR-200 | Contemporary prospective understanding of migraine real-world evidence (CAPTURE): Baseline patient-reported outcomes

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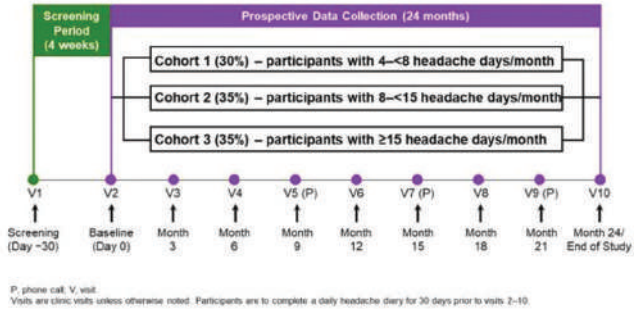
Background and Aims: CAPTURE is a 2-year, international, prospective, longitudinal study aiming to elevate the understanding of disease burden and treatment patterns among people living with migraine, stratified by headache frequency.

Methods: Adults with migraine diagnosed for ≥1 year, aged <50 years at onset, and taking ≥1 medication indicated for migraine with ≥4 monthly headache days (MHDs) in the prior 3 months were assigned to cohorts based on headache frequency (cohort 1: 4 to <8 MHDs; cohort 2: 8 to <15 MHDs; cohort 3: ≥15 MHDs; Figure). Descriptive data for baseline characteristics and patient-reported outcomes (PROs) (Migraine Disability Assessment [MIDAS], Migraine-Specific Quality of Life questionnaire v2.1 [MSQv2.1], Work Productivity and Activity Impairment Questionnaire [WPAI], Headache Impact Test-6, Patient Global Impression–Severity, Hospital Anxiety and Depression Scale, Migraine Interictal Burden Scale) are presented. Endpoints include durations of current/subsequent migraine treatment use and change from baseline of clinical outcomes (e.g., MHDs, medication use, PROs).

Figure. CAPTURE Study Design



P, phone call; V, visit.
Visits are clinic visits unless otherwise noted. Participants are to complete a daily headache diary for 30 days prior to visits 2–10.

CAPTURE Study Design.

Results: Among 239 participants (as of December 2023; cohort 1: $n=68$; cohort 2: $n=104$; cohort 3: $n=67$) (Table 1), baseline PROs indicated greater impairment and poorer quality of life with higher MHDs (Table 2). For cohorts 1, 2, and 3, respectively, baseline mean (SD) MIDAS total scores were 29 (40), 33 (30), and 61 (52); MSQv2.1 Role Function–Restrictive scores were 58.9 (17.5), 53.4 (20.8), and 44.8 (22.0); and WPAI migraine-related impairment was 39.4 (27.2), 40.6 (24.8), and 52.0 (22.8).

TABLE 1: Baseline demographic characteristics.

Characteristic	Cohort 1: 4 to <8 MHDs (n=68)	Cohort 2: 8 to <15 MHDs (n=104)	Cohort 3: ≥15 MHDs (n=67)
Age, mean (SD), y	42.3 (12.5)	42.6 (12.7)	40.8 (12.4)
Sex, n (%)[a]			
Female	52 (77.6)	87 (86.1)	57 (91.9)
Male	15 (22.4)	14 (13.9)	5 (8.1)
Missing	1	3	5
Race, n (%)[a]			
White	64 (95.5)	102 (100.0)	62 (96.9)
Black or African American	1 (1.5)	0	0
Asian	2 (3.0)	0	0
American Indian or Alaska Native	0	0	2 (3.1)
Missing	1	2	3
Region, n (%)[a]			
North America	15 (22.1)	23 (22.1)	14 (20.9)
Europe	53 (77.9)	80 (76.9)	53 (79.1)
South America	0	1 (1.0)	0

MHDs, monthly headache days; SD, standard deviation.
[a]Percentages calculated using nonmissing values.

TABLE 2: Baseline patient-reported outcome measures.

Assessment, mean (SD)	Cohort 1: 4 to <8 MHDs (n=68)[a]	Cohort 2: 8 to <15 MHDs (n=104)[a]	Cohort 3: ≥15 MHDs (n=67)[a]
HAD-S total score	11.2 (6.7)	12.4 (6.8)	14.7 (8.7)
Anxiety	6.7 (3.9)	7.3 (4.1)	8.0 (4.7)
Depression	4.5 (3.4)	5.0 (3.5)	6.7 (4.9)
HIT-6 total score	61.1 (6.0)	61.8 (6.1)	64.1 (5.9)
MIBS-4	4.5 (2.9)	5.4 (3.6)	6.2 (3.7)
MIDAS total score[b]	28.8 (40.1)	32.7 (29.5)	61.0 (52.3)
Absenteeism	14.1 (23.7)	15.2 (16.8)	25.1 (24.4)
Presenteeism	14.7 (18.3)	17.5 (16.1)	35.9 (34.1)
MSQv2.1 domain score			
Role Function-Restrictive	58.9 (17.5)	53.4 (20.8)	44.8 (22.0)
Role Function-Preventive	41.9 (11.0)	40.1 (13.0)	35.5 (14.1)
Emotional Function	30.1 (10.2)	26.7 (12.3)	22.5 (12.4)
PGI-S	1.6 (0.8)	1.8 (0.8)	2.2 (0.7)
WPAI domain score[c]			
Percent work time missed (absenteeism)	5.8 (15.0)	2.8 (5.0)	6.5 (12.4)
Percent impairment while working (presenteeism)	29.8 (25.8)	39.9 (24.1)	50.7 (22.2)
Percent overall impairment	34.0 (27.3)	41.4 (24.2)	52.8 (23.1)
Percent activity impairment due to migraine	39.4 (27.2)	40.6 (24.8)	52.0 (22.8)

HAD-S, Hospital Anxiety and Depression Scale; HIT-6, Headache Impact Test; MHD, monthly headache day; MIBS-4, Migraine Interictal Burden Scale; MIDAS, Migraine Disability Assessment; MSQ, Migraine-Specific Quality-of-Life Questionnaire v2.1; PGI-S, Patient Global Impression-Severity; WPAI, Work Productivity and Activity Impairment Questionnaire: Migraine.
[a]Numbers of participants with available data for this analysis are as follows: cohort 1, n=64; cohort 2, n=101; cohort 3, n=65.
[b]MIDAS scores were available for 100 participants in cohort 2.
[c]WPAI absenteeism, presenteeism, and percent overall impairment scores were calculated among participants reporting full-time employment: cohort 1, n=47; cohort 2, n=71; cohort 3, n=41.

Conclusion: Baseline PROs suggest greater disease burden among participants with higher MHD frequency. CAPTURE will provide critical data on migraine disease patterns and the associated burden over time.

Disclosure: This study was supported by AbbVie.

EPR-201 | Primary headache in transgender women compared with cisgender women and cisgender men: A case-control study

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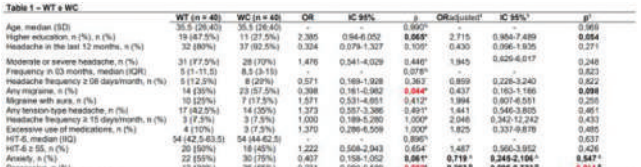
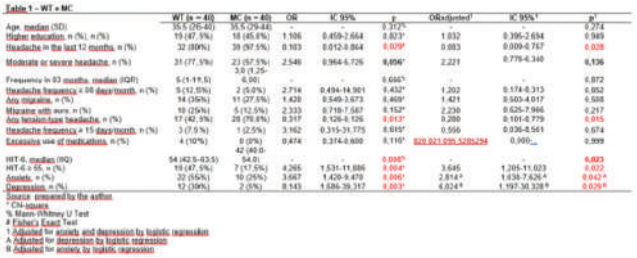
Background and Aims: The prevalence of headaches in transgender individuals using crossed hormone replacement therapy is not well established in the literature. The project aimed to evaluate the frequency, characteristics, and impact of headaches among transgender women on gender-affirming hormone therapy compared to cisgender women, and cisgender men.

Methods: We performed a case-control study carried out at a university hospital in northeast Brazil (HC-UFPE). Cases: 40 transgender women, aged 18 years or older and undergoing estrogen replacement therapy. Controls: 40 age-matched cisgender women, and 40 age-matched cisgender men. A semi-structured questionnaire, the Headache Impact Test (HIT-6), and the Hospital Anxiety and Depression Scale were performed. We performed logistic regression for the possible confounding variables. The research project was approved by the Research Ethics Committee of HC-UFPE (CAAE:58822022.2.0000.8807/number: 5.509.844).

Results: We included 120 individuals, 40 of whom were transgender women. The median age was 35.5 among the 3 groups (Mann–Whitney; $p=0.990$, and $p=0.312$). There was no statistical difference in the prevalence of migraine after logistic regression for anxiety and depression between transgender women group and cisgender women group. Cisgender women had higher rates of depression than transgender women (Mann–Whitney; $p=0.002$). We did not observe difference in the prevalence of migraine between transgender women and cisgender men group. There was a statistical difference in the prevalence of impact, anxiety, and depression in the transgender women group compared with cisgender men group (Mann–Whitney; $p=0.004/p=0.006/p=0.003$), respectively.



Sample characterization and WT × WC analysis.



Sample characterization and WT × MC analysis.

Conclusion: Transgender women had less depression than cisgender women. Transgender women had more impact of headache, anxiety, and depression rates than cisgender men.

Disclosure: We do not have conflicts of interest to declare.

Movement disorders 3

EPR-202 | Analysis of four randomized placebo-controlled trials supports pridopidine's treatment benefit in Huntington disease

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Background and Aims: In PROOF-HD, pridopidine demonstrated improvements across key measures of HD clinical progression (cUHDRS), function (TFC), cognition (SWR), motor (Q-Motor), and quality-of-life, in participants off antidopaminergic medications (ADMs).

Methods: To assess if participants off ADMs from prior pridopidine studies have consistent findings with PROOF-HD, we performed a pooled analysis from four randomized, double-blind, placebo-controlled trials assessing pridopidine in early HD (TFC 7–13) (HART, MermaiHD, PRIDE-HD and PROOF-HD).

Results: In the analysis of 435 participants ($n=227$, placebo and $n=208$, pridopidine), pridopidine showed treatment benefit versus placebo in TFC at Week 26 (Δ0.31, $p=0.03$), 39 (Δ0.43, $p=0.01$), 52 (Δ0.38, $p=0.02$), and 78 (Δ0.49, $p=0.02$), and on cUHDRS at Week 26 (Δ0.39, $p=0.006$) and 39 (Δ0.55, $p=0.003$) with a meaningful treatment benefit of Δ0.36 at Week 78 (PRIDE-HD did not measure SWR and was excluded). In the revised cUHDRS without SWR, pridopidine showed improvement above baseline up to Week 52, with benefits versus placebo at Week 26 (Δ0.30, $p=0.006$), 39 (Δ0.45, $p=0.002$), 52 (Δ 0.29, $p=0.04$), and 78 (Δ0.34, $p=0.07$). All trials contribute positively to the observed benefits. A significant benefit across all Q-motor measures was observed. For example, pridopidine shows improvement from baseline in finger tapping to Week 52 with a significant treatment benefit at Week 12 (Δ-31 msec, $p=0.046$), 26 (Δ-27 msec, $p<0.001$), 52 (Δ-25 msec, $p=0.02$), and Week 78 (Δ-25 msec, $p=0.05$). The placebo group shows an expected decline in all Q-motor measures.

Conclusion: This analysis strongly supports and validates PROOF-HD findings of a consistent, sustained, and meaningful treatment benefits of pridopidine in patients off ADMs.

Disclosure: Full disclosures will be presented.

EPR-203 | Metabolic brain correlates of visuoperceptual impairment and visual hallucinations in Parkinson's disease

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Background and Aims: This study investigated whether the same brain metabolic correlates underlie both visual hallucinations and perceptual impairment in Parkinson's disease (PD).

Methods: Eleven non-demented idiopathic PD patients experiencing visual hallucinations (PD-VH) and 9 non-demented, age-matched PD patients without a history of visual hallucinations (PD-NVH) participated in the study. They underwent positron emission tomography (PET) with [18F]fluorodeoxyglucose tracer. The University of Miami Parkinson's disease Hallucinations Questionnaire (UM-PDHQ) was administered to assess the burden of visual hallucinations. Perceptual performance was evaluated using two sets of illusory figures. A voxel-wise group comparison using 18-FDG-PET tomography was conducted, following the SPM12 software guidelines. Additionally, partial correlations between voxel-wise relative regional cerebral glucose metabolic rate, UM-PDHQ scores, and perceptual performance scores were performed.

Results: PD-VH patients showed poorer perceptual performance than PD-NVH patients ($p < 0.050$). Unlike PD-NVH patients, PD-VH patients exhibited significant relative hypermetabolism in both right and left fronto-parietal lobes ($p < 0.05$, Threshold Free Cluster Enhancement-False Discovery Rate-corrected). Additionally, in PD-VH patients, the metabolic rate of a similar set of regions positively correlated with UM-PDHQ scores ($p < 0.001$, uncorrected) and inversely correlated with perceptual performance scores ($p < 0.001$ to $p < 0.050$, uncorrected).

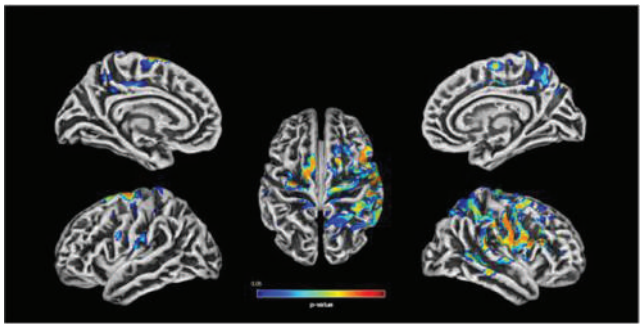

FIGURE 1: Hypermetabolic regions in Parkinson's disease patients with visual hallucinations (Threshold Free Cluster Enhancement – False Discovery Rate corrected, $p < 0.05$).

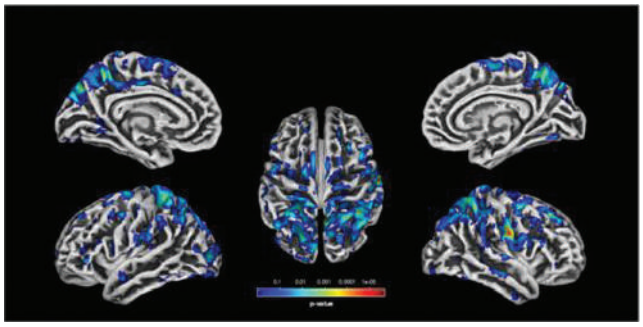

FIGURE 2: Partial positive correlation (covariates: age, sex) between University of Miami Parkinson's disease Hallucinations Questionnaire (UM-PDHQ) scores and cerebral regional relative glucose metabolic rate.

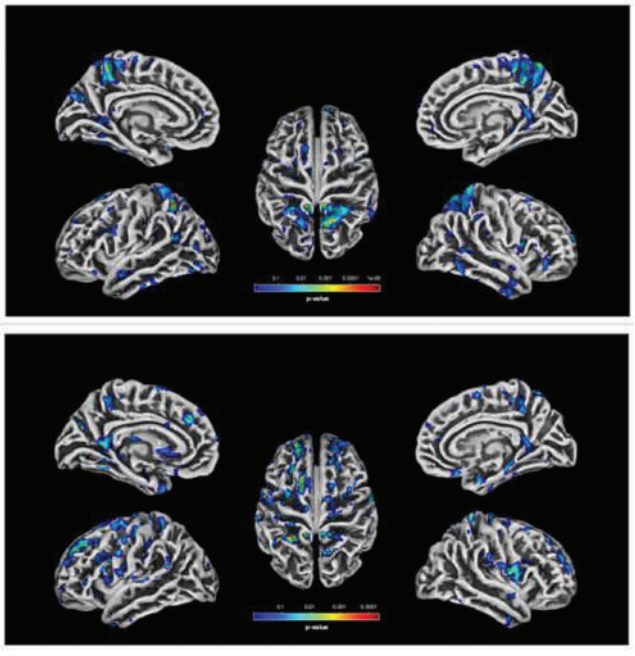

FIGURE 3a: Partial negative correlation (covariates: age and sex) between the size shrinkage of amodal completion illusion test scores and the cerebral regional relative glucose metabolic rate in the group of Parkinson's disease patients with visual hallucination.

Conclusion: Fronto-parietal hypermetabolism appears to be a common underlying factor for both visual hallucinations and perceptual impairment in Parkinson's disease. Future studies with a larger sample size could provide more precise localization of these alterations.
Disclosure: The authors declare no competing interests for this study.

EPR-204 | Safety of deutetrabenazine for tardive dyskinesia in the European population: The open-label RIM-TD year 4 study

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Background and Aims: Tardive dyskinesia (TD) is a hyperkinetic movement disorder that has few treatment options. Deutetrabenazine (DTBZ) is a vesicular monoamine transporter 2 inhibitor approved in 6 countries for the treatment of TD in adults. Data from the first 3 years of an open-label extension study (RIM-TD; NCT02198794) support the tolerability and efficacy of DTBZ for TD in adults, but the safety beyond this period in the European population is unknown.
Methods: Patients in the Czechia, Germany, Hungary, Poland, and Slovakia were eligible to enrol in an additional 52 weeks of DTBZ treatment (RIM-TD year 4). Safety assessed via adverse event (AE) reporting throughout year 4 is reported here.
Results: Of the 80 patients enrolled in year 4, the mean (SD) age at the start of year 4 was 61.4 (13.5) years, and 52 (65%) patients were female. Concomitant medications included antipsychotics (52 [65%]), antidepressants (31 [39%]), anxiolytics (15 [19%]), and antiepileptics (26 [33%]). At week 39 of year 4, the mean (SD) total daily dose of DTBZ was 39.1 (11.8) mg/day. AEs and treatment-related AEs were reported for 23 (28.8%) and 3 (3.8%) patients, respectively. 73 (91%) patients completed year 4; reasons for discontinuation were patient withdrawal ($n = 3$ [4%]), AEs (2 [3%]), and death (2 [3%]; due to cardiac failure and acute respiratory and circulatory failure).
Conclusion: Year 4 safety data from this European cohort of patients with TD are consistent with the 3-year RIM-TD parent study and support the safety and tolerability of DTBZ beyond 3 years.
Disclosure: This study was supported by funding from Teva Branded Pharmaceutical Products R&D, Inc. Robert A. Hauser, Stewart A. Factor, Joohi Jimenez-Shahed, and Karen E. Anderson have received fees and/or honoraria from Teva Pharmaceuticals. Krzysztof Duma, Nayla Chaijale, Steve Barash, Nicholas Gross, Leslie Marinelli, and Mark Forrest Gordon are employees and stockholders of Teva Pharmaceuticals.

EPR-205 | Inhaled levodopa in fluctuating Parkinson's disease: Post-commercialization experience in a movement disorders unit

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Background and Aims: Levodopa, the primary Parkinson's disease (PD) treatment for over 50 years, becomes less effective as the disease progresses, leading to motor fluctuations. Current treatments for these fluctuations are scarce. CVT-301, a newly available inhaled levodopa powder, has shown efficacy in clinical trials for managing OFF periods in PD without significant pulmonary side effects. It offers rapid symptom improvement and it is easy to administer, making it suitable for OFF periods uncontrolled by oral medications. However, post-commercialization data on the use of inhaled levodopa is lacking. In this study we describe the experience in our Movement Disorders Unit.
Methods: observational study at a specialized Parkinson's center in Spain. Patients treated with inhaled levodopa from April to October 2023 were included in a retrospective way. Clinical and demographic characteristics were described. All patients had been trained in treatment usage by a neurologists or specialized nurse to ensure a correct administration.
Results: Eighteen patients (55.6% females, mean age 65.17 years, mean PD duration 9 years) were included. Thirteen (77.2%) reported OFF symptom improvement (median PGI-C score 3, IQR 2–3.75). Clinical improvement was described within the first 10 min of administration. The average maximum daily usage was 1.5 (IQR: 1–3). Side effects were reported by 12 (66.7%) patients, mainly cough and dyskinesias, leading to a 11.1% discontinuation rate.
Conclusion: In our cohort, inhaled levodopa provided rapid and substantial improvement in our cohort and was overall well tolerated with a discontinuation rate of 11%.
Disclosure: IP has received honoraria as speaker in scientific meetings from Zambon, Abbvie, Exeltis Healthcare SL Sociedad Extremeña de Neurología, Sociedad Española de Neurología and travel support for scientific meetings from Esteve. Pablo Ros-Arlanzón and

Noelia Valverde-Mata contributed equally to this work and share first authorship.

EPR-206 | Post hoc subgroup analysis: Age of Friedreich ataxia onset in MOXIe trial of omaveloxolone

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Background and Aims: Age of onset is an important predictor of clinical progression in patients with Friedreich ataxia (FA). This post hoc analysis evaluated change in modified Friedreich Ataxia Rating Scale (mFARS) scores by age of onset subgroups using data from MOXIe Part 2 (NCT02255435; EudraCT2015-002762-23) and propensity-matched data from the MOXIe open-label extension (OLE) and the FA-COMS natural history study (NCT03090789).

Methods: MOXIe Part 2 randomized patients 1:1 to placebo or omaveloxolone 150 mg once daily (primary endpoint: change from baseline in mFARS at Week 48). MOXIe OLE (ongoing study to assess long-term safety and tolerability of omaveloxolone) patients were propensity score-matched 1:1 to FA-COMS patients. Changes in mFARS scores by age of onset subgroups were analyzed using mixed models repeated measures.

Results: In MOXIe Part 2 (median age of FA onset: 15 years), patients with age of onset >15 years versus ≤15 years had lower mean baseline mFARS scores (Table 1). Placebo-treated patients with age of onset ≤15 years versus >15 years had more progression by Week 48, whereas omaveloxolone-treated patients demonstrated a similar change from baseline regardless of age of onset. In both subgroups, progression directionally favored omaveloxolone versus placebo-treated patients at Week 48 (Table 1) and versus propensity-matched FA-COMS controls after 3 years (Table 2).

TABLE 1: MOXIe Part 2: Key demographics and baseline characteristics by age of FA onset subgroups (FAS), and mFARS results by age of FA onset subgroups (FAS).

	Age of FA Onset ≤15 Years		Age of FA Onset >15 Years	
	Placebo (N=22)	Omaveloxolone (N=23)	Placebo (N=20)	Omaveloxolone (N=17)
Age (years) Mean (SD) Median [min, max]	18.3 (2.40) 17.0 [16, 24]	20.8 (4.87) 20.0 [16, 34]	29.4 (7.54) 28.0 [18, 40]	28.8 (5.58) 28.0 [20, 39]
Age of FA onset (years) Mean (SD) Median [min, max]	11.1 (3.04) 12.0 [5, 15]	12.0 (2.25) 12.0 [7, 15]	19.5 (3.58) 18.0 [16, 30]	21.1 (4.88) 21.0 [16, 36]
mFARS				
Baseline, mean (SD)	40.83 (9.086)	43.39 (10.503)	36.52 (12.683)	37.64 (9.559)
Week 48 change from baseline				
LS mean (SE)	2.03 (0.896)	−1.56 (0.960)	−0.40 (0.935)	−1.47 (1.039)
LS mean difference (SE)	—	−3.60 (1.313) p=0.0077	—	−1.07 (1.377) p=0.4411

Abbreviations: FA=Friedreich ataxia; FAS=full analysis set; LS=least squares; max=maximum; mFARS=modified Friedreich Ataxia Rating Scale; min=minimum; SD=standard deviation; SE=standard error.

TABLE 2: Propensity-matched analysis: Baseline age, age of onset, and mFARS results by age of onset subgroups (primary pooled population).

	Age of FA Onset ≤15 Years		Age of FA Onset >15 Years	
	Matched FA-COMS (N=92)	MOXIe Extension (N=75)	Matched FA-COMS (N=44)	MOXIe Extension (N=61)
Age (years) Mean (SD) Median [min, max]	20.4 (10.38) 18.0 [6, 64]	22.7 (5.64) 21.0 [16, 37]	38.3 (11.80) 36.0 [16, 61]	31.3 (6.16) 32.0 [18, 41]
Age of FA onset (years) Mean (SD) Median [min, max]	9.8 (3.42) 10.0 [2, 15]	11.7 (2.76) 12.0 [5, 15]	26.6 (11.17) 21.5 [16, 52]	20.0 (3.93) 19.0 [16, 36]
mFARS				
Baseline, mean (SD)	43.70 (15.98)	45.23 (11.55)	35.46 (15.06)	38.53 (12.94)
Year 3 change from baseline				
LS mean (SE)	6.77 (0.807)	3.45 (0.896)	5.94 (1.109)	2.47 (1.002)
LS mean difference (SE)	—	−3.33 (1.198) p=0.0057	—	−3.47 (1.478) p=0.0193

Abbreviations: FA=Friedreich ataxia; FA-COMS=Friedreich Ataxia - Clinical Outcome Measures; LS=least squares; max=maximum; mFARS=modified Friedreich Ataxia Rating Scale; min=minimum; SD=standard deviation; SE=standard error.

Conclusion: Although MOXIe Part 2 was not powered to detect efficacy by age of onset subgroups, results directionally favored omaveloxolone versus placebo regardless of age of FA onset. Similar trends were observed after 3 years in MOXIe OLE relative to propensity-matched FA-COMS patients.

Disclosure: This study was funded by Reata Pharmaceuticals. Reata was acquired by Biogen in 2023. S Chimalapati, W Costello, A Goldsberry, S Rich, and C Ruhl are employees of Biogen. D Lynch reports grants from FARA, the Muscular Dystrophy Association (MDA), the National Institutes of Health (NIH), Reata Pharmaceuticals, and Retrotope.

EPR-207 | Suvecaltamide pharmacokinetics, safety, & tolerability–Phase 1, randomized, double-blind, multiple ascending dose study

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Background and Aims: Suvecaltamide (JZP385), a highly selective CaV3 channel modulator, is currently in Phase 2b development to treat essential tremor (NCT05122650) and Parkinson's disease tremor (NCT05642442). This Phase 1, double-blind, parallel design, within-participant, multiple ascending dose study evaluated the pharmacokinetics (PK), safety, and tolerability of this once-daily (QD) suvecaltamide formulation.

Methods: Healthy participants (18–75 years) were randomized to suvecaltamide or placebo (Part 1: 8 mg QD, days 1–7; Part 2: 8 mg QD, days 1–7; 16 mg QD, days 8–14; 24 mg QD, days 15–21; 36 mg QD, days 22–25). PK, time-matched electrocardiograms, treatment-emergent adverse events (TEAEs), and food-effect data were collected.

Results: Participants (suvecaltamide: $n = 20$/formulation/part; placebo: $n = 10$/part) were similar in age, sex, race, and baseline characteristics across treatment groups and study parts. Fasted, steady-state PK parameters for suvecaltamide and its major active metabolites (JZZ05000034 = M01, JZZ05000035 = M02) were approximately dose proportional (Table). A high-fat/high-calorie meal had negligible effect on suvecaltamide Cmax and AUC, but prolonged tmax. For all doses, the upper bound 90% CI of the placebo-corrected change from baseline in Fridericia's corrected QT interval at each analyte's mean Cmax was substantially below the 10-msec regulatory threshold of concern. Across study parts, the most common TEAEs were dizziness (suvecaltamide, 25%; placebo, 10%), insomnia (suvecaltamide, 20%; placebo, 20%), and headache (suvecaltamide, 18%; placebo, 30%). Most TEAEs were mild to moderate in severity, and their incidence tended to decrease with increasing dose.

Table. Suvecaltamide pharmacokinetic parameters at steady state (with fasting)

	Suvecaltamide			M01 (JZZ05000034)				M02 (JZZ05000035)			
Dose[a]	C_{max} (ng/mL)[b]	AUC_{tau} (h·ng/mL)[b]	t_{max} (h)[c]	C_{max} (ng/mL)[b]	AUC_{tau} (h·ng/mL)[b]	t_{max} (h)[c]	MR C_{max}	MR AUC_{tau}	C_{max} (ng/mL)[b]	AUC_{tau} (h·ng/mL)[b]	t_{max} (h)[c]	MR C_{max}	MR AUC_{tau}
8mg	233 (47.6)	3184 (857.6)	1.0 [0.5–6.0]	152 (33.1)	3183 (719.1)	4.3 [0.5–23.6]	0.67	1.04	90 (29.4)	1691 (356.7)	5.1 [1.1–16.0]	0.37	0.51
16mg	439 (100.0)	5859 (1932.5)	1.0 [0.5–2.0]	317 (111.1)	6806 (2334.3)	2.5 [0.5–23.6]	0.74	1.14	188 (58.1)	3612 (1101.5)	2.5 [1.0–8.0]	0.41	0.63
24mg	631 (146.6)	8213 (3003.1)	1.0 [0.5–2.5]	507 (149.5)	10,530 (3230.7)	2.3 [0.5–23.6]	0.82	1.17	261 (68.9)	5189 (1965.2)	4.0 [1.5–23.6]	0.39	0.54
36mg	962 (216.1)	12,180 (3579.6)	1.0 [0.5–6.0]	696 (184.5)	14,300 (4253.1)	2.3 [1.0–23.6]	0.79	1.20	392 (114.2)	7429 (2648.6)	2.5 [1.0–8.0]	0.41	0.58

[a]8mg data is from Day 6, 16mg data is from Day 14, 24mg data is from Day 21, 36mg data is from Day 25.
[b]PK data presented as mean (SD).
[c]t_{max} is presented as median [minimum – maximum].
AUC_{tau}, area under the curve over the dosing period, tau, at steady state tau is defined as 24 hours; C_{max}, maximum observed concentration; h, hour; MR, molar ratio (metabolite to parent); PK, pharmacokinetic; SD, standard deviation; t_{max}, time of maximum concentration.

Suvecaltamide pharmacokinetic parameters at steady state (with fasting).

Conclusion: Results from this Phase 1 study expand our understanding of suvecaltamide PK, safety, and tolerability, supporting further clinical development of the QD formulation of suvecaltamide.

Disclosure: Supported by Jazz Pharmaceuticals. All authors are full-time employees of Jazz Pharmaceuticals who, during this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc.

EPR-208 | Diagnostic accuracy of skin biopsy in disclosing early PD

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Background and Aims: To analyse the diagnostic accuracy of phosphorylated α-synuclein (p-syn) in autonomic skin fibers in identifying early Parkinson's disease (PD).

Methods: One hundred twenty-nine participants with early parkinsonian signs (onset within the last 18 months) were included in the study. Proximal and distal skin sites were taken to analyse p-syn by immunofluorescence. Patients also underwent clinical evaluation including focused scales (UPDRS and HY, MoCA, COMPASS-31, NMSQuest) and smell analysis. Clinical evaluation was repeated over a follow-up of 18 months in all patients whereas skin biopsy was repeated in 45 patients in the follow-up. Clinical diagnosis of PD was defined according to the Movement Disorder Society (2019) criteria.

Results: Seventy-seven patients fulfilled clinical criteria for PD and 69 of them (90%) presented p-syn in autonomic fibers or plexus. By contrast, twenty-three patients meet clinical criteria of tauopathy, vascular PD or MSA. P-syn was absent in these patients except a single MSA patient showing the typical somatic p-syn. Accordingly, the overall specificity of p-syn in skin autonomic nerves was 100%. Twenty-nine patients showed an undefined clinical picture both at baseline and follow-up. PD patients showed higher smell dysfunctions, RBD incidence, UPDRS, HY and COMPASS-31 scales without any correlation with p-syn.

Conclusion: Our results showed that skin biopsy and skin p-syn in autonomic nerve fibers presented an excellent diagnostic accuracy in disclosing early PD with high sensitivity and specificity. Our study corroborates the use of skin biopsy for the diagnosis of early PD.

Disclosure: No disclosures to report.

EPR-209 | Beyond the concept of "occupational dystonia"

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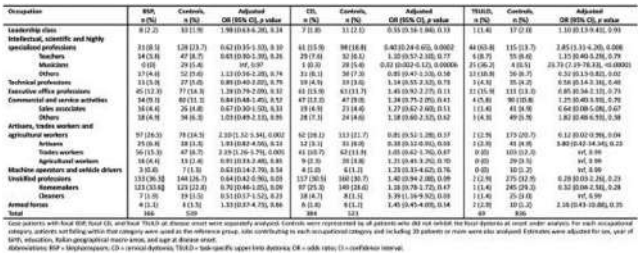
Background and Aims: Development of idiopathic adult-onset dystonia (IAOD) in different body parts is associated with specific demographic and clinical characteristics, as well as with specific risk factors. This study aimed to investigate the association between specific occupations and specific forms of idiopathic dystonia at onset, namely blepharospasm (BSP), cervical dystonia (CD), and task-specific upper limb dystonia (TSULD).

Methods: Data from 905 IAOD patients enrolled in the Italian Dystonia Registry were analyzed. Each patient was assigned to the corresponding occupational category by specialists in occupational medicine according to the Italian National Institute of Statistics classification. Logistic regression models (adjusted for sex, year of birth, age at dystonia onset, education, and Italian geographical areas) were computed to assess the association between occupation and a specific dystonia at onset, using the patients who developed focal dystonia in other body parts as controls.

ISTAT occupational category (n. patients)	Jobs (n. patients)
Leadership class (18)	Entrepreneurs (8); executives (4); restaurateurs (3); hotel managers (2); garage managers (1).
Intellectual, scientific and highly specialized professions (159)	Teachers (61); musicians (29); students (15); chartered accountants (7); healthcare professionals (7); lawyers (7); clergy members (6); engineers (5); surveyors (4); journalists (3); computer scientists (2); dancers (2); freelancers (2); research scientists (2); actors (1); biologists (1); consultants (1); home economists (1); physicists (1); project managers (1); writers (1).
Technical professions (38)	Nurses (13); real estate agents (4); commercial agents (3); insurance agents (3); programmers (2); travel agents (2); agronomists (1); oenologists (1); fitness trainers (1) interior designers (1); jewelry sales representatives (1); maritime brokers (1); opticians (1); pilots (1); radiologic technologists (1); sales representatives (1); swimming instructors (1).
Executive office professions (122)	Unclassifiable (96); secretaries (6); administrative employees (6); accountants (2); bank employees (2); municipal clerks (2); cashiers (1); customs brokers (1); postal service clerk (1); railway office workers (1); switchboard operators (1); social security administrators (1); tax consultants (1); technical officers (1).
Commercial and service activities (94)	Sales associates (42); hospitality workers (19); personal care assistants (16); hairdressers/beauticians (12); warehouse workers (2); automotive parts salespersons (1); flight attendants (1); petrol station attendants (1).
Artisans, trades workers and agricultural workers (175)	Trades workers (103); artisans (43); agricultural workers (29).
Machine operators and vehicle drivers (10)	Drivers (7); marine plants (1); train conductors (1); truck drivers (1).
Unskilled professions (277)	Homemakers (246); cleaners (26); concierges (3); nursery school attendants (2).
Armed forces (12)	Police officers (4); municipal police officers (3); unspecified (3); carabinieri (1); firefighters (1).

Distribution of specific jobs across Italian National Institute of Statistics (ISTAT) occupational categories.

Results: Compared to other professions, trades workers exhibited an increased risk for BSP at onset (OR = 2.19, 95% CI 1.26–3.79), cleaners for CD (OR = 3.39, 95% CI 1.16–9.92), and musicians for TSULD (OR = 23.73, 95% CI 7.19–78.33). The longer the duration of employment before the onset of dystonia, the greater the risk of developing the specific dystonia.



Associations between main lifetime occupation categorized according to the Italian National Institute of Statistics (ISTAT) classification and site of dystonia onset.

Site of dystonia onset	Occupation	OR (95% CI), *p* value
BSP (n = 352)	Non-trades workers	1 (reference)
	Trades workers for <22 years	1.45 (0.63-3.33), 0.38
	Trades workers for ≥22 years	2.34 (1.04-5.24), 0.04
CD (n = 383)	Non-cleaners	1 (reference)
	Cleaners for <17 years	2.43 (0.42-14.16), 0.32
	Cleaners for ≥17 years	8.93 (1.06-75.24), 0.04
TSULD (n = 53)	Non-musicians	1 (reference)
	Musicians for <14 years	Inf, 0.99
	Musicians for ≥14 years	10.09 (1.50-67.70), 0.02

Each occupational exposure was stratified according to the median duration. Estimates were adjusted by sex, year of birth, education, Italian geographical macro-areas, and age at disease onset.
Abbreviations: BSP = blepharospasm; CD = cervical dystonia; TSULD = task-specific upper limb dystonia; OR = odds ratio; CI = confidence interval.

Impact of occupational duration in trades work, cleaners, and musicians on the risk of developing blepharospasm, cervical dystonia, and task-specific upper limb dystonia, respectively.

Conclusion: We provided novel information indicating that exposure to certain occupations may trigger specific forms of IAOD, namely BSP, CD, and TSULD. The associations highlighted by this study probably reflect common pathophysiological mechanisms among different focal dystonias, relying on the frequent performance of repetitive movements in a specific body part.
Disclosure: Nothing to disclose.

EPR-210 | Validity and reliability of the Spanish version of the King's Parkinson's Pain Scale (KPPS)

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Background and Aims: The King´s Parkinson´s Pain Scale (KPPS) has been recently translated and cross-culturally adapted to Spanish. We aim to assess its test-retest reliability, measurement error, and criterion and convergent validity in Spanish-speaking individuals experiencing Parkinson´s Disease (PD)-related pain.
Methods: Fifty-three PD patients suffering from otherwise explained pain participated. They were evaluated in one session by the KPPS, Brief Pain Inventory, two Pain Pressure Thresholds (PPT) in a painful and a non-painful location, and Conditioned Pain Modulation (CPM). A retest of the KPPS was performed via phone call by the same evaluator 7–15 days later. Internal consistency (Cronbach's alpha), test-retest reliability (Intraclass Correlation Coefficient), Standard Error of Measurement, and criterion and convergent validity (Pearson's *r*) were obtained.
Results: Internal consistency was acceptable (Cronbach's alpha = 0.77, 95% CI = 0.67–0.85). The mean test and retest Total KPPS scores were similar (test = 34.83 ± 23.50 points, retest = 35.87 ± 26.23 points), and test-retest reliability was good (ICC = 0.85, 95% CI = 0.75–0.91). Measurement error was SEM = 9.1 points. Regarding criterion validity, the Total KPPS score was not correlated to the BPI intensity subscale ($r = 0.18$, $p = 0.19$) but it was moderately and positively correlated to the interference subscale ($r = 0.43$, $p = 0.001$). Related to convergent validity, the Total KPPS was moderately and negatively correlated to both the non-painful PPT ($r = -0.4$, $p = 0.003$) and WMH ($r = -0.38$, $p = 0.005$). No statistically significant correlations were found with painfulPPT or CPM ($p > 0.05$).

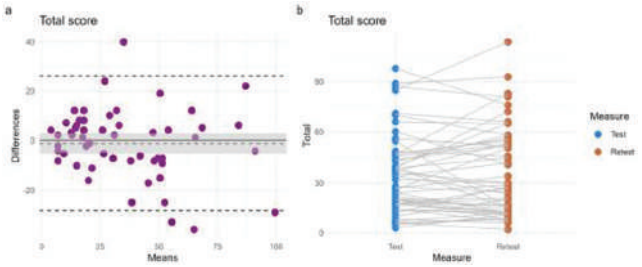

FIGURE 1: Test-retest reliability of the Spanish King's Parkinson's Disease Pain Scale (KPPS) total score.

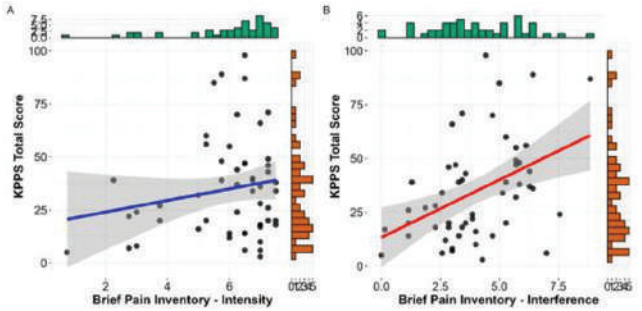

FIGURE 2: Criterion validity of the Spanish King's Parkinson's Disease Pain Scale (KPPS) total score.

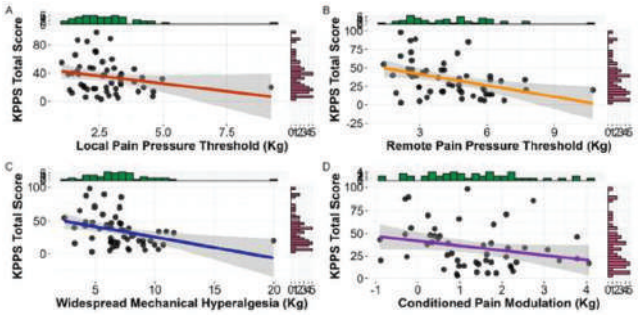

FIGURE 3: Convergent validity of the Spanish King's Parkinson's Disease Pain Scale (KPPS) total score.

Conclusion: The present study provides evidence that the Spanish version of the KPPS has good reliability, minimal measurement error, and sufficient criterion and convergent validity.
Disclosure: The availability of this scale will assist Spanish clinicians in crafting individualized treatment plans for PD patients by pinpointing characteristics such as the severity and frequency of their pain.

Movement disorders 4

EPR-211 | Postganglionic autonomic dysfunction and cutaneous alpha-synuclein deposits in MSA: Role in disease progression

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Background and Aims: Multiple system atrophy (MSA) is a progressive neurodegenerative disease clinically characterized by parkinsonism (MSA-P) and/or cerebellar dysfunction (MSA-C) associated with autonomic failure. Autonomic dysfunction is generally considered to be caused by a preganglionic fibers involvement. However, growing evidence supports the presence of postganglionic autonomic involvement together with skin denervation, suggesting the concomitant peripheral nervous system involvement. The study aimed to assess peripheral autonomic involvement through sudomotor and cardiovascular tests and skin biopsy to establish their role in predicting disease progression and severity.
Methods: A cross-sectional study on patients with "clinically established" MSA diagnosis was performed. Complete clinical workup, MIBG cardiac scintigraphy, cardiovascular autonomic tests, Dynamic sweating test, skin biopsies for epidermal and dermal nerves, and p-syn quantitation at three body sites were performed.
Results: 31 patients (21 MSA-P, 10 MSA-C) were enrolled. No difference in demographic and clinical scales scoreswase found. DST was impaired in all tested patients. Cutaneous p-syn deposits were found in 81% of patients, with a topographic distribution following a distal-proximal gradient and no difference between clinical subtypes. P-syn deposits were found in both somatic and autonomic fibers, with greater prevalence in the former. The presence of widespread skin nerve p-syn deposits was associated with higher UMSARS Part II scores and with OH. Neither p-syn deposition nor sudomotor dysfunction correlated with disease duration.
Conclusion: This study highlights the presence of functional abnormalities of postganglionic sudomotor pathway in MSA and provides a preliminary support for the use of cutaneous p-syn quantitation as a prognostic biomarker in MSA in clinical practice and research studies.
Disclosure: Nothing to disclose.

EPR-212 | Prediction of cognitive heterogeneity in Parkinson's disease: A 4-year longitudinal study

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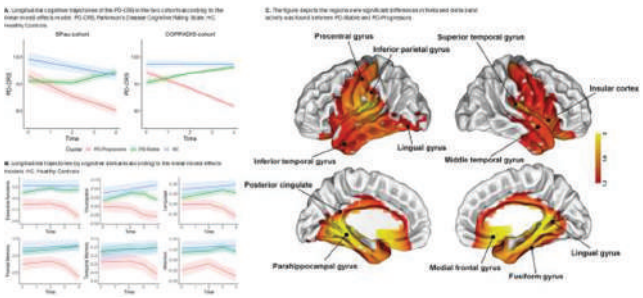
Background and Aims: Cognitive impairment in Parkinson's disease (PD) can exhibit a very heterogeneous trajectory among patients. Here we explored the mechanisms involved in the expression and prediction of different cognitive phenotypes over 4 years.
Methods: In two independent cohorts (total $n=475$), we performed a cluster analysis to identify trajectories of cognitive progression. Baseline and longitudinal Level-II neuropsychological assessments were conducted, and baseline resting EEG and NfL plasmatic quantification were done. Linear mixed-effects models were used to study longitudinal changes. Risk of mild cognitive impairment (PD-MCI) and dementia were estimated using multivariable hazard regression. Spectral power density from the EEG at baseline and source localization were computed.
Results: Two cognitive trajectories were identified. Cluster 1 presented stability (PD-Stable) over time, whereas Cluster 2 showed progressive cognitive decline (PD-Progressors). Both clusters showed equivalent clinical and sociodemographic characteristics at baseline, but the PD-Progressors group showed an increased risk for evolving to PD-MCI (Hr = 2.09; 95% CI, 1.11–3.95) and a marked risk for dementia (Hr = 4.87; 95% CI, 1.34–17.76), in turn with a pattern of worsening in posterior-cortical-dependent cognitive processes. NfL levels were equivalent between groups at baseline. Conversely, the PD-Progressors group showed a fronto-temporo-occipital and parietal slow-wave power density increase, that was in turn related to worsening at 2 and 4 years in different cognitive measures.



Cognitive trajectories and topography of slow wave activity.

Conclusion: In the absence of baseline clinical signs and markers of structural damage, further development of an aggressive cognitive decline in PD is associated with increased slow-wave power density and with a different profile of worsening in several posterior-cortical-dependent tasks.
Disclosure: Nothing to disclose.

EPR-213 | Correlates of mutant huntingtin, NfL and MRI in Huntington's disease, a multimodal analysis

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Background and Aims: This study aims to investigate correlations between mHtt and NfL levels and MRI findings in individuals at different stages of HD, including presymptomatic and symptomatic individuals. Understanding these correlations may provide valuable insights into disease pathogenesis and facilitate the development of effective therapeutic strategies.
Methods: Longitudinal study with cross-sectional analysis of a cohort of individuals with genetic confirmation for Huntington's disease (HD) and controls. They were grouped into presymptomatic (preHD) at the motor level (DLC <4) and symptomatic (HD) (DCL = 4). Levels of NfL in CSF (Simoa, Quanterix) and mHTT in CSF (SMC Erenna platform, Merck) were quantified. MRI 3 Tesla and gray matter analysis using VBM and cortical thickness using FreeSurfer were performed. Correlations between NfL and mHtt biomarkers and neuroimaging were established using SPM.
Results: Sixty-one participants, including 27 presymptomatic, 24 symptomatic, and 10 controls, showed age differences between groups (age covaried). Presymptomatic individuals exhibited elevated NfL and mHtt levels compared to controls, with further increases in symptomatic individuals. NfL levels correlated with caudate, putamen, and cerebellar atrophy in presymptomatics ($p < 0.005$), while mHtt levels showed weaker correlation ($p < 0.05$). In symptomatics, NfL levels correlated with thalamic, posterior cortical, and prefrontal atrophy, whereas mHtt levels correlated less with posterior cortical atrophy, suggesting NfL's higher sensitivity in detecting neurodegeneration and/or involvement of non-Huntingtin-dependent processes.
Conclusion: Levels of NfL exhibit greater sensitivity in detecting the neurodegenerative process compared to mHtt, showing a correlation with atrophy in the caudate and putamen in presymptomatic individuals that extends to cortical areas as the disease progresses.
Disclosure: Nothing to disclose.

EPR-214 | Reliability of neurophysiological and cerebral tremor features in Parkinson's disease

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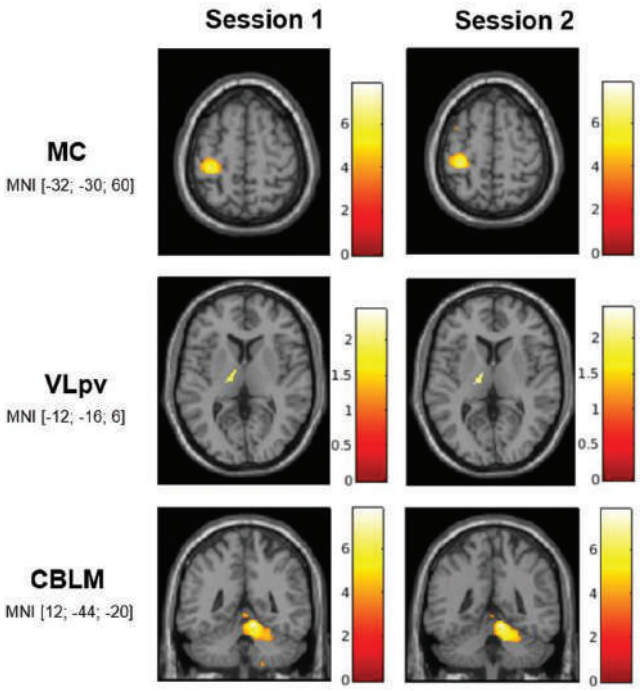
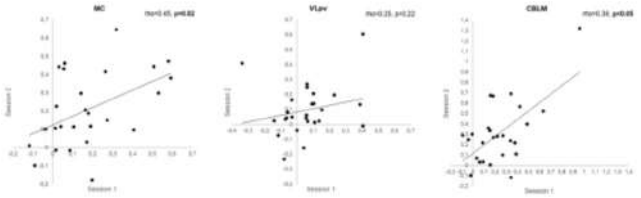
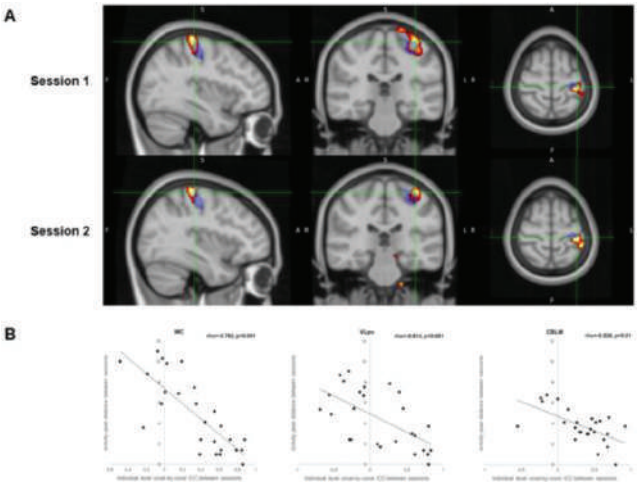
Background and Aims: The cerebello-thalamo-cortical (CTC) circuit plays a key role in pathophysiology of tremor in Parkinson's Disease (PD). Better understanding the underlying mechanisms is crucial for advancing treatment strategies. We aim to assess the test-retest reliability of clinical, neurophysiological and neuroimaging PD tremor parameters on an individualized level.
Methods: We evaluated 26 tremor-dominant PD patients OFF medication in two sessions two months apart. Evaluations included standardized clinical scales, quantitative analysis of tremor using accelerometry, and a resting state-fMRI co-registered with rest tremor accelerometric assessment. Both group and individual level analyses were conducted.
Results: At group level, clinical and accelerometric data did not change across sessions, and showed good to excellent reliability for rest and postural tremor. Significant tremor-related activity was observed in the three nodes of the CTC circuit (Figure 1). A positive correlation across sessions was also observed for the mean tremor-related activity in motor cortex (MC) and cerebellum (CBLM) (MC: $\rho = 0.45$, $p = 0.02$; CBLM: $\rho = 0.39$, $p = 0.05$) (Figure 2). At individual level, tremor-related activity evaluated voxel-by-voxel correlated significantly across sessions in 69.23%, 50%, and 76.92% of patients for MC, thalamus (VLpv) and CBLM respectively (all $p < 0.01$). Subjects with stronger correlation showed lower distance between activity peaks across sessions (Figure 3), and smaller changes in rest tremor amplitude were associated with higher reliability of tremor-related activity in MC (all $p < 0.01$).



Tremor-related activity in the three regions of the CTC circuit. For graphical representation, the cluster-forming threshold was set at $p < 0.001$ (uncorr.) for MC and CBLM; for VLpv, activity within the ROI with a threshold set at $p < 0.05$ (uncorr.) is shown.



Correlation of mean tremor-related activity in each CTC circuit region between sessions. Spearman's correlations applied. Significant *p*-values are shown in bold.



A: Tremor-related activity in MC in one patient (yellow-red) and MC ROI (blue). The ROI activity peak (green lines cross) in this case is in the same voxel in the two sessions. B: Correlation between voxel-by-voxel ICC and activity peak distance in CTC.

Conclusion: Our study demonstrates the robust reliability of neurophysiological and functional neuroimaging measures in investigating tremor mechanisms in PD. These findings support personalized treatments and targeted neuromodulation, advancing PD tremor management.

Disclosure: Supported by International Federation of Clinical Neurophysiology.

EPR-215 | Towards a clinical identification of a cholinergic subtype of Parkinson's disease

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Background and Aims: Several non-motor subtypes of Parkinson's disease (PD) underpinned by specific neurotransmitter dysfunctions have been proposed and clinical tools to identify the noradrenergic subtype have been suggested. In this report, we describe PD cognitive profiles indicating cholinergic versus dopaminergic predominance, aiming at clinically identify a cholinergic subtype of PD, characterized by cognitive dysfunction and disability.

Methods: Data were obtained from the Non-Motor Longitudinal International Study (NILS). Potential cholinergic and dopaminergic cognitive components were identified using two simple cognitive tasks, similarly to the CamPaIGN study: intersecting pentagons copying (P) and lexical fluency (F). Patients were categorized as having impairment in both tests (PF), in one test (P, F) or no impairment (NC). Relationships between cognitive profiles and Clinical Impression of Severity Index (CISI-PD) for Cognition and Disability were investigated with multiple logistic regressions.

Results: Among 1004 patients, PF was observed in 3.9%, P and F were detected in 11.6% and 8.8% respectively, while NC was found in 75.8%. Demographic and clinical differences among groups are shown in Table 1. After including other significant predictors (age, education, disease duration, motor/non-motor burden), PF phenotype was the strongest predictor of moderate/severe cognitive problems (Or = 18.57, $p < 0.001$) and moderate/severe disability (Or = 2.81, $p = 0.023$) (Table 2).

TABLE 1: Group characteristics and differences in demographic and clinical features.

	PF Pentagon copy and Lexical fluency Impairment N = 39	P Pentagon Copy Impairment N = 116	F Lexical Fluency Impairment N = 88	NC No Impairment N = 761	*p* value
Age (years)*	74.4 (7.7)	71.2 (9.8)	67.3 (10.3)	64.83 (10.9)	**< 0.001**[a]
Sex (F/M)	17/22	52/63	31/57	267/495	0.138
Education (years)*	11.0 (2.8)	13.3 (4.4)	14.0 (4.4)	15.1 (4.3)	**< 0.001**[b]
Disease duration (years)*	5.4 (5.5)	5.8 (5.4)	4.1 (4.6)	4.6 (5.0)	**0.022**[c]
SCOPA Motor Part A**	14.1 (4.8)	13.0 (5.6)	12.4 (5.7)	9.8 (5.0)	**< 0.001**[d]
NMSS Total**	46.2 (38.5)	52.0 (40.5)	60.9 (40.1)	44.9 (35.0)	**< 0.001**[e]
MMSE**	22.6 (3.4)	26.6 (2.6)	27.3 (2.7)	28.9 (1.7)	**< 0.001**[f]
MMSE-11**	22.6 (3.4)	26.6 (2.6)	26.3 (2.7)	27.9 (1.7)	**< 0.001**

Symbol "*" means abnormal test, while "-" indicates normal test.
Data are presented as mean (standard deviation) or frequencies, where appropriate.
*Assessed with Kruskal-Wallis test.
*Assessed with Pearson Chi Square test.
**Assessed with Quade's non-parametric ANCOVA (covariates: age, sex, education, disease duration).
a. Significant difference for PF vs F; PF vs NC; F vs NC; P vs NC
b. Significant difference for PF vs F; PF vs P; PF vs NC; PF vs NC; P vs NC; F vs NC
c. Significant difference for PF vs F; PF vs P; PF vs NC; PF vs NC; P vs NC; F vs NC
d. Significant difference for F vs P; P vs NC
e. Significant difference for PF vs NC; P vs NC; F vs NC
f. Significant difference for PF vs P; F vs P; P vs NC
g. Significant difference for PF vs P; PF vs F; PF vs P; F vs P; F vs NC; P vs NC
Abbreviations: C: Cognitive profile; H&Y: Hoehn & Yahr; SCOPA: Scales for Outcome in PArkinson's disease; NMSS; Non-Motor Symptoms Scale; MMSE: Mini Mental State Examination; MMSE-11: minus item 11 (intersecting pentagons copying)

TABLE 2: Multiple logistic regression models for Cognitive Status and Disability.

	Model 1 Moderate/Severe Cognitive Problems		*Model 2 Moderate/Severe Disability*	
	OR	***p* value**	**OR**	***p* value**
C classification		**<0.001**		**0.047**
PF	18.565	**<0.001**	2.807	**0.023**
P	7.532	**<0.001**	1.545	0.098
F	2.168	0.374	1.128	0.679
Age	1.050	0.066	1.013	0.113
Education	1.122	**<0.001**	-	-
Disease duration	1.007	0.911	1.101	**<0.001**
SCOPA Motor A	1.141	**0.003**	1.268	**<0.001**
NMSS Total	1.005	0.425	1.017	**<0.001**

Predictors were selected if significant on a simple logistic regression basis.
Abbreviations: C: Cognitive profile; SCOPA: Scales for Outcome in PArkinson's disease; NMSS; Non-Motor Symptoms Scale;

Conclusion: The use of two simple bedside tests may support the clinical identification of cognitive profiles in PD with cholinergic versus dopaminergic predominance and provide valuable insight on cognitive status and overall disability. This could enable subtype-specific management as outlined in the recently published Dashboard of PD.
Disclosure: Nothing to disclose.

EPR-216 | Exploring spatial and temporal optimisation of deep brain stimulation in Parkinson's disease using adaptive stimulation

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Background and Aims: Although deep brain stimulation (DBS) is an established advanced therapy in Parkinson's disease (PD), there are still limitations in terms of efficacy and side-effects. Recently, this has been challenged by either applying directional or adaptive stimulation. So far, both approaches have not been combined. Here we investigated this combined approach.
Methods: DBS was applied in a care as usual setting in PD patients with either omnidirectional or directional (SenSight) DBS leads and a Percept PC neurostimulator that could adapt stimulation based on the presence of local field potential (LFP) activity (ADAPT-PD Trial, NCT04547712). If adaptive DBS (aDBS) was possible (alpha-beta peak power ≥1.2 μV) and tolerated, subjects were randomized to two aDBS algorithms (single [ST] or dual threshold [DT]) each for 30 days.
Results: Eighty-five subjects were enrolled in the trial ($n = 68$ Primary Cohort, $n = 17$ Directional Stimulation Cohort; including $n = 54$ omnidirectional, $n = 31$ SenSight leads). aDBS evaluation phase included 60 subjects ($n = 53$ DT, $n = 45$ ST; $n = 26$ SenSight leads). 96.8% (30/31) of SenSight leads had adequate alpha-beta power (≥1.2 μV). Combining cohorts, similar "On" time without troublesome dyskinesia was observed versus continuous DBS in DT (94.3%); and in ST mode (93%). TEED trended lower during aDBS (median −12% DT, −12% ST). 59/60 subjects chose to continue aDBS in long-term follow-up. No serious adverse device events occurred through the evaluation phase.
Conclusion: SenSight leads detected alpha-beta peaks at a high rate. aDBS resulted in similar "On" time without troublesome dyskinesia, with a trend for reduced TEED for patients with omnidirectional and directional stimulation.
Disclosure: the study was initiated by medtronic, some authors are medtronic employees.

EPR-217 | Developing a neuromodulation target for GTS: A TMS-EEG study

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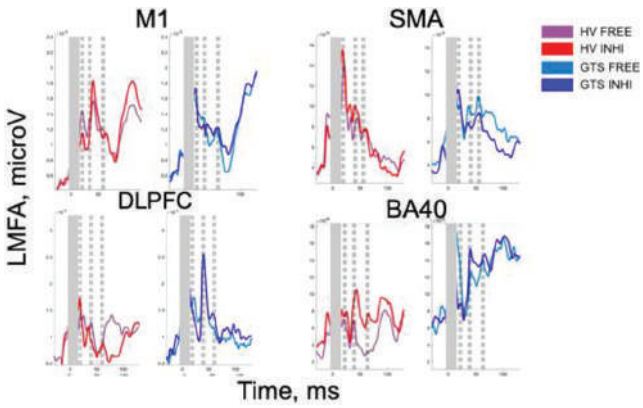
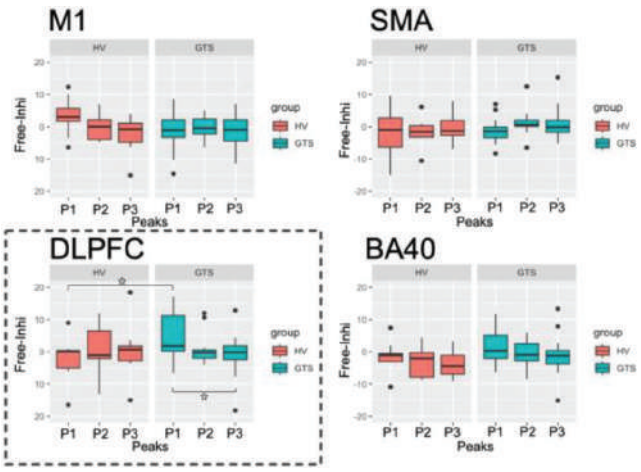
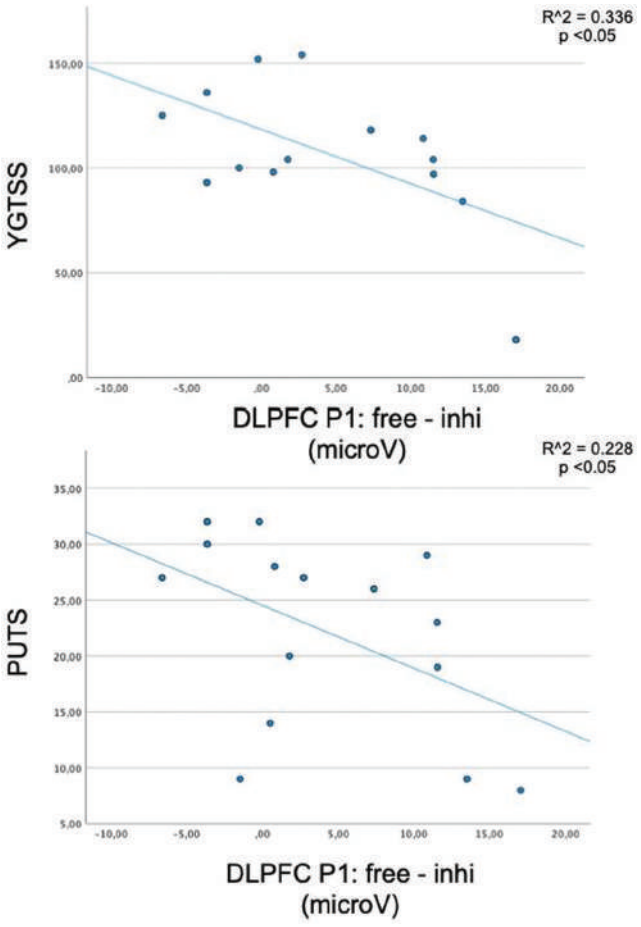
Background and Aims: Neuromodulation techniques have shown efficacy in a series of neurological disorders, but their efficacy depends on appropriate disease-specific targets. TMS-EEG can be used to probe the causal role of network hubs in neurological diseases. Gilles de la Tourette syndrome (GTS) is characterized by vocal and motor tics preceded by a premonitory urge (PU), which is considered the drive of tics. Tics can be voluntarily inhibited at the expense of increasing the PU. We used a transcranial magnetic stimulation (TMS)-EEG integrated approach to identify possible neuromodulation targets aimed at treating disease symptoms. We probed areas involved in PU and tic generation, such as M1, the dorsolateral prefrontal cortex (DLPFC), the Supplementary motor area (SMA) and the Brodmann Area 40 (BA40).
Methods: Seventeen GTS patients and ten healthy volunteers (HVs) underwent TMS-EEG. We collected TMS-evoked potentials (TEPs) from left M1, SMA, DLPFC and BA40 in two conditions: free to tic and voluntary tic suppression, a condition that worsens PU that was matched in HVs by eye blink suppression. We collected clinical scales for tics, PU, and psychiatric symptoms severity.
Results: Contrary to HVs, GTS showed suppression-related negative modulation of DLPFC local TEPs. This correlated negatively with PU Tics Scale and Yale Global Tic Severity scores.



LMFA TEPs of the four stimulated areas. Dotted lines represent the peaks from which the signal was extracted to perform further analysis. Grey bars cover the stimulation artifact.



Boxplots of free-inhi differences across the first three peaks (P1, P2 and P3) for each area. Only DLPFC showed significant peak*group interaction. Stars represent significant post-hoc comparisons.



Clinical correlations. Correlation analysis within the GTS group showed significant negative correlation of free-inhi difference at P1 with PUTS and YGTSS.

Conclusion: Negative DLPFC modulation during tics suppression and its correlation with PU and tics severity suggest a crucial role of this area in GTS pathophysiology. The DLPFC could hence be a promising target for neuromodulation to reduce symptoms in GTS.

Disclosure: Nothing to disclose.

EPR-218 | First steps in noninvasive brain stimulation of subthalamic nucleus in Parkinson's disease

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Background and Aims: Temporal Interference stimulation (TIS) is a novel non-invasive brain electrical stimulation technique that has a potential to reach small size deep brain regions. The approach utilizes two high frequency signals (>1 kHz), which constructively interfere to create low frequency envelope modulating the target structure. The main goal of this pilot work was to verify the capability of TIS to focus the subthalamic nucleus (STN). Second goal was to compare the effect of TIS and conventional deep brain stimulation (DBS) on the pathological beta oscillations in Parkinson's disease.

Methods: Implanted DBS leads were temporally externalized for local field potentials (LFP) recording in 4 patients with Parkinson's disease indicated for STN-DBS therapy. TIS was performed by 2 pairs (f1 = 9.00 kHz; f2 = 9.13 kHz, 2 mA per pair max.) of scalp electrodes placed in frontoparietal regions to focus the maximum of 130 Hz interference envelope into the motor part of the STN.

Results: The maximal amplitude of 130Hz envelope was localized in the motor part of STN. The comparison of the reference LFPs and recordings after TIS and after conventional DBS 5 min sessions showed substantial suppression of beta power peak after both types of stimulation in all patients. Moreover, the power of 130 Hz envelope was significantly ($p < 0.05$) anticorrelated with pathological beta activity during TIS in three patients.

Conclusion: This pilot testing confirmed that TIS is capable to effectively focus STN. The power increase in 130Hz envelope corresponds to the decrease of the pathological beta activity in STN during TIS.

Disclosure: The work was supported by Ministry of Health of the Czechia, grant No. NU21-04-00445 and project LX22NPO5107 (MEYS) financed by European Union-Next Generation EU.

EPR-219 | The height of third ventricle discriminates the gait phenotype in patients with idiopathic normal pressure hydrocephalus

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Background and Aims: Given the high variability of phenomenology, the higher-level gait disorder (HLGD) of patients with idiopathic normal pressure hydrocephalus (iNPH) can be classified into a disequilibrium (wide-based) subtype or a locomotor (parkinsonian) subtype. First, we aimed to obtain several magnetic resonance imaging (MRI) indices used for diagnostic and research purposes in order to assess differences between the two gait phenotypes of iNPH. Second, we explored potential correlations of MRI features with clinical severity scores.

Methods: We enrolled 86 patients (53 males; age range: 69–88 years) diagnosed as probable iNPH. Based on gait evaluation, we identified 29 subjects with disequilibrium subtype and 57 patients with locomotor subtype of HLGD. All patients underwent a comprehensive clinical assessment, including neuropsychological tests, and performed a brain MRI scan for the morphometric measurement of eight linear radiological indices.

Results: Gait phenotypes differed with respect to the height of the third ventricle, which was higher in the locomotor subtype and showed a trend of correlation with the motor score of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS III) and with the continence score of the iNPH Rating Scale.

Conclusion: A greater height of the third ventricle could be a neuroimaging marker of the locomotor phenotype of HLGD in iNPH patients. An increase of this radiological index may reflect a secondary top-down compression on the midbrain. Consequently, the reduced mesencephalic volume may increase the severity of gait disturbance, parkinsonism and urinary dysfunction in iNPH patients.

Disclosure: Nothing to disclose.

MS and related disorders 3

EPR-220 | Exploring the relationship between cognitive impairment, retinal damage, and brain atrophy in multiple sclerosis

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Background and Aims: Cognitive impairment is a debilitating feature of Multiple Sclerosis (MS). Brain atrophy, measured by MRI, is correlated to such clinical scenario. Optical coherence tomography (OCT) may represent a rapid, low-cost, and non-invasive method evaluating neurodegeneration in MS. Our objective was to explore the relationship between cognitive performance, retinal damage, and brain atrophy in people with MS (pwMS).

Methods: 100 pwMS, consecutively enrolled at our MS Center, underwent: neurological examination; cognitive assessment through the Brief Repeatable Battery of Neuropsychological Tests and STROOP test; 3T-MRI scan for the evaluation of brain T2-lesion load and brain volumetric measures using SIENAx software; OCT for the evaluation of peripheral retinal nerve fiber layer (pRNFL) and ganglion cell–inner plexiform layer (GCIPL) thickness. Correlation and regression analyses between cognitive performance, retinal layers mean thickness and brain volumes were performed using SPSS. A p-value ≤0.05 was considered statistically significant.

Results: We found a significant correlation between pRNFL and GCIPL thinning and worse cognitive performance measured by SDMT, and STROOP tests, exploring information processing speed (IPS) and executive functions. T2 lesion volume (T2LV) and normalized white matter volume (nWMV) correlate with cognitive performance in the same cognitive domains. As expected, normalized gray matter volume (nGMV) and normalized brain volume (nBV) showed a significant correlation with cognitive performance in many cognitive domains.

Conclusion: Our results showed a relationship between retinal damage and cognitive performance in the same cognitive domains (IPS and executive functions) related with WM damage. Retinal damage (measured by OCT) may be a useful marker for cognitive decline in pwMS.

Disclosure: Nothing to disclose.

EPR-221 | First assessment of sNfL integration in everyday clinical practice – Lessons from NeofiLos

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Background and Aims: Neuroaxonal damage results in release of neurofilaments such as neurofilament light chain (NfL) with elevated NfL potentially indicating RMS disease activity 1–3. Elevated levels may reveal "subclinical" disease before lesions or clinical symptoms appear4. Measuring sNfL may help elucidate subclinical disease activity potentially contributing to optimized decision making. NeofiLos enables office-based centers to access serum NfL (sNfL) testing aiming to investigate utility and practical embedding of serial measurements into everyday clinical practice in Germany.

Methods: NeofiLos is an ongoing prospective data collection at ~80 office-based neurologists assessing utility of sNfL from physician's perspective in RMS patients treated with ofatumumab or other disease-modifying therapies. sNfL will be measured at baseline followed by quarterly interval up to 5× per patient. Values embedded into scientific context using patient demographics are reported to neurologists evaluating value and assessing implementation of sNfL into clinical routine setting.

Results: These interim results will depict the assessment of integrating sNfL measurements into everyday clinical practice over time by highlighting challenges, possibilities and further needs. At baseline, physicians stated that sNfL-testing can be integrated into their daily practice routine without major restructuring (Median6.6; 7-point-Lickert-scale, SD1.1, $n = 61$). Furthermore, data will show details on accessibility and reimbursement as prerequisites for implementation in daily practice.

Conclusion: This sNfL pilot project in clinical routine setting is highlighting the importance of sNfL as additional parameter for optimal MS patient management gathering insights into translation of sNfL-testings into clinical practice. Thus, NeofiLos is a highly valuable source for defining actual gaps and optimizing future patient care.

Disclosure: Thebault S et al. Mult Scler. 2022; 28(10):1491–1497. Dietmann AS et al. J Neurol. 2023; 270(3): 1416–1429. Kuhle J et al. Mult Scler. 2020; 26(13): 1691–1699. Akgün K et al. Neurol Neuroimmunol Neuroinflamm. 2019; 6(3): e555. TZ reports personal fees for lecturing and consulting from Biogen, BMS, F. Hoffmann-La Roche Ltd, Merck, Novartis, Sanofi, Teva and Almirall; and grants or research support from Biogen, F. Hoffmann-La Roche Ltd, Teva, Sanofi and Novartis KS and ISS are employees of Novartis.

EPR-222 | Hyperreflective foci in the inner retina are not associated with optic neuritis in multiple sclerosis

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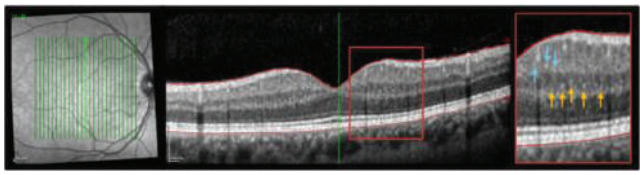
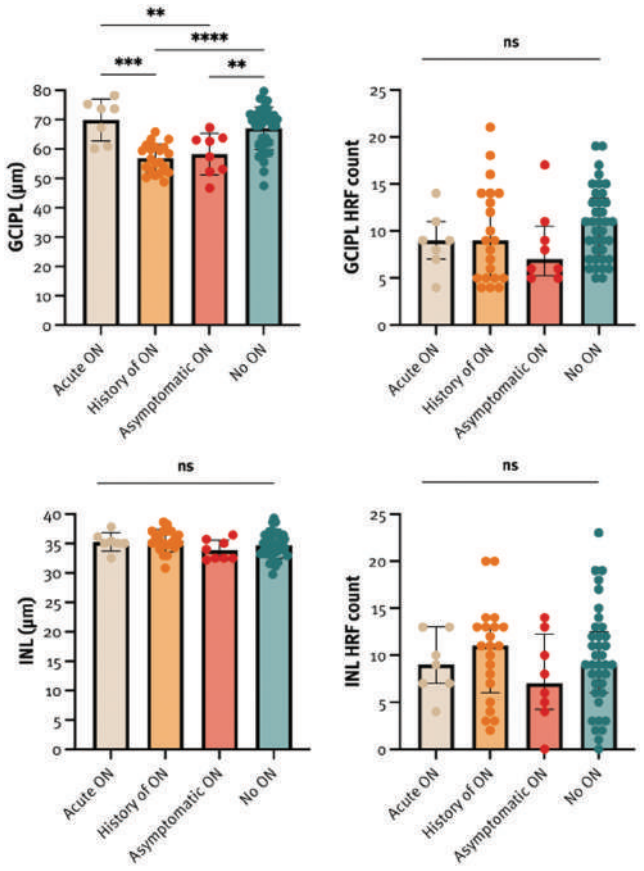
Background and Aims: Optic neuritis (ON) is a common symptom of multiple sclerosis (MS), with activated microglia being associated with neuroaxonal damage and its associated thinning of the ganglion cell-inner plexiform layer (GCIPL). Retinal microglia may be visualized as hyperreflective foci (HRF) by optical coherence tomography (OCT).

Methods: In this cross-sectional retrospective study, we included patients with MS (pwMS) who had undergone an OCT scan. HRF counting was performed separately in the GCIPL and the inner nuclear layer (INL). Eyes were grouped into four categories: (i) acute ON (≤7 days), (ii) clinical history of ON (≥6 months), (iii) asymptomatic ON (interocular asymmetry of ≥5 μm for pRNFL and/or ≥4 μm for GCIPL), and (iv) no ON.



HRF Protocol. Macular scan and HRF visualisation in a patient with MS. HRF were defined as isolated, small sized (<30 μm), punctiform elements with moderate reflectivity but without any back shadowing.

Results: In all, 71 eyes of 36 pwMS (47.2% female, median age 31.5 years (24.9–43.8), median disease duration 1.8 years (0.1–10.2), median EDSS 1.0 (0–2.5)) were included. The GCIPL thickness was significantly lower in patients with a history of ON ($n = 21$; 56.8 μm (4.8)) and/or asymptomatic ON ($n = 8$; 58.2 μm (7.0)) compared to acute ON ($n = 7$; 69.8 μm (7.2)) and eyes without ON ($n = 37$; 69.8 μm (7.2); all $p < 0.01$). We found no differences in the INL thickness, and the GCIPL HRF and INL HRF count.



The GCIPL thickness was significantly lower in eyes with a history of ON and asymptomatic ON compared to with acute ON and eyes without ON. No differences in the INL thickness, and the GCIPL HRF and INL HRF count were found.

Conclusion: HRF count does not seem to be affected by ON, implying that (i) the HRF count may not represent activated retinal microglia, and/or (ii) microglia may be activated in the stages of ON that were not included in the study. Further studies are needed to clarify the pathophysiology of MS.

Disclosure: Nothing to disclose.

EPR-223 | Circulating extracellular vesicles exhibit immune cell surface marker enrichment in multiple sclerosis patients

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Background and Aims: Relapsing-remitting multiple sclerosis (RRMS) is a prevalent autoimmune CNS disease but pathophysiologically more heterogeneous than other demyelinating disorders such as Neuromyelitis Optica Spectrum Disorder (NMOSD) or Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD). In the present study, we hypothesized that the detection of immune cell surface markers in extracellular vesicles (EVs) may allow to discriminate RRMS from NMOSD and MOGAD.

Methods: EVs were isolated using a size exclusion-based-technique (SmartSEC, System Biosciences) in plasma samples from RRMS patients ($n=22$), NMOSD ($n=17$) and MOGAD ($n=10$). The concentration and the size of EVs were assessed by Nanoparticle Tracking Analysis (NTA, Malvern Panalytical). Morphological examination of EVs was carried out by cryo-electron microscopy (cryo-EM). The level of EV surface markers was assessed using MACSPlex Capture Beads (Miltenyi) allowing simultaneous detection of 37 EV markers, including a majority of immune cell-specific proteins, in individual samples, by flow cytometry.

Results: Intact EVs were visualized by cryo-EM. EVs were predominantly in the range of exosomes according to NTA measurements. With this method, a lower concentration of EVs was observed in RRMS than in NMOSD/MOGAD samples, although the mean EV size was similar. Strikingly, MACSPlex/flow cytometry measurements revealed significantly higher levels of immune cell markers such as CD19, CD29, CD40, CD44 and CD69P in RRMS than in NMOSD/MOGAD EVs. No difference was found between NMOSD and MOGAD.

Conclusion: The enrichment of specific immune cell surface markers in EV preparations may represent an immunological signature of RRMS.

Disclosure: A.C. has received speakers'/board honoraria from Actelion (Janssen/J&J), Alexion, Almirall, Bayer, Biogen, Celgene (BMS), Genzyme, Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Teva, all for hospital research funds. He received research support from Biogen, CSL Behring, Genzyme, and UCB, the European Union, and the Swiss National Foundation. He serves as associate editor of the European Journal of Neurology, on the editorial board for Clinical and Translational Neuroscience and as topic editor for the Journal of International Medical Research. M.E.E. has received travel grants and consulting fees from Biogen, Novartis, Teva, Merck, and Roche. K.G., N.M. and C.S. are employees of CSL Behring. V.L.F., K.D. and V.P. have no disclosures.

EPR-224 | Assessment of RFC1 gene expansion in multiple sclerosis patients

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Background and Aims: Biallelic expansion of the AAGGG sequence in the Replication Factor C Subunit 1 (RFC1) gene is implicated in the pathogenesis of Cerebellar Ataxia with Neuropathy and Vestibular Areflexia syndrome (CANVAS). The spectrum of RFC1-related neurological disorders is growing; some case reports have shown the association between the AAGGG expansion and central nervous system inflammatory lesions, but this relationship remains unclear. We explored the prevalence of RFC1 expansion in multiple sclerosis (MS) patients.

Methods: A cohort of 2788 MS patients and 415 healthy controls (HC), with already available whole-genome genetic data obtained with different Illumina genotyping platforms, were eligible to the study. The presence of the homozygous haplotype linked to AAGGG expansion was evaluated by assessing four single-nucleotide polymorphisms (SNPs; rs2066790, rs11096992, rs17584703, and rs6844176) previously observed to be shared by CANVAS patients.

Results: Within our cohort, 58 individuals were carriers of the homozygous haplotype, 54 MS and 4 HC. A twofold increase in the haplotype frequency was observed in MS patients compared to HC (1.94% vs. 0.96%). Among the 54 MS patients, 72% were women, the average age at symptom onset was 32 years and 20.3% had a diagnosis of primary progressive MS.

Conclusion: Our study revealed the presence of the investigated haplotype in a small proportion of MS patients. Polymerase Chain Reaction analyses are ongoing to validate this finding, providing comprehensive insight into the observed association. If confirmed, our data suggest the importance of excluding RFC1-associated spectrum disorders when performing a diagnosis of MS.

Disclosure: G. Visentin, A. Giordano, S. Sciré, G. Bellantuono, M. Sorosina, E. Mascia, K. Misra, P. Carrera: nothing to disclose. M. Filippi is Editor-in-Chief of the Journal of Neurology, Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology; received compensation for consulting services, direction of educational events, participation on Advisory Boards and/or speaking activities from Alexion, Almiral, Bayer, Biogen, Bristol-Myers Squibb, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda, and TEVA; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health and Research, and Fondazione Italiana Sclerosi Multipla. F. Esposito has received honoraria from Merck and Biogen.

EPR-225 | Ocrelizumab-induced colitis in patients with multiple sclerosis: An emerging safety issue

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Background and Aims: Drug-induced colitis is being increasingly diagnosed in people on biological therapy, including patients with Multiple Sclerosis (pwMS) under ocrelizumab. The exact pathophysiology is unknown, but immunological dysregulation through B-cell depletion has been proposed as a possible mechanism. We present a case of ocrelizumab-associated colitis (OAC) and review available literature on the topic.

Methods: We report the case of a pwMS with suspected OAC, who presented to our Center in December 2023. A retrospective literature search on OAC was also conducted from March 2020 to January 2024.

Results: A 38-year-old female with relapsing-remitting MS started ocrelizumab on April 2022 after having failed fingolimod. Several weeks after treatment initiation, she developed watery diarrhea, vomiting and lower abdominal pain, exacerbated by ocrelizumab re-treatment in December 2022, requiring hospitalization. History of infection, fever, travelling, ill contact or bowel disease was denied. Flexible sigmoidoscopy was normal and biopsies of various part of duodenum and left colon showed non-specific chronic inflammation. Patient was treated with oral prednisone with improvement and a diagnosis of suspected OAC was made. Table 1 summarizes published reports of OAC among pwMS. Furthermore, an analysis of the Food and Drug (FDA) Adverse Event Reporting System pharmacovigilance database revealed 43 OAC cases, out of 15.701 adverse events reported for ocrelizumab.

TABLE 1: Summary of ocrelizumab-associated colitis ($n = 12$) among patients with multiple sclerosis.

MS= multiple sclerosis, yr: years; OCRE= ocrelizumab; GI= gastrointestinal; IBD= inflammatory bowel disease; PPMS= primary progressive multiple sclerosis; SPMS= secondary progressive multiple sclerosis; RRMS= relapsing remitting multiple sclerosis; M= male subjects; F= female subjects; UC= ulcerative colitis; ASA= acetylsalicylic acid; IV= intravenous; ER= endoscopic; CMV= cytomegalovirus; NA= data not available.

Conclusion: FDA recently issued a warning regarding OAC, which could be potentially severe. We highlight the importance for clinicians of being aware of this safety risk and of a prompt intervention with multidisciplinary approach, including endoscopic evaluation and timely treatment.

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EPR-226 | Cladribine tablets in highly-active relapsing MS real-world effectiveness in UK clinical practice (CAMELOT-MS)

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Background and Aims: Real-world evidence increasingly informs treatment choice in multiple sclerosis (MS). Cladribine tablets (CladT) received EU marketing authorisation in August 2017 in high-disease activity relapsing-remitting MS (HDA-RRMS). The aim of the study was to understand effectiveness and safety of CladT in UK real-world setting up to 5 years after CladT initiation.

Methods: Phase 4 observational multi-centre study for patients who initiated CladT monotherapy for HDA-RRMS.

Results: 116 patients were enrolled, 40 (34.5%) were disease-modifying therapies (DMT) naïve. 112 patients (96.6%) completed both treatment courses and 4 (3.4%) discontinued treatment. Annualized relapse rate (ARR) during pre-treatment (-1-0 years) was 0.595 (95% CI: 0.470; 0.753). A declining ARR trend was observed after CladT initiation with an ARR of 0.101 (95% CI: 0.052; 0.194) during 0–1 years, 0.052 (95% CI: 0.023; 0.115) for 1–2 years and 0.063 (95% CI: 0.024; 0.169) for 4–5 years. Relapse-free rate after CladT initiation was 0.75 (95% CI: 0.58; 0.86) at 5 years. Only TEAEs of special interest were reported. Serious TEAE was reported in 1 (0.9%) patient; no TEAEs led to death. CladT-related TEAEs were lymphopenia (33/116, 28.4%), herpes zoster (4/116, 3.4%), onychomycosis and oral herpes (1/116, 0.9% each).

Conclusion: Overall ARR showed a declining trend over 5 years after CladT initiation in both DMT naïve and platform therapy groups. There was no significant difference in relapse-free rates. This study showed a tolerable safety profile with CladT.

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has received travel support, speaker honoraria and consultation fees from Genzyme, from Merck, Novartis, Roche, the MS Academy and the Italian Multiple Sclerosis Foundation (FISM). Nikos Evangelou: speaker fees and honoraria from Biogen, Merck, Novartis, and Roche. Tarunya Arun has received speaker fees, support for scientific meetings and honoraria for advisory work from Merck, Novartis, Roche, and Genzyme. Ei Zune The: None. Paul Gallagher: funding for research, speaking honoraria, travel or educational support from Sanofi Genzyme, Novartis, Biogen, Merck, Bristol Myers Squibb, and Roche pharmaceuticals. Hannah Evans is an employee of Merck Serono Ltd., Feltham, UK, an affiliate of Merck KGaA.

EPR-227 | Misdiagnosis and underdiagnosis of multiple sclerosis: A systematic review and meta-analysis

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Background and Aims: Misdiagnosis and underdiagnosis of multiple sclerosis (MS) pose significant risks to patients and healthcare systems. Yet, there is a lack of high-level evidence on the frequency of such errors. We here conducted a systematic review and meta-analysis of the prevalence of MS misdiagnosis and underdiagnosis, time delay to correct diagnosis, and the impact of sex.

Methods: An Ovid Medline and Embase database search until September 16, 2023, yielded 3910 studies. Based on pre-defined criteria (original studies on MS diagnostic errors with ≥10 individuals, excluding conference abstracts and reviews) 62 were included for qualitative synthesis and 24 for random-effects meta-analyses, assessing bias with the Newcastle-Ottawa scale. Main outcomes included the proportion of misdiagnosis, underdiagnosis, and diagnostic delay.

Results: Frequency of MS misdiagnosis (incorrect assignment of MS diagnosis) ranged from 5% to 41%, with a pooled proportion of 15% [95%-CI: 9%–26%, 1621 cases] (Figure 1A). Delay to rectify MS misdiagnosis ranged from 0.3 to 15.9 years. MS underdiagnosis (unrecognized diagnosis of MS) ranged from 3% to 58%, with a pooled proportion of 36% [95%-CI: 20%–55%, 728 cases] (Figure 1B). Diagnostic delay for underdiagnosed cases was 1.5 years [95%-CI: 1.1–1.9] (Figure 2). A sub-analysis of 8 studies indicated that women were 2.1 times more likely to be misdiagnosed with MS compared to men [95% CI: 1.53–2.86] (Figure 3).

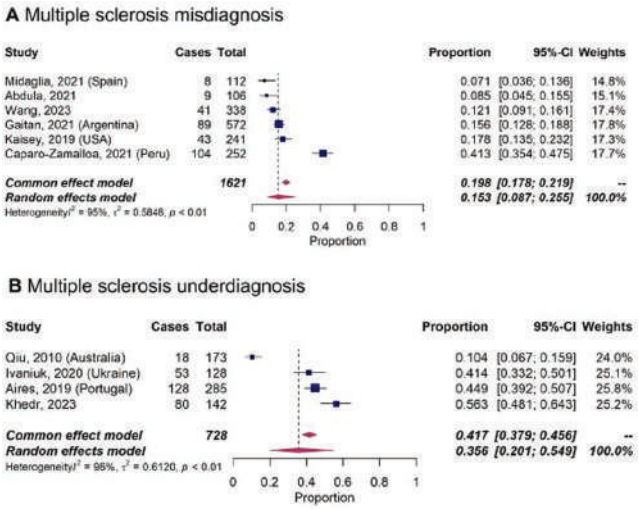

FIGURE 1: Meta-analysis on misdiagnosis and underdiagnosis proportions in multiple sclerosis (MS).

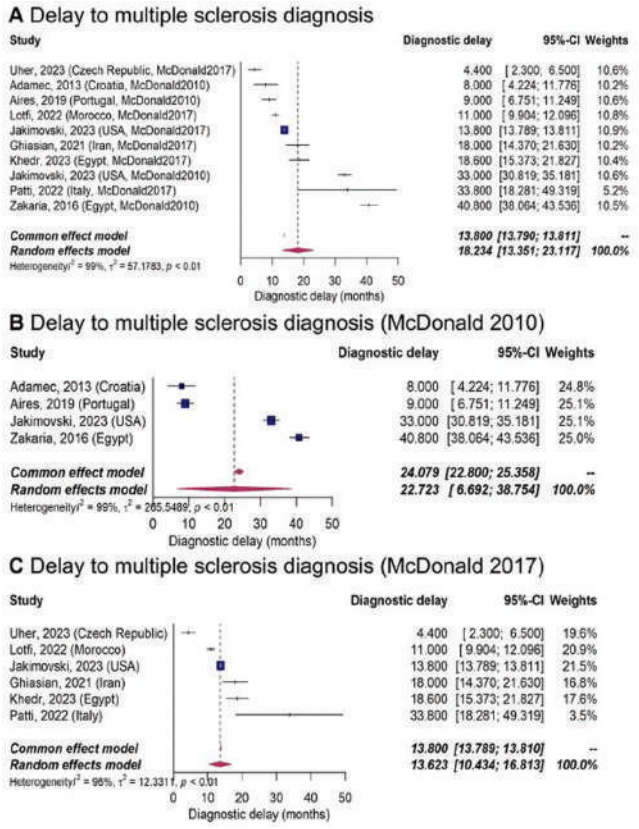

FIGURE 2: Meta-analysis on diagnostic delay in cases with MS underdiagnosis.

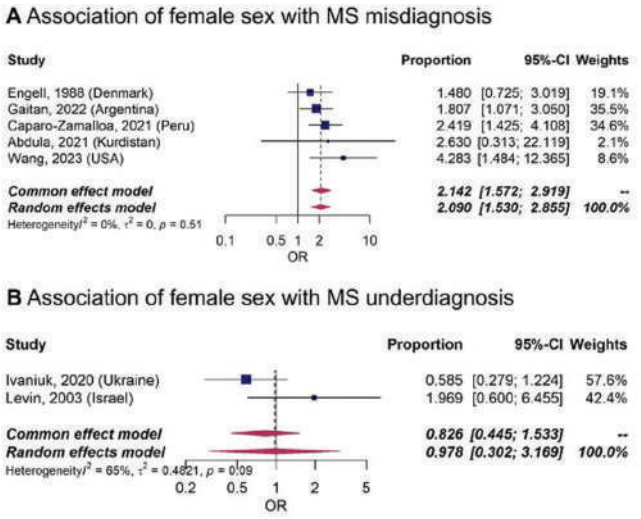

FIGURE 3: Meta-analysis on association of female sex with multiple sclerosis misdiagnosis and underdiagnosis.

Conclusion: This study provides high-level evidence for the high prevalence of MS misdiagnosis and underdiagnosis. Future studies should explore the causes of diagnostic challenges, the influence of sex, and interventions to improve diagnostic accuracy.

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EPR-228 | **Liver injury in patients with multiple sclerosis: A case series**

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Background and Aims: Increase in liver enzymes among patients with multiple sclerosis (pwMS) is frequent, but often underreported and insufficiently investigated. Incidence and predictive factors are unknown. We describe liver injury (LI) in pwMS, documenting histological liver disease pattern, diagnosis and consequences for therapy.

Methods: PwMS who underwent liver biopsies because of increased liver enzymes during/after DMTs were included. Indices of hepatocellular damage, autoimmune antibodies and viral serology were evaluated, along with liver biopsies.

Results: Nine patients were included: baseline characteristics are reported in Table 1. Table 2 summarizes LI course and characteristics in each patient. Five pwMS developed LI under treatment with DMTs, 3 with fingolimod and 2 with natalizumab, while 1 subject was untreated. Four subjects were under intravenous methylprednisolone. In 6/9 patients anti-nucleus autoantibodies were found and autoimmune hepatitis was suspected. No patients had viral infection. There was no evidence of metabolic or storage liver disease. On liver biopsies, no patient had histology consistent with autoimmune hepatitis. PwMS under methylprednisolone and natalizumab developed severe acute hepatitis, with confluent necrosis. Moderate inflammation in the portal tracts was found in one case of methylprednisolone and in another treated with natalizumab. Patients treated with fingolimod exhibited vascular alterations, suspicious for porto-sinusoidal vascular disease, with minimal lobular inflammation. One subject, undergoing methylprednisolone during fingolimod treatment, had overlapping features with pwMS under methylprednisolone. Figure 1 displays slides of histological findings.

TABLE 1: Demographic and clinical characteristics of study population.

	ALL PATIENTS
Total N (Female n, %)	9 (7, 77.8)
Age at liver enzyme elevation (y), mean (SD)	37.0 (10.7)
MS Duration at liver enzyme elevation (y), median (IQR)	7.7 (3.3-12.7)
EDSS at liver enzyme elevation, median (IQR)	1.5 (1.0-2.0)
Relapsing Remitting Phenotype, N (%)	9 (100)
Treatment characteristics Ongoing treatment at liver enzyme elevation, N (%) •Fingolimod •Natalizumab •Methylprednisolone •Untreated	 3 (33.3) 2 (22.2) 4 (44.4) 1 (11.1)
Time between treatment start and liver enzyme elevation (m), mean (SD) •Fingolimod •Natalizumab •Methylprednisolone	 38.7 (60.1) 8.0 (1.4) 0.3 (1.0)
Time between treatment start and liver enzyme elevation in each treated patient (m) •Case 1, fingolimod •Case 2, fingolimod •Case 3, natalizumab •Case 4, fingolimod and methylprednisolone •Case 6, methylprednisolone •Case 7, methylprednisolone •Case 8, methylprednisolone •Case 9, natalizumab	 3.0 5.0 8.0 108.0 and 3.0 1.0 1.0 2.0 2.0

N= number of subjects; Y= years; M= months; SD= standard deviation; IQR= interquartile range; MS= Multiple Sclerosis; EDSS= Expanded Disability Status Scale.

TABLE 2: Livery injury course and characteristics in each patient.

M= male subjects; F= female subjects; DMT= Disease Modifying Treatment; NTP= methylprednisolone; AST= aspartate aminotransferase; ALT= alanine aminotransferase; GGT= gamma-glutamyl transferase; U/L= unit per liter; d= days; ANA= antinuclear antibody; ASMA= anti-smooth muscle antibody; NASH= non-alcoholic steatohepatitis; PSVD= porto-sinusoidal vascular disorder; DMF= dimethyl fumarate; OCRE= ocrelizumab; OFA= ofatumumab; NA= data not available.

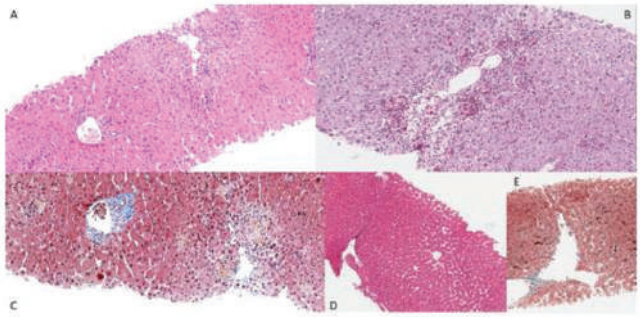

FIGURE 1: Slides of histological findings. A, B, C: methylprednisolone and natalizumab induced liver injury; D, E: fingolimod.

Conclusion: LI in pwMS is a concern. Vigilant monitoring and a multidisciplinary approach are fundamental. Liver biopsy can contribute in differential diagnosis and informing therapeutic decisions.

Disclosure: CZ: Astrazeneca, Biogen, Bristol Myers Squibb, Janssen, Merck, Novartis, Roche, Sanofi. VV, JS, MM, MR and FP: nothing to disclose. LM: Alexion, Biogen, Celgene, Merck, Novartis, Roche, Sanofi. MAR: Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva. She receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and Fondazione Italiana Sclerosi Multipla. She is Associate Editor for Multiple Sclerosis and Related Disorders. MF: Alexion, Almirall, Biogen, Bristol-Myers Squibb, Horizon, Merck, Novartis, Roche, Sanofi; Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Horizon, Janssen, Neopharmed Gentili, Novo Nordisk, Takeda, TEVA. He is Editor-in-Chief of the Journal of Neurology, Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA.

MS and related disorders 4

EPR-229 | **Abstract withdrawn**

EPR-230 | **Frexalimab reduces plasma neurofilament light chain in relapsing multiple sclerosis: Week 48 data from a phase 2 trial**

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Background and Aims: Frexalimab, a second-generation anti-CD40L monoclonal antibody, demonstrated safety and efficacy in participants with relapsing multiple sclerosis (pwRMS) in the 12-week (W) double-blind period of a phase 2 trial (NCT04879628), with an 89% reduction in new gadolinium-enhancing lesions in the high-dose group versus placebo. This was accompanied by a 24% reduction in plasma neurofilament light (pNfL), a biomarker of neuroaxonal damage. Here, we describe changes in pNfL levels with frexalimab treatment until W48.

Methods: 129 pwRMS were randomized 4:4:1:1 to frexalimab-high, frexalimab-low, placebo-high, or placebo-low groups; participants receiving placebo switched to respective frexalimab groups at W12. Plasma samples were collected at baseline, W12, W24 and W48, and pNfL levels were measured using the Simoa® NF-LIGHT™ assay. Here, geometric means are reported at baseline and W48. A one-way ANOVA was used to examine differences in pNfL levels across treatment groups at baseline. Differences from baseline were calculated using percent change.

Results: 125/129 (97%) participants completed the double-blind period and entered the open-label extension. At baseline ($n=123$), pNfL levels (geometric mean [SD]) were similar across groups ($F=0.09$, $p=0.97$): 11.9 [2.0] in frexalimab-high, 12.7 [1.8] in frexalimab-low, 12.5 [1.9] in placebo-high/frexalimab-high, and 12.2 [1.8] pg/mL in placebo-low/frexalimab-low. At W48 ($n=108$), pNfL levels were reduced to 6.7 [2.0] in frexalimab-high, 8.1 [1.7] in frexalimab-low, 9.6 [1.7] in placebo-high/frexalimab-high, and 7.8 [2.1] pg/mL in placebo-low/frexalimab-low corresponding to a 41%, 35%, 24%, and 33% reduction from baseline, respectively.

Conclusion: The observed reduction in pNfL through W48 provides evidence that frexalimab markedly reduces neuroaxonal damage in pwRMS.

Disclosure: Jens Kuhle: speaker fees, research support, travel support, and/or served on advisory boards of the Swiss MS Society, Swiss National Research Foundation (320030_189140/1), University of Basel, Progressive MS Alliance, Bayer, Biogen, Celgene, Merck, Novartis, Octave Bioscience, Roche, and Sanofi. Patrick Vermersch: Received honoraria and/or consulting fees (Janssen, Biogen, Sanofi, Novartis, Teva, Merck, Roche, Imcyse, AB Science, and BMS-Celgene) and research support (Novartis, Sanofi, and Roche). Biljana Djukic, Svend S. Geertsen, Andrea T. Shafer, Philippe Truffinet:

Employees of Sanofi (may hold shares and/or stock options in the company). Gavin Giovannoni: Received compensation over the last five years for receiving research support or serving as a consultant or speaker (AbbVie, Actelion, Atara Bio, Biogen, Canbex, Celgene, EMD Serono, Japanese Tobacco, Sanofi, Genentech, GlaxoSmithKline, GW Pharma, Merck, Novartis, Roche, Synthon BV, and Teva).

EPR-231 | Pregnancy outcomes after glucocorticosteroid and apheresis in pregnancy in women with multiple sclerosis

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Background and Aims: Information on pregnancy outcomes after high-dose intravenous glucocorticosteroid (ivGC) and apheresis exposure in women with Multiple Sclerosis (MS) is scarce. TOur objective is to assess pregnancy outcomes after ivGC and apheresis treatment in women with MS.

Methods: Pregnancies with ivGC and/or apheresis exposure, documented in the German Multiple Sclerosis and Pregnancy Registry are presented. Information on pregnancy outcomes was collected with a standardized questionnaire in regular telephone interviews during pregnancy and postpartum. For analysis, this cohort was stratified into the following groups: (i) ivGC only (ii) Apheresis with or without ivGC iii) DMT matched unexposed control group.

Results: 313 pregnancies were exposed to ivGC, 30 to apheresis (25 in combination with ivGC, 5 to apheresis only) and 938 matched controls. IvGC versus controls showed a significant difference in small for gestational age (SGA) (26.2% vs. 18.6%, $p=0.005$), and lower birthweight (3134 g ±600 g vs. 3259 g ±587 g, $p=0.001$) whereas major congenital malformations (4.47% vs. 4.16%, $p=0.94$) did not. Preterm birth (PTB) (12.7% vs. 8.74%, $p=0.057$) showed a positive trend towards significance. In the apheresis group, birthweight (2731 g ±783 g vs. 3134 g ±600 g, $p=0.010$) was significantly lower compared to ivGC, whereas PTB (23.3% vs. 12.7%, $p=0.156$) and SGA (36.7% vs. 26.2%, $p=0.310$) showed no significant differences. Further adjusted analysis will be presented at the time of the conference.

Conclusion: IvGC exposure showed statistically significant impact on SGA and decreased mean birth weight significantly. Compared to ivGC alone, pregnancies exposed to apheresis have a higher risk of PTB and SGA, but differences did not reach statistical significance. Our data adds useful information on pregnancies with generally healthy newborns after treatment with ivGC and apheresis in pregnancy but is limited by the small sample of apheresis pregnancies.

Disclosure: KDK has nothing to disclose. SH has nothing to disclose. NB received payment for manuscript writing from Thieme. NF received speakers' honoraria and a sponsorship for congress participation from Biogen GmbH. LW received travel grants from Novartis. RG has received speaker honoraria and research support from Bayer-Schering Healthcare, Biogen-Idec Germany, Chugai, Eisai, Merck Serono, Nikkiso Pharma, Novartis, Roche, Sanofi-Genzyme and TEVA, has received consulting honoraria from CSL Behring, Baxter, Janssen and Talecris and has stock options in Bayer, Merck and Roche. KH has received speaker honoraria and research support from Bayer, Biogen, Merck, Novartis, Sanofi-Genzyme, Roche and Teva, has received support for congress participation from Bayer, Biogen, Merck, Roche, Sanofi Genzyme and Teva, and has served on scientific advisory boards for Bayer, Biogen, Sanofi, Teva, Roche, Novartis and Merck. S.T. received speakers' honoraria from Bayer Healthcare and Biogen GmbH, payment for manuscript writing from HEXAL AG as well as sponsorship for congress participation from Biogen GmbH.

EPR-232 | Remibrutinib, a BTKi, has no impact on serum immunoglobulin levels: Insights from chronic spontaneous urticaria

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Background and Aims: Remibrutinib is a highly selective, potent, covalent, oral Bruton's tyrosine kinase inhibitor (BTKi) that downregulates B cell as well as myeloid cell activation without cellular depletion. Here, we report on serum immunoglobulin (Ig) levels over time in a Phase 2b core (NCT03926611) and extension (NCT04109313) study of remibrutinib in patients with chronic spontaneous urticaria (CSU), receiving various doses for up to 52 weeks including 100 mg b.i.d.,

the dosing regimen being evaluated in the Phase 3 REMODEL trials (NCT05147220, NCT05156281) in relapsing multiple sclerosis (MS).

Methods: Patients were randomized to receive various doses of remibrutinib (10–100 mg q.d./b.i.d.) or placebo for up to 12 weeks (core study). Eligible patients entered a 52-week open-label extension study with remibrutinib 100 mg b.i.d. Total serum levels of different immunoglobulins were assessed at baseline, Week 12 (end of core) and Week 52 (end of extension).

Results: Of the 309 patients included in the analysis, 194 rolled-over to the 52-week extension. No relevant changes in the total serum immunoglobulin levels up to Week 12 and Week 52 were observed. In the 194 patients receiving remibrutinib 100 mg b.i.d. in the extension study (mean age: 45.5 years; % female: 71.6), mean baseline and Week 52 IgG levels (μg/mL) were 11.0 ±2.41 and 10.5 ±2.47, respectively, and the corresponding mean IgM levels were 1.0 ±0.80 and 0.9 ±0.73.

Conclusion: Remibrutinib treatment did not affect total immunoglobulin levels in CSU patients of phase 2 studies, including with long-term treatment up to 52 weeks with 100 mg b.i.d., the dose used in MS clinical trials.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-233 | TYSABRI® observational program: Intravenous to subcutaneous natalizumab efficacy and safety switch analysis

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Background and Aims: The Tysabri® Observational Program (TOP) is the largest real-world observational study to inform on long-term safety and effectiveness of natalizumab (Biogen, NTZ-B) in relapsing remitting multiple sclerosis in clinical practice. This analysis compares efficacy and safety outcomes in patients switching from intravenous (IV) to subcutaneous (SC) NTZ-B.

Methods: Annualized relapse rates (ARR) were compared in the 6-month periods before and after switch. Mean annual increase in Expanded Disability Status Scale (EDSS) scores was compared between the periods of 4 clinical visits pre-switch and 2 visits post-switch. Serious adverse events (SAEs) were assessed in the period 6 months post-switch. Sub-analysis was also performed for patients treated with SC NTZ-B with an extended 6-week dosing interval (Q6W).

Results: As of May 2023, TOP included 6321 patients. 448 patients switched from IV to SC NTZ-B and had ≥6 months follow-up on SC NTZ-B. ARR was 0.080 (95% confidence interval [CI]: 0.051, 0.126) pre-SC NTZ-B and 0.076 (95% CI: 0.047, 0.121) post-SC NTZ-B switch ($p=0.847$). Mean annual EDSS increase was 0.026 pre-SC NTZ-B and 0.077 ($p=0.085$) post-SC NTZ-B switch. A total of 11 SAEs were reported in 10 patients (2.2%), none related to NTZ-B treatment or MS relapse. In the Q6W sub-analysis ARR was 0.042 (95% CI: 0.016, 0.112) prior to SC switch, compared to 0.085 (95% CI: 0.043, 0.167) post-SC switch ($p=0.258$). There was no significant difference in EDSS score change.

Conclusion: Efficacy and safety appear to be maintained in patients switching from IV to SC NTZ-B formulation, also with Q6W dosing interval.

Disclosure: Study supported by Biogen. LK: no personal compensation; institutions received research support for: steering committee, advisory board & consultancy fees (Abbvie, Actelion, Auriga Vision, Bayer HealthCare, Biogen, Celgene, df-mp, Eli Lilly, EMD Serono, Genentech, Genzyme, GSK, Janssen, Merck, Minoryx, Novartis, Roche, Sanofi, Santhera, Senda Biosciences, Shionogi, Wellmera); speaker fees (BMS, Celgene, Janssen, Merck, Novartis, Roche); educational activities (Biogen, Desitin, Novartis, Sanofi, Teva); license fees for Neurostatus products; grants (EU, Innosuisse, Novartis, Roche, Swiss MS Society, Swiss National Research Foundation). HW: honoraria (AbbVie, Actelion, Alexion, Biogen, Cognomed, Evgen, F Hoffmann-La Roche, MedDay, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva); research support (Biogen, GSK, Roche, Sanofi). HB: institution received compensation for: consulting, talks & advisory/steering board activities (Alfred Health, Biogen, Genzyme, Merck, Novartis); research support (Biogen, Merck, MS Research Australia, National Health and Medical Research (Australia), Novartis, Oxford Health Policy Forum, Pennycook Foundation, Roche). MT: consultancy honoraria (Biogen, Merck Serono, Novartis, Roche); speaker honoraria (Biogen, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva); research grants for institution (Biogen, Merck Serono, Novartis, Roche). TS: consultancy honoraria & travel fees (Biogen, Novartis). ZS/AD: employees of & own stock/stock options in Biogen.

EPR-234 | Disability trajectories over time in pediatric and adult-onset multiple sclerosis patients

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Background and Aims: To compare disability trajectories over time and the risk of reaching the first progression independent of relapse activity (PIRA) event in pediatric onset (POMS; ≤18 years), adult onset (AOMS; 19–49 years) and late onset (LOMS; >49 years) relapsing-remitting multiple sclerosis (RRMS).

Methods: MS patients with a first visit within 1 year from onset, ≥5-year follow-up and ≥1 visit every 6 months were selected from the Italian MS Registry. Disability trajectories over time and risk of PIRA event were assessed by longitudinal models for repeated measures (adjusted for sex, proportion of follow-up time spent on active treatment and relapses) and multivariable Cox models, respectively. The adjusted disability evolution over time was assessed by calculating the mean annual estimated EDSS changes compared to baseline estimated values (delta-EDSS).

Results: 3777 RRMS patients (268 POMS, 3282 AOMS and 227 LOMS) were included. The slope of disability trajectories over 5 years was significantly lower in POMS than in AOMS and LOMS ($p < 0.004$). The POMS and LOMS curves diverged from the beginning of the follow-up and reached a difference of the estimated EDSS score of 0.62 (0.40; 0.84, $p < 0.0001$) at year 5. A first PIRA event occurred in 844 (22.3%) patients. The risk of PIRA was 54% higher in LOMS than in POMS. Age significantly predicted the risk of PIRA ($p = 0.02$).

Conclusion: These findings indicate that age remains highly relevant in determining onset and rate of disability progression in MS. POMS show a less steep increase in EDSS scores over time than older patients.

Disclosure: The authors report no conflicts of interest with respect to the contents of the current study, but note that the patients in the study were treated with a number of disease-modifying drugs and that authors have received advisory board, membership, speakers honoraria, travel support, research grants, consulting fees or clinical trial support from the manufacturers of those drugs, including Actelion, Allergan, Almirall, Bayer Schering, Biogen, Celgene, Excemed, Genzyme, Forward Pharma, Ipsen, Medday, Merck, Merz, Mylan, Novartis, Sanofi, Roche, Teva and their local affiliates.

EPR-235 | Exploring the therapeutic landscape of NMOSD: Patterns of use over time, efficacy and factors influencing attack risk

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Background and Aims: In neuromyelitis optica spectrum disorder (NMOSD), attack prevention is crucial to avoid disability accumulation. Considering a changing therapeutic landscape with recent drug approvals, we explored use and effectiveness of long-term immunosuppressive therapies.

Methods: Longitudinal cohort study on NMOSD (2015 IPND criteria) from the Neuromyelitis Optica Study Group (NEMOS; database closure October 2022). Calculating treatment episodes, we compared established & new immunotherapies for annualized attack rates (AAR), survival analysis (time until next attack) and multivariate Cox proportional hazard regression (attack risk factors).

Results: We included 364 patients: 320 with AQP4-IgG+ and 44 with seronegative NMOSD (also MOG-IgG-seronegative). Median follow-up was 8.6 and 10.0 years, respectively. Rituximab (980 patient years) was most commonly used, with comparable attack rates in both subgroups. The therapeutic landscape changed over time,

with an increase of rituximab (52.9% in AQP4-IgG+, 73.1% in seronegative) up to 2018, while new therapies increased post 2019, with approval of eculizumab for AQP4-IgG+ NMOSD. All treatments, except specific MS medications, reduced AAR for AQP4-IgG+ (untreated 0.80 (CI 0.69–0.96), treated 0.48 (CI 0.41–0.56)) and seronegative NMOSD (untreated 0.42 (CI 0.30–0.59), treated 0.33, (CI 0.21–0.53)). Survival analysis supported these findings. Attack risk factors were younger age, prior attack under same therapy and female sex. Significant attack risk reduction were only observed for rituximab (HR 0.68, CI 0.51–0.89, $p = 0.006$) and eculizumab (<0.001, CI NA, $p < 0.001$) for AQP4-IgG+ NMOSD.

Conclusion: Our data indicate a dynamic pattern, with emerging monoclonal antibody therapies delivering increasingly efficacious attack prevention in NMOSD.

Disclosure: Project support by Alexion AstraZeneca Rare Disease and NEMOS e.V.

EPR-236 | Race and ethnicity in multiple sclerosis phase 3 clinical trials, a systematic review

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Background and Aims: Distinctive differences in multiple sclerosis (MS) have been observed by race and ethnicity, probably driven by social determinants of health (SDoH). In this context, it is imperative that research can be generalized to the overall population, including minorities. We aim to (1) assess how often race or ethnicity was reported in ClinicalTrials.gov, (2) evaluate whether the population was diverse enough, (3) make comparisons with the corresponding published material.

Methods: This systematic review included all the MS phase 3 clinical trials registered on ClinicalTrials.gov between September 2007 and December 2023. When race/ethnicity was reported, we searched for the corresponding published results using PubMed as well as a machine learning-based web tool.

Results: Out of the 99 included studies, 56% reported race or ethnicity, of which only 26% of those registered before 2017, when reporting race/ethnicity in ClinicalTrials.gov, if collected, became mandatory. Studies reporting race or ethnicity contributed to a total of 33,891 participants, mainly enrolled in Eastern Europe (60%). Most were white (93%) and the median percentage of White participants in the studies was 93% (IQR 86%–98%), compared to 3% for Black (IQR 1%–12%) and 0.2% for Asian (IQR 0%–1%). Eight trials completely omitted race/ethnicity in the main official publication and even when information was reported, some differences in terminology were identified and categories with fewer participants were often collapsed.

Conclusion: More efforts should be done to improve transparency and representativeness of data, in publications as well as at a design phase, by addressing SDoH that historically limit the enrollment of underrepresented population.

Disclosure: Nothing to disclose.

EPR-237 | Longer-term (up to 6 years) efficacy of ofatumumab in recently diagnosed treatment-naive relapsing multiple sclerosis

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Background and Aims: Ofatumumab demonstrated superior efficacy and similar safety versus teriflunomide in the Phase 3 ASCLEPIOS I/II overall relapsing multiple sclerosis (RMS) population and in recently diagnosed treatment-naive (RDTN) participants (diagnosed ≤3 years). Data from ALITHIOS (open-label extension study) previously demonstrated sustained efficacy for up to 5 and 4 years in the overall and RDTN subgroups, respectively. Here, of atumumab's efficacy in RDTN participants up to 5 years is reported, with 6-year data to be presented at Congress.

Methods: These analyses (data cut-off: 25-Sep-2022 [up to 5 years]/25-Sep-2023 [up to 6 years]) include cumulative data from RDTN participants originally randomized to ofatumumab (continuous group) and those originally randomized to teriflunomide and switched to ofatumumab in ALITHIOS (switch group).

Results: The RDTN subgroup comprised 314/301 in the continuous/switch groups (mean age at baseline: 36.8/35.7 years; 69.1%/65.8% female; mean EDSS: 2.30/2.28). In the 5-year analyses, the continuous group sustained a low annualized relapse rate (ARR) over Years 1–5 (0.1–0.01). Marked reductions in ARR in the switch group from Year 2–3 (0.1–0.053) were sustained through Years 3–5 (0.053–0.037). T2 lesion activity was suppressed in the continuous group up to Year 5, and from Year 3–5 in the switch group. The odds of achieving no evidence of disease activity (NEDA-3) in the continuous/switch groups increased from 89%/36% at Year 2 to ≥90% in both groups at Year 5 (Figure 1).

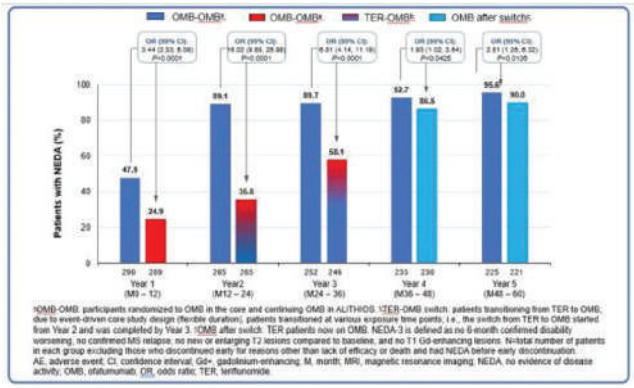

FIGURE 1: NEDA-3 status up to 5 years of ofatumumab treatment.

Conclusion: Ofatumumab demonstrates sustained long-term efficacy in people with RDTN RMS, supporting its use early in the disease course.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

EPR-238 | **Abstract withdrawn**

Muscle and neuromuscular junction disorder 2

EPR-239 | **Interleukin-6 inhibition in myasthenia gravis: A case series using tocilizumab**

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Background and Aims: Inhibition of interleukin-6 (IL6) with satralizumab is currently in clinical trials for myasthenia gravis (MG). Existing evidence supporting IL6 blockade is however limited to rare case reports with tocilizumab. Our objective was to examine a possible clinical utility in MG.

Methods: Single center retrospective observational cohort study. Patients exposed to ≥1 dose of subcutaneous/intravenous tocilizumab were included. Clinical effectiveness was assessed by Quantitative Myasthenia Gravis (QMG) score, prednisolone dose, rescue treatment and/or additional immunosuppressive drugs.

Results: We identified 19 MG patients. Clinical characteristics at baseline were: Mean age 45.8 years (standard deviation, SD 17.6), 42% Females, 58% Acetylcholine receptor antibody-positive, 53% Early onset MG, 16% Thymoma-associated MG and, 95% generalized MG. Disease duration was 9.1 years (SD 10.5), QMG score 9 (SD 6), prednisolone dose 13 mg (SD 15), 85% were previously exposed to rituximab. Treatment indication was refractory disease (79%), increased susceptibility to infections (16%) and/or severe new onset disease (21%). Mean follow-up time was 2.0 years (SD 2.0), with 37% with still ongoing treatment (reasons to discontinue; time-limited rescue treatment 25%, stable disease 8%, lack of effect 25%, adverse events 17%, mortality 17%, or other 17%). Effectiveness outcomes will be included in the final presentation.

Conclusion: IL6 inhibition represents a novel approach to treat MG and benefits from robust safety data obtained from rheumatic conditions. While firm conclusions about clinical effectiveness in MG awaits ongoing trials, our data provide an initial indication of clinical utility in certain clinical scenarios.

Disclosure: SB has received in non-restricted research grants from UCB Pharma and Janssen, not related to this study. FP has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

EPR-240 | **Efficacy and safety of tocilizumab in patients with refractory generalized myasthenia gravis**

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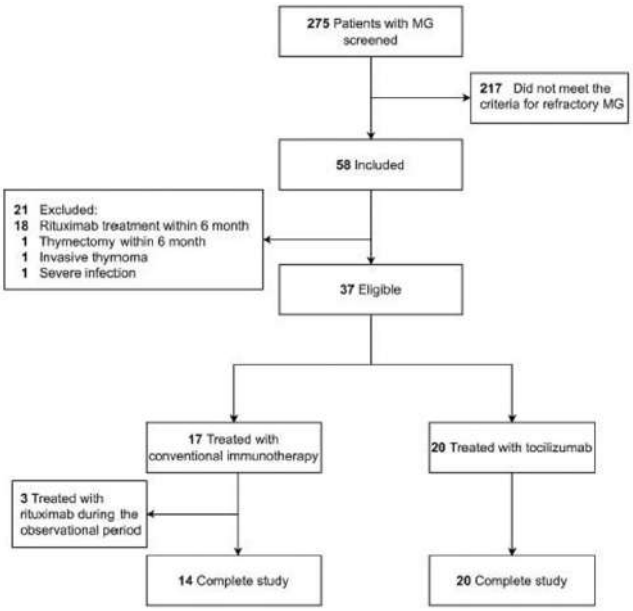
Background and Aims: We aimed to compare the efficacy of tocilizumab with conventional immunotherapy in refractory patients with acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG).

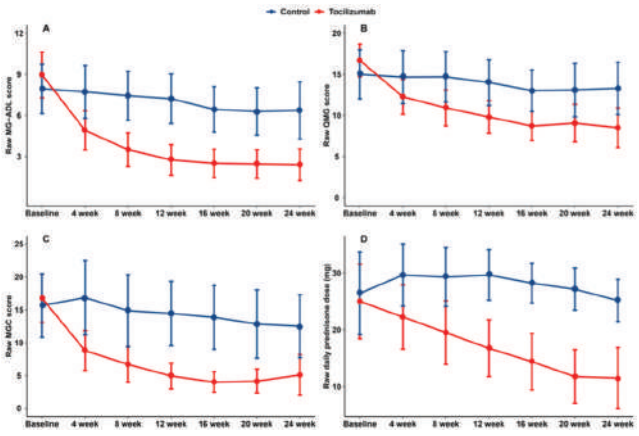
Methods: This single-center prospective cohort study was based on patients from an MG registry study in China and conducted from February 10, 2021 to March 31, 2022. Adult refractory patients with AChR-Ab+ gMG were assigned to tocilizumab or conventional immunotherapy groups. The primary efficacy outcome was the mean difference of MG activities of daily living (MG-ADL) change at weeks 4, 8, 12, 16, 20, 24 corresponding to that at baseline between the two groups. A generalized estimating equation (GEE) model was used for the primary outcome analysis. Safety was assessed based on adverse events (AEs).

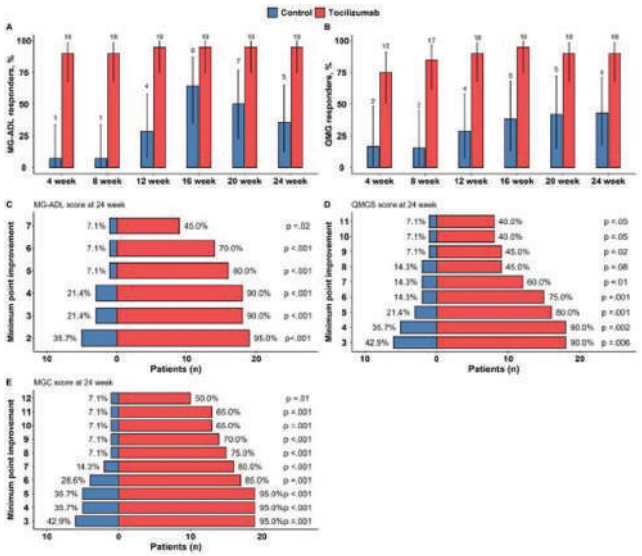
Results: Of 34 eligible patients, 20 (mean [standard deviation] age, 53.8 [21.9] years; 12 [60.0%] female) received tocilizumab and 14 received conventional immunotherapy (45.8 [18.0] years; 8 [57.1%] female). The tocilizumab group had greater reduction in MG-ADL score at week 4 (adjusted mean difference, −3.4; 95% CI, −4.7 to −2.0; $p < .001$) than the conventional immunotherapy group. At week 24, the proportion of patients achieving higher levels of MG-ADL (up to 7-point reduction) and QMG (up to 11-point reduction) scores improvement was significantly greater with tocilizumab. Tocilizumab had acceptable safety profiles without severe or unexpected safety issues.



Study flowchart showing the selection process for patients with MG.

Mean changes in MG-ADL (A), QMG (B), MGC (C) scores, and the daily prednisone dose (D) from baseline to 24 weeks in the tocilizumab and control groups.





Sensitivity analyses

Conclusion: Tocilizumab is safe and effective in improving the MG-ADL score and reducing prednisone dose in refractory AChR-Ab+ gMG, suggesting tocilizumab has the potential to be a valuable therapeutic option for such patients.

Disclosure: Nothing to disclose.

EPR-241 | Response over time with zilucoplan in generalized myasthenia gravis: Post hoc analysis of RAISE-XT 60-week follow-up

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Background and Aims: In an interim analysis of RAISE-XT (NCT04225871), an ongoing open-label extension (OLE) study, zilucoplan, a macrocyclic peptide complement component 5 inhibitor, showed clinically meaningful and significant improvements in myasthenia gravis-specific outcomes in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG). In this post hoc analysis, we assessed the long-term outcomes of Myasthenia Gravis Activities of Daily Living (MG ADL)

and Quantitative Myasthenia Gravis (QMG) responders or non-responders at Week 12 of a qualifying, double-blind study (Phase 2, NCT03315130 or Phase 3, NCT04115293).

Methods: Eligible adults with gMG self-administered daily subcutaneous injections of zilucoplan 0.3 mg/kg in RAISE-XT. MG-ADL and QMG responder rates (≥3-point and ≥5-point reductions from double-blind baseline without rescue therapy, respectively) were exploratory endpoints.

Results: Of 93 patients randomized to zilucoplan 0.3 mg/kg in the double-blind studies, 74.2% ($n=69/93$) were MG-ADL and 59.8% ($n=55/92$) were QMG responders at Week 12. Among Week 12 responders, responder rates were >88% for MG-ADL (Figure 1) and >90% for QMG throughout the OLE up to Week 60. Among Week 12 non-responders, 50.0% (12/24) were MG-ADL responders and 47.2% (17/36) were QMG responders at Week 14; 42.9% (6/14) and 47.8% (11/23) were Week 60 responders, respectively (Figure 2).

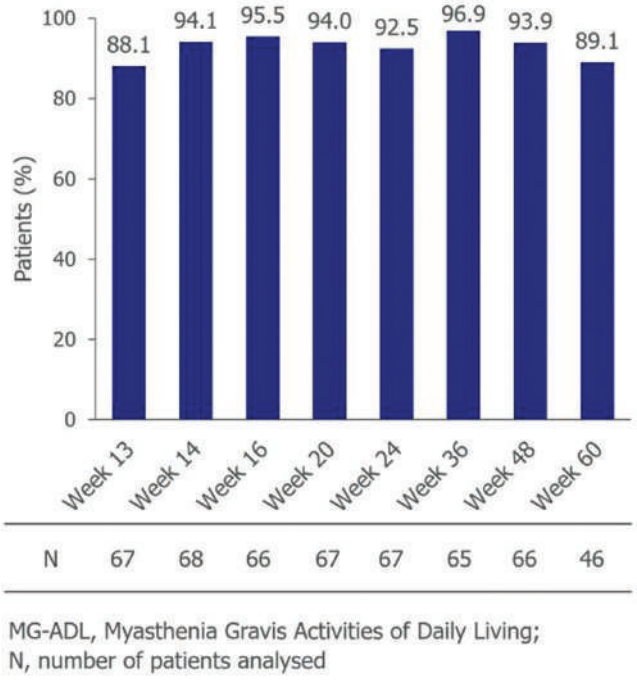

FIGURE 1: Proportion of MG-ADL responders at Week 12 who responded during RAISE-XT visits up to Week 60.

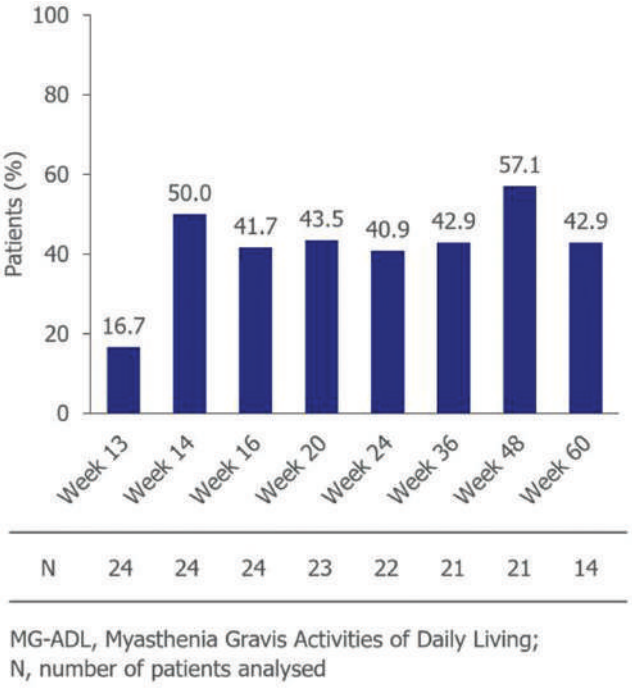

FIGURE 2: Proportion of MG-ADL non-responders at Week 12 who responded during RAISE-XT visits up to Week 60.

Conclusion: Most patients on zilucoplan were responders at Week 12 of the double-blind studies and, among them, responder rates remained high (>88%) throughout the OLE up to Week 60. Of patients who were non-responders at Week 12, approximately half became responders during the OLE, suggesting the benefit of continuing zilucoplan treatment beyond Week 12.

Disclosure: This study was funded by UCB Pharma. Raphaelle Beau Lejdstrom, Babak Boroojerdi, Fiona Grimson and Natasa Savic are employees and shareholders of UCB Pharma. Full disclosure of all industry relationships will be made during congress presentation if accepted.

EPR-242 | Ravulizumab and efgartigimod in myasthenia gravis: A real-world study

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Background and Aims: Myasthenia gravis (MG) is an autoimmune disease leading to localized or general muscle weakness. The complement inhibitor ravulizumab and neonatal Fc-receptor antagonist efgartigimod have recently been approved for the treatment of acetylcholine receptors (AChR) antibody-positive MG. Both therapies led to sustained meaningful improvement in the MG-specific Activities of Daily Living scale (MG-ADL), the primary endpoint in pivotal placebo-controlled phase III clinical trials, but comparative studies are lacking.

Methods: In this prospective, exploratory study we aimed to estimate the clinical efficacy of ravulizumab and efgartifgimod and profiled their biological effects on Auto-Ab features in a real-world cohort of patients with AChR-Ab+ generalized MG.

Results: A total of 42 patients starting with ravulizumab and 21 patients starting with efgartigimod were prospectively included between January 2023 and December 2023. Baseline MG-ADL and quantitative myasthenia gravis (QMG) scores were clinically similar in both groups. MG-ADL-based response rates in our real-world cohorts were considerably lower and clinical efficacy assessed by the QMG scale did not reach statistical significance in either treatment group after 4, 8, and 10 weeks compared to the pivotal randomized controlled phase III trials that led to approval of ravulizumab and efgartigimod. Ravulizumab reduced terminal complement activation, but neither treatment showed significant effects on complement pathways proximal to C5 or functional capacities of AChR-Abs.

Conclusion: Our data suggest that durable disease control in MG requires continuous administration of both fast-acting agents. Combination with more deeply intervening immunotherapies might restrain pathogenicity of AChR-Abs, improving long-term therapeutic efficacies.

Disclosure: F.S. received travel/accommodation/meeting expenses from Alexion Pharmaceuticals and argnx and received speaking

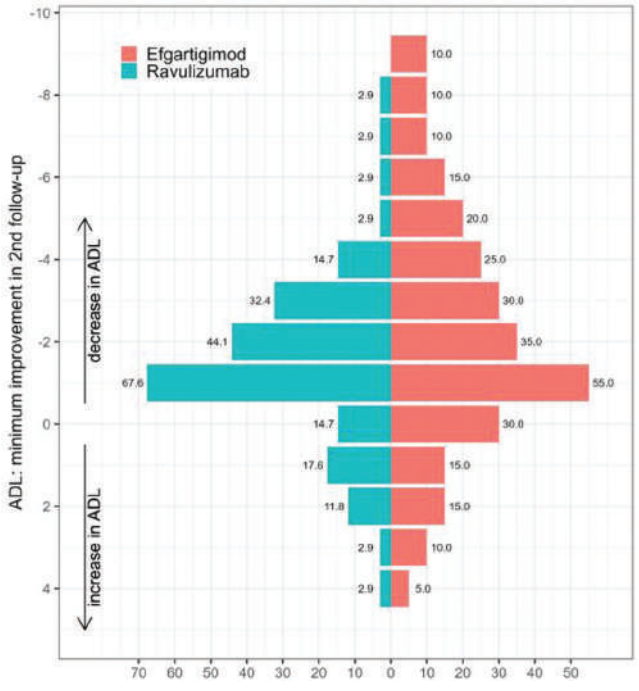

FIGURE 1A: Clinical response to ravulizumab and efgartigimod in patients with AChR-Ab-positive gMG. Bar chart for the distribution of clinically meaningful improvement in MG-ADL score from baseline to second follow-up (week 8 or week 10).

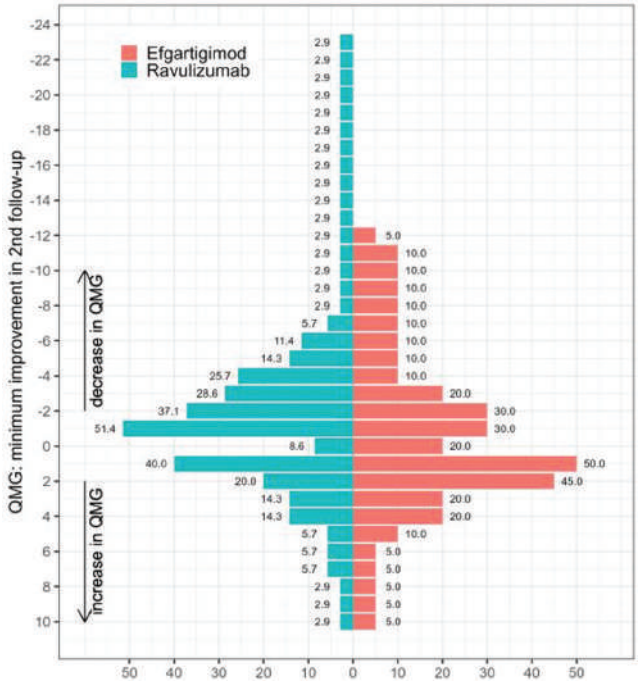

FIGURE 1B: Clinical response to ravulizumab and efgartigimod in patients with AChR-Ab-positive gMG. Bar chart for the distribution of clinically meaningful improvement in QMG score from baseline to second follow-up (week 8 or week 10).

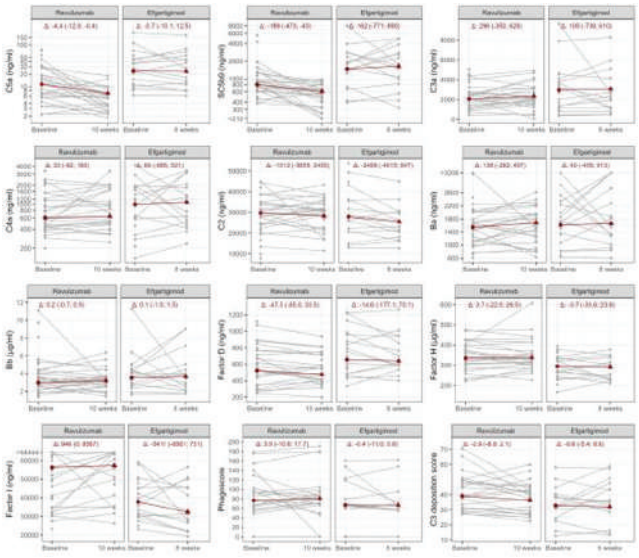

FIGURE 2: Profiling activated complement protein levels and AChR-specific antibody effector functions upon treatment initiation with ravulizumab and efgartigimod.

honoria and honoria for attendance at advisory boards from Alexion Pharmaceuticals, argnx and UCB pharma. H. W. received speaker honoraria from Alexion, Biogen, Bristol Myers Squibb, Genzyme, Merck, Neurodiem, Novartis, Ology, Roche, TEVA, and WebMD Global. He received honoraria for consulting services from Abbvie, Actelion, Argenx, BD, Bristol Myers Squibb, EMD Serono, Fondazione Cariplo, Gossamer Bio, Idorsia, Immunic, Immunovant, INmune Bio_Syneos Health, Janssen, Merck, NexGen, Novartis, Roche, Sanofi, Swiss Multiple Sclerosis Society, UCB and Worldwide Clinical Trials. A. M. received speaker or consultancy honoraria or financial research support (paid to his institution) from Alexion Pharmaceuticals, argenx, Axunio, Destin, Grifols, Hormosan Pharma, Janssen, Merck, Octapharma, UCB, and Xcenda. J. D. L. has received speaker fees, research support, travel support, and/or served on advisory boards by Abbvie, Alexion, Argenx, Biogen, Merck, Moderna, Novartis, Roche, Sanofi and Takeda, and is member of the medical advisory board of the German Myasthenia Gravis Society. The other authors report no conflict of interest.

EPR-243 | DNTH103: Preventing nerve damage in a NHP CIDP model via sustained complement inhibition

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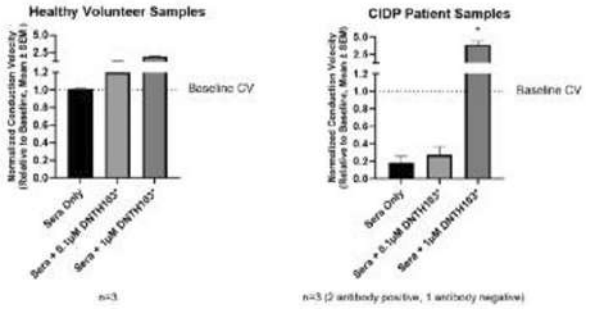
Background and Aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune disease with complement pathway involvement.1 DNTH103 is a fully human, potent, monoclonal antibody with a long half-life that selectively blocks the classical complement pathway.

Methods: The aim of these studies was to demonstrate the selectivity, potency, and efficacy of DNTH103 in a CIDP model and sustained pharmacokinetic/pharmacodynamic activity in nonhuman primates (NHPs). Study 1: Real-time binding of DNTH103 to C1s and proC1s by surface plasmon resonance (Biacore). Study 2: Characterisation of DNTH103 pharmacokinetic/pharmacodynamic by ligand-binding assay and CH50 haemolysis (Haemoscan) in NHPs. Study 3: DNTH103 functional activity was characterized with Human-on-a-Chip Motoneuron Axon Model using healthy iPSC-derived motoneurons, Schwann cells, and sera from 3 healthy and 3 CIDP patients (2 anti-NF155+). Conduction velocity was assessed in serum conditions with and without DNTH103.

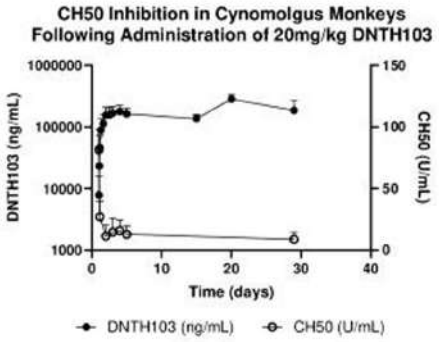
Results: DNTH103 bound selectively to active C1s with high affinity (KD: 7.1 pM) with minimal binding to proC1s (KD: ~500 nM). After a single subcutaneous administration of 20 mg/kg DNTH103 in NHPs, drug levels reached a Cmax of 191 μg/mL between 60 and 72 h; the circulating level of drug resulted in a sustainable >90% reduction in CH50 levels for the duration of the study period. DNTH103 prevented nerve conduction velocity slowing in antibody-positive CIDP patient sera.

Figure 1: DNTH103 Prevents Conduction Velocity Slowing in CIDP Sera Samples



Note: Fisher's LSD one-way ANOVA multi-comparison statistical analysis performed. *$p = 0.320$ CIDP, chronic inflammatory demyelinating polyneuropathy; CV, conduction velocity; SEM, standard error of the mean.

Figure 2: PK/PD of DNTH103 in NHP Following a 20 mg/kg Single Acute Dose by Subcutaneous Administration



NHP, nonhuman primate; PD, pharmacodynamics; PK, pharmacokinetics.

Conclusion: DNTH103 selectively binds to active C1s and effectively blocks complement-mediated inhibition of conduction detected in sera from CIDP patients. DNTH103 is an attractive research candidate for CIDP due to its potent activity, selectivity for active C1s, and extended circulating half-life.

Disclosure: This study was funded by Dianthus Therapeutics. The authors declare no conflicts of interest.

EPR-244 | Efgartigimod in generalized myasthenia gravis: A Chinese multicenter cohort study

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Background and Aims: Efgartigimod is a neonatal Fc receptor antagonist that facilitates antibody degradation including pathogenic IgGs. Recently, the ADAPT study showed that efgartigimod was well tolerated and efficacious in generalized myasthenia gravis (gMG). However, there is very limited evidence from China, and it remains inconclusive about which kind of patients are selected to preferentially receive efgartigimod in real-world settings.

Methods: This multicenter study included gMG patients from 14 neuromuscular reference centers in China. The Myasthenia Gravis Activities of Daily Living (MG-ADL) score, immunosuppressants, and safety profile were prospectively collected. Clinically meaningful improvement (CMI) was defined as the change in ADL of ≥2. Minimal symptom expression (MSE) was defined as MG-ADL total score of 0–1.

Results: Of 1640 gMG patients admitted between September to December 2023, 60 (3.6%) patients (M:F = 3:7) received efgartigimod for at least one treatment cycle and completed the 12-week follow-ups. Among them, 55 patients (91%) were AChR antibody-positive, 4 were MuSK antibody-positive and 1 was seronegative. Thymoma-associated Myasthenia gravis accounts for the majority (45%, 27/60), while the principal cause for efgartigimod initiation was MG acute exacerbation (MGAE) (48%, 29/60) or myasthenic crisis (MC) (15%, 9/60). CMI was rapidly achieved in 97% (58/60) of patients with a mean time of 1.3 weeks. By Week 4, the maximum reduction in MG-ADL was 7.9 and 45% (27/60) achieved MSE. Overall, all but 1 patient did not require additional rescue therapies after efgartigimod initiation.

Conclusion: This multicenter clinical cohort study demonstrated that efgartigimod provides rapid disease control for gMG in real-world clinical practice.

Disclosure: Nothing to disclose.

EPR-245 | Long-term zilucoplan in generalized myasthenia gravis: 96-week follow-up interim analysis of RAISE-XT

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Background and Aims: Long-term data from RAISE-XT (NCT04225871), an ongoing, Phase 3, open-label extension study, will enhance understanding of the safety and efficacy of the macrocyclic peptide complement component 5 inhibitor, zilucoplan, in patients with acetylcholine receptor autoantibody-positive generalized myasthenia gravis (gMG). We assessed responder rates for Myasthenia Gravis Activities of Daily Living (MG-ADL), Quantitative Myasthenia Gravis (QMG) and minimal symptom expression (MSE) up to 96 weeks.

Methods: RAISE-XT enrolled adults with gMG who completed a qualifying, double-blind study (NCT03315130/NCT04115293). Patients self-administered daily subcutaneous injections of zilucoplan 0.3 mg/kg. Primary outcome: incidence of treatment-emergent adverse events (TEAEs). Exploratory outcomes included responder rates for MG-ADL, QMG and MSE (reduction of ≥3 points, ≥5 points, or an MG-ADL score 0 or 1, respectively, without rescue therapy).

Results: Overall, 200 patients had enrolled at data cut-off (11 May 2023); median (range) exposure was 1.8 (0.11—5.1) years. Of 183 who received zilucoplan 0.3 mg/kg or placebo in the qualifying study, 93 continued zilucoplan 0.3 mg/kg; 90 switched from placebo

to zilucoplan 0.3 mg/kg. At RAISE-XT baseline (double-blind study Week 12), MG-ADL, QMG and MSE responder rates were 74.2%, 59.8% and 19.4% for zilucoplan ($n=93$) and 52.2%, 37.1% and 7.8% for placebo ($n=90$), respectively. At Week 96, pooled zilucoplan ($n=183$) MG-ADL, QMG and MSE responder rates had improved to 88.2% (Figure 1), 80.3% and 48.2%. TEAEs occurred in 191/200 (95.5%) patients; 71/200 (35.5%) patients experienced a serious TEAE (Table 1).

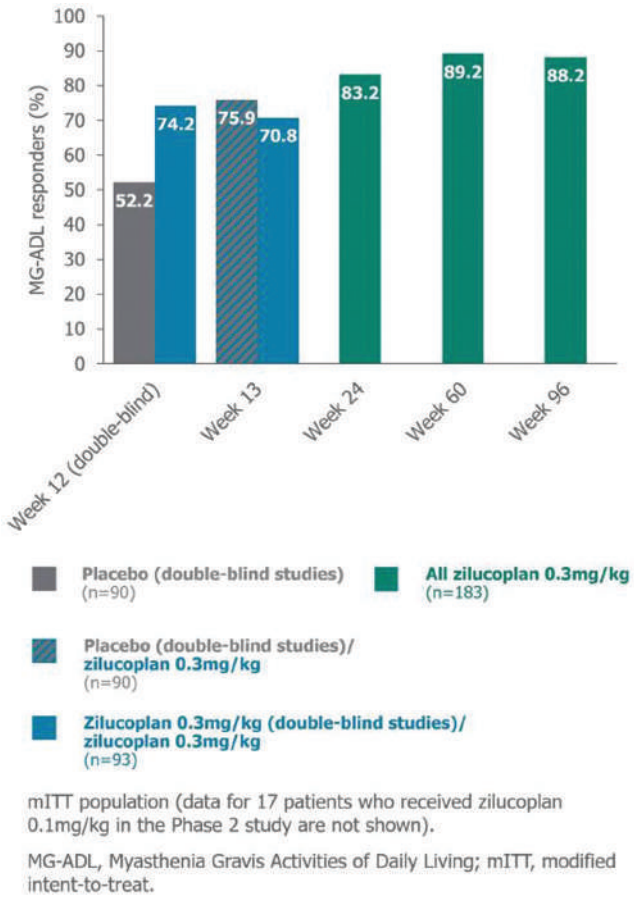

FIGURE 1: MG-ADL responder rates through to Week 96.

TABLE 1: Overview of TEAEs.

	All zilucoplan (N=200)
Any TEAE, n (%)	191 (95.5)
Serious TEAE, n (%)	71 (35.5)
TEAE resulting in permanent withdrawal from IMP,* n (%)	19 (9.5)
Treatment-related TEAE, n (%)	70 (35.0)
Severe TEAE, n (%)	64 (32.0)
TEAE leading to death, n (%)	4 (2.0)

Safety set, includes all patients who entered RAISE-XT.

*Includes the four deaths, which were: two cardiac arrests in patients with major cardiovascular risk factors, and one head injury. For one participant, the cause of death was unknown: a non-serious and severe TEAE of pneumonia reported two days prior to death, but it is not known whether the cause of death was related to pneumonia. None of the deaths were considered treatment-related (as determined by the investigator).

IMP, investigational medicinal product; TEAE, treatment-emergent adverse event.

Conclusion: In this interim analysis, zilucoplan demonstrated a favourable safety profile and improved MG-ADL, QMG and MSE responder rates, sustained up to 96 weeks of treatment.

Disclosure: This study was funded by UCB Pharma. Babak Boroojerdi, Guillemette de la Borderie, Petra W. Duda and Mark Vanderkelen are employees and shareholders of UCB Pharma. Full disclosure of all industry relationships will be made during congress presentation if accepted.

EPR-246 | Phenotypic description of 40 patients with p.Ser55Phe variant in the MYOT gene: The MYOT-MUR study

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Background and Aims: The Spanish myotilinopathy cohort is the most extensive to date (Olive et al., 2011). While most patients, especially those carrying the p.Ser55Phe variant, may have originated from a founding population in Murcia, South-Eastern Spain, there is a lack of published data regarding the phenotypic spectrum of this original population.

Methods: A clinical assessment of patients with the p.Ser55Phe variant in the MYOT gene was conducted, involving the collection

of genealogical diagrams, neuromuscular history, and a neurological exam.

Results: Forty patients from 12 families in Murcia were included. All patients had familial antecedents. The mean age of symptom onset was 48 years for men and 56 years for women, with two female patients older than 60 years remaining asymptomatic. The most common initial symptom was unilateral foot drop (90.4%), progressing to upper limbs after 6–8 years for male patients and within the first year for female patients. Two patients presented with a limb-girdle muscular dystrophy phenotype.

Conclusion: The Spanish region of Murcia might host the largest cluster of myopathy linked to MYOT variants. In our study, we described a phenotype for female patients not previously documented, characterized by early involvement of the upper limbs and a more favorable course, with a later onset and the existence of asymptomatic carriers. This broadening of the phenotype underscores the need to enhance knowledge of the natural history of myotilinopathies, particularly in areas of high prevalence.

Disclosure: Nothing to disclose.

Monday, July 01 2024

Neuropathies

EPR-247 | Clinical findings in a couple of Italian siblings of Romani ancestry with CMT4D and review of the current literature

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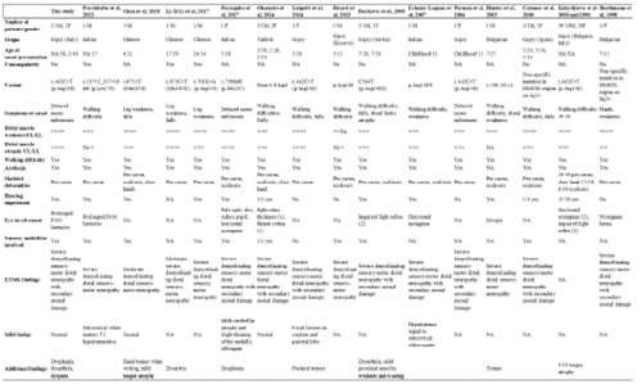
Department of Neurology, Policlinico Ospedale Maggiore di Milano, University of Milan, Milan, Italy

Background and Aims: Charcot-Marie-tooth disease type 4D (CMT4D) is an early onset form of CMT characterized by severe demyelinating motor-sensory neuropathy, muscle weakness and atrophy and hearing impairment. It is caused by mutations in the N-myc downstream-regulated gene 1 (NDRG1). Eight different mutations in NDRG1 have been identified so far. We report the case of two siblings of Romani ancestry, a 38-year-old man and a 40-year-old woman, with a NDRG1 mutation, p.R148, and provide a review of the literature.

Methods: Disease staging was assessed through a battery of clinical and instrumental examinations: CMT neuropathy score, electromyography, fiberoptic endoscopic evaluation of swallowing, pulmonary function tests and visual evoked potentials. The review included all articles focusing on CMT4D available online, published from 1998 to 2022.

Results: Both patients showed severe muscle weakness and atrophy, mild dysphagia, mild pulmonary restrictive syndrome and sensorineural deafness. Neurophysiological parameters showed a severe motor-sensory polyneuropathy. Fifteen articles were included in the review. The age at onset, in the first decade of life, and the clinical features were in line with the literature. The variant p.R148 accounts for the majority of CMT4D cases, almost all of Romani ancestry. Because of the lack of data regarding other pathogenic variants, it is difficult to provide a comparison between potential differences in clinical phenotypes. Nevertheless, it is interesting to notice that all the patients who had an onset with delayed motor milestones were p.R148 variant carriers.



Demographic, genetic, clinical, neuropsychological and radiological characteristics of patients carrying NDRG1 mutations.

Conclusion: Additional research into NDRG1 variants and phenotypic characteristics may provide further information about potential genotype-phenotype correlations and prognosis.

Disclosure: Nothing to disclose.

EPR-248 | Phase 3 trial designs evaluating riliprubart, a C1s-complement inhibitor, in CIDP

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[1]Cedars Sinai Medical Center, Los Angeles, California, USA; [2]Department of Neurology, Division of Neuromuscular Medicine, University of Minnesota, Minneapolis, Minnesota, USA; [3]Department of Neurology, Maastricht University Medical Center, The Netherlands; Curaçao Medical Center, Willemstad, Curaçao; [4]Erasmus MC, University Medical Center, Rotterdam, The Netherlands; [5]Neurologische Klinik und Poliklinik, Universitätsklinikum Würzburg, Germany; [6]Sanofi R&D, Neurology Development, Cambridge, Massachusetts, USA; [7]Sanofi R&D, Biostatistics and Programming, Bridgewater, New Jersey, USA; [8]Neuromuscular Diseases Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; Centro para la Investigación Biomédica en Red en Enfermedades Raras (CIBERER), Madrid, Spain

Background and Aims: Standard-of-care (SOC) therapies (immunoglobulins/corticosteroids) for chronic inflammatory demyelinating polyneuropathy (CIDP) have variable efficacy and side-effects. Riliprubart, a first-in-class, humanized, IgG4-monoclonal antibody, selectively inhibits activated-C1s and has low-volume subcutaneous route of administration. Phase 2 trial (NCT04658472) results

indicated promising clinical benefits with a favourable benefit-risk profile. We present two Phase 3 trial designs which will evaluate riliprubart in two different CIDP populations with high unmet needs: patients refractory to SOC therapies and responders to intravenous immunoglobulins (IVIg) with residual disability.

Methods: Two global, multicentre, randomized, Phase 3 trials are planned: MOBILIZE, a placebo-controlled trial targeting SOC-refractory patients; VITALIZE, a double-dummy trial targeting IVIg-treated patients with residual disability. Each trial consists of a 24-week double-blinded period (Part-A), then a 24-week open-label period (Part-B). In Part-A, participants will be randomized (1:1) to receive riliprubart or placebo (MOBILIZE; $N \leq 140$), and riliprubart plus IVIg-placebo or IVIg plus riliprubart-placebo (VITALIZE; $N \leq 160$). Sample sizes will be re-estimated based on a pre-defined interim analysis during Part-A. Eligible adults with CIDP diagnosed based on 2021 EAN/PNS guidelines with Inflammatory Neuropathy Cause and Treatment (INCAT) score 2–9 (score 2 exclusively from legs) can be included. Primary endpoint is percentage of participants responding, defined as ≥1 point decrease from baseline in adjusted INCAT score at Week-24 (Part-A). Key secondary endpoints include change from baseline in additional disability/impairment measures (Part-A) and long-term efficacy (Part-B).

Results: Both trials are expected to begin enrolment in 2024.

Conclusion: These Phase 3 trials aim to demonstrate riliprubart efficacy for CIDP, including people with refractory disease or residual disability.

Disclosure: RAL: Consultant – CSL Behring, Grifols, Pfizer, Sanofi, argenx, Pharnext, Roche, J&J, Takeda, Boehringer Ingelheim, Momenta; Scientific advisory board – Alnylam Akcea; Medical advisory board – The GBS-CIDP Foundation International. JA: Consultant – Sanofi, Alexion, Alnylam, argenx, Annexon, CSL Behring, J&J, Grifols, Takeda, Immunovant, Immunopharma, Pfizer. ISJM: Grants – Talecris Talents program, GBS/CIDP Foundation International, FP7 EU program; Honoraria for participation in steering committee of Talecris Immune Globulin Intravenous (CIDP Study), CSL, Behring, Octapharma, LFB, Novartis, Union Chimique Belge, J&J, argenx, Octapharma. PAvD: Consultant – Annexon, argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi; Grant – Prinses Beatrix Spierfonds, Sanquin, Grifols. CS: Consultant – Alnylam, Air Liquide, Bayer, Immunic, Ipsen, LFB, Merz, Nevro, Pfizer, Roche Takeda; Honoraria – Alnylam, CSL Behring, Grifols, Lilly, Merck, Novartis, Pfizer TEVA. EW, XL, MAA, NA: Employees of Sanofi, may hold shares and/or stock options. LQ: Grant- Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, UCB and Grifols; Speaker/expert testimony honoraria – CSL Behring, Novartis, Sanofi, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, argenx, UCB, Dianthus, LFB, Avilar Therapeutics, Octapharma, Roche; Clinical Trial Steering Committee member (Sanofi); Principal Investigator – UCB's CIDP01 trial.

EPR-249 | Phase 2 efficacy and safety of riliprubart, a C1s-complement inhibitor, in CIDP

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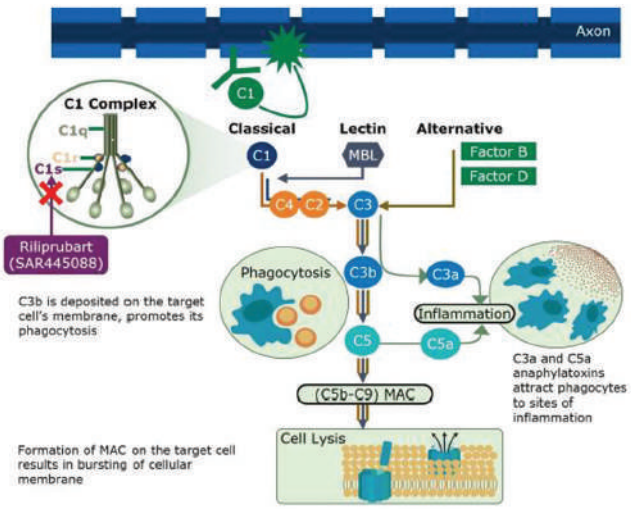
Background and Aims: Riliprubart, a first-in-class humanized IgG4-monoclonal antibody, selectively inhibits activated-C1s within the classical-complement pathway (Figure). We report efficacy and safety of riliprubart in chronic inflammatory demyelinating polyneuropathy (CIDP).



Riliprubart targeting C1s and the classical complement pathway.

Methods: Global, multicentre, Phase-2, open-label trial (NCT04658472) evaluating riliprubart across three subgroups: Standard-of-care (SOC)-Treated, SOC-Refractory, and SOC-Naïve. Participants undergo 24-week treatment (Part-A), followed by optional treatment-extension (Part-B: 52-weeks, Part-C: until end-of-study). In Part-A, primary endpoint is %-participants with relapse (SOC-Treated) or response (SOC-Refractory/Naïve), defined as ≥1-point change in adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score from baseline up to 24-weeks. Part-B evaluates efficacy durability based on % relapse-free

participants (SOC-Treated) or those with sustained-response (SOC-Refractory/Naïve), defined as no-increase in adjusted INCAT score ≥2-points relative to 24-weeks. Exploratory endpoints include additional efficacy measures (INCAT, I-RODS, MRC-SS, grip-strength), change in total-complement, and plasma neurofilament-light chain (NfL). Safety is also evaluated.

Results: As of May-2023, Part-A results from pre-specified interim-analysis show 88% (*N* = 22/25) SOC-Treated participants improved/remained stable (44%; *N* = 11/25 improved), and 12% relapsed (*N* = 3/25). 50% (*N* = 9/18) SOC-Refractory participants responded to riliprubart. Clinically meaningful improvements were observed across secondary efficacy measures. Sustained inhibition of complement-activity and reduction in NfL-levels were also observed in these subgroups. Treatment-emergent adverse events occurred in 60% (*N* = 15/25) of SOC-Treated and 72% (*N* = 13/18) of SOC-Refractory participants. Two deaths were reported in participants with significant medical comorbidities aside from CIDP. Available Part-A and Part-B data for three subgroups will be presented at the meeting.

Conclusion: These preliminary results support proof-of-concept for riliprubart in CIDP, with a favourable benefit-risk profile, supporting further investigation in Phase-3.

Disclosure: LQ: Received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, UCB and Grifols. He received speaker or expert testimony honoraria from CSL Behring, Novartis, Sanofi, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, argenx, UCB, Dianthus, LFB, Avilar Therapeutics, Octapharma and Roche. He serves at Clinical Trial Steering Committee for Sanofi, and was Principal Investigator for UCB's CIDP01 trial. RAL: Consultant with CSL Behring, Grifols, Pfizer, Sanofi (Steering Committee), argenx, Pharnext, Roche, Johnson & Johnson, Takeda, Boehringer Ingelheim (DSMB), and Momenta. He is also part scientific advisory boards Alnylam and Akcea and medical advisory board The GBS-CIDP Foundation International. HPH: Consultant with Sanofi and Octapharma. He has received fees for serving on Steering and Data Monitoring Committees from Biogen, BMS Celgene, GeNeuro, Merck, Novartis, Octapharma, Roche, and TG Therapeutics. PAvD: Consultant with Annexon, argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi (Institutional research fund received all honoraria), and received grants from the Prinses Beatrix Spierfonds, Sanquin, and Grifols. EW, KA, XL, MAA, NA: Employees of Sanofi and may hold shares and/or stock options in the company. RACH: Consultant with Hansa Biopharma, and Sanofi.

EPR-250 | Empasiprubart (ARGX-117) in multifocal motor neuropathy: Initial safety and efficacy data of the phase 2 ARDA study

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Background and Aims: Multifocal motor neuropathy (MMN) is a rare immune-mediated neuropathy resulting from motor nerve conduction block leading to axonal degeneration and progressive asymmetric limb weakness with absence of sensory loss. Currently, IVIg is the only proven efficacious therapy. Empasiprubart blocks the activation of classical and lectin complement pathways via C2 binding. ARDA (NCT05225675) is a phase 2, multicentre, randomized, placebo-controlled, double-blinded, parallel-group study that will assess the safety, efficacy, and tolerability of empasiprubart in adults with MMN.

Methods: ARDA enrolled 52 participants with probable or definite MMN (2010 EFNS/PNS guidelines). All had proven IVIg dependency and were on stable IVIg regimen leading to randomisation. MMN diagnosis and IVIg dependency were confirmed by committee. Enrolled participants were assigned to one of two dosing cohorts; each randomized 2:1 to empasiprubart or placebo. Key efficacy endpoints include IVIg retreatment, change in muscle strength, and disability scores.

Results: Cohort 1 randomized 27 participants. During double-blind treatment period, empasiprubart demonstrated a 91% reduction (HR [95% CI]: 0.09 [0.02, 0.44]) in the risk for IVIg retreatment compared with placebo (Figure 1). Since starting therapy, 94% of empasiprubart-treated patients rated their condition improved, with 55% being much/very much improved (Figure 2) (Patient Global Impression of Change scale). 89% of placebo patients had no change/worsened. Empasiprubart was well tolerated overall. Most adverse events were mild or moderate. Additional results presented at the congress.

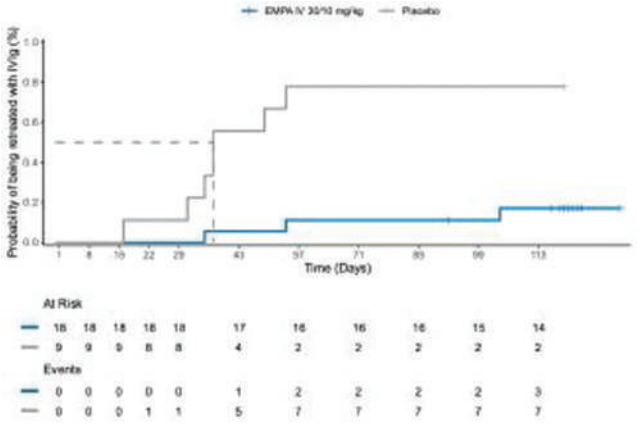

Figure 1 Time to first retreatment with IVIg during treatment period. During double-blind treatment period, empasiprubart demonstrated a 91% reduction (HR [95% CI]: 0.09 [0.02, 0.44]) in the risk for IVIg retreatment compared with placebo. Time to first retreatment with IVIg is defined as the time from last IVIg administration before randomisation (including unscheduled visits) up to the first IVIg retreatment during double-blind trial period.

FIGURE 1

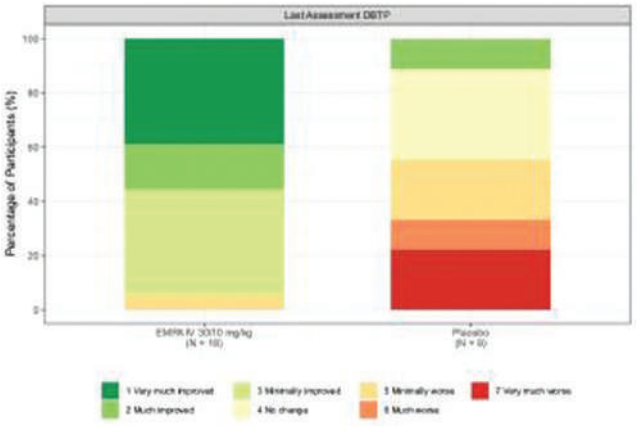

Figure 2 PGIC: Actual values at last assessment during treatment period. Since starting therapy, 94% (31/18) of treated patients rated their condition improved, with 55% being much/very much improved (Patient Global Impression of Change scale). Conversely, 89% (8/9) of placebo patients had no change/worsened.

FIGURE 2

Conclusion: Early efficacy and safety signals in cohort 1 from the ongoing ARDA study support proof of concept of empasiprubart in MMN.

Disclosure: LQ received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, UCB and Grifols; speaker or expert testimony honoraria from CSL Behring, Novartis, Sanofi-Genzyme, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, ArgenX, UCB, LFB, Avilar Therapeutics, Octapharma and Roche; serves at Clinical Trial Steering Committee for Sanofi Genzyme; and was Principal Investigator for UCB's CIDP01 trial. WLvdP employer received fees for ad hoc consultancy from Argenx, Takeda, Biogen, Roche and Novartis gene therapies. SP received lecture honoraria from argenx, Viatris, Pfizer, Teva Actavis, Berlin Chemie Menarini, Mylan, Worwag, Adoc, Remedica and Salveo; research grants from argenx, Kedrion Biopharma and Octapharma; consultant fees from argenx, Dianthus Therapeutics and Mylan; and travel grants from Octapharma, Kedrion, Teva Actavis, Sanofi Genzyme, Pfizer, Roche, ADOC, Wörwag, Medis, and Berlin–Chemie Menarini; and reports no other conflicts of interest outside or related to this work. YH Nothing to disclose. IVW, IVH, EP are employees of argenx. OVS works as a consultant for argenx. MV, OM, SC work as consultants for argenx and PPD. JA has received consulting honoraria from argenx, Alexion, Akcea, CSL Behring, Johnson & Johnson, Grifols, Takeda, and Sanofi.

EPR-251 | Photobiomodulation for managing chemotherapy-induced peripheral neuropathy: Follow-up of a randomized, controlled trial

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Background and Aims: Chemotherapy-induced peripheral neuropathy (CIPN) is one of the most common side effects of chemotherapy (CTx) and severely impacts the patients' quality of life. Managing CIPN is often based on CTx dose reduction or a premature stop of treatment. Photobiomodulation (PBM) therapy stimulates cell repair by using (near)-infrared light and previous research shows its efficiency in preventing CIPN. This trial evaluated the effectiveness of PBM in treating CIPN while optimizing the PBM dosage.

Methods: A randomized, controlled trial was conducted at the Jessa Hospital (Hasselt, Belgium) including 60 cancer patients diagnosed with CIPN. Patients were randomly allocated to the PBM-1 (6 J/cm^2, $n=28$) or PBM-2 group (8 J/cm^2, $n=32$). PBM was applied twice a week for three weeks. The severity of CIPN was assessed using the modified Total Neuropathy Score (mTNS), while the Numeric Rating Scale (NRS) was used to evaluate the patient's pain. Outcome measures were collected at baseline, the end of PBM, and three weeks post-PBM. The NRS was also assessed at six months and a year post-PBM.

Results: The NRS score decreased significantly over time in the PBM-1 ($p=0.02$) and PBM-2 group ($p=0.017$). Post-hoc analysis showed a significant difference between baseline and one-year follow-up in the PBM-1 group ($p=0.007$). The mTNS also decreased significantly over time in both groups ($p=0.007$, and $p=0.029$, respectively).

TABLE 1: Patient-, disease- and treatment-related characteristics.

Characteristics	PBM-1 (n = 28)		PBM-2 (n = 32)		
	Mean ± SD		*Mean ± SD*		*P*[a]
Age (years)	63.79 ± 11.45		60.97 ± 11.84		0.35
BMI (kg/m²)	24.41 ± 3.77		26.69 ± 3.95		**0.03**
	n	%	*n*	%	*P*[b]
Sex					0.23
Female	19	67.86	26	81.25	
Male	9	32.14	6	18.75	
Smoking					0.19
Current	2	7.14	2	6.25	
Former	11	39.29	6	18.75	
Never	15	53.57	24	75.00	
Alcohol consumption					0.68
Never or < 1 unit a week	13	46.43	13	40.63	
1-3 units a week	10	35.71	14	43.75	
4-10nits a week	4	14.29	5	15.63	
10-20 units a week	1	3.57	0	0.00	
Exercise frequency					0.94
Never	3	10.71	4	12.50	
Once a week	5	17.86	7	21.88	
2-3 times a week	11	39.29	14	43.75	
3-4 times a week	5	17.86	4	12.50	
≥ 5 times a week	4	14.29	3	9.38	
Tumor location					0.59
Breast	14	50.00	19	59.38	
Head- and neck	1	3.57	1	3.13	
Prostate	1	3.57	0	0.00	
Colorectal	4	14.29	3	9.38	
Ovarian	1	3.57	1	3.13	
Endometrial	0	0.00	2	6.25	
Bladder	0	0.00	1	3.13	
Lung	0	0.00	1	3.13	
Other	7	25.00	4	12.50	
T-stage					0.37
x	1	7.14	2	6.25	
1	3	10.71	7	21.88	
2	14	50.00	15	46.88	
3	8	25.00	8	25.00	
4	2	7.14	0	0.00	
N-stage					0.22
x	1	7.14	2	6.25	
0	6	21.43	15	46.88	
1	14	50.00	9	28.13	
2	6	21.43	5	15.63	
3	1	0.00	1	3.13	
M-stage					0.98
x	4	14.29	4	12.50	
0	16	57.14	19	59.38	
1	8	28.57	9	28.13	
Type of chemotherapy[*]					
Paclitaxel	13	46.43	22	68.75	0.07
Docetaxel	3	10.71	0	0.00	0.10
Oxaliplatin	11	39.29	6	18.75	0.07
Cisplatin	0	0.00	3	9.38	0.15
Carboplatin	5	17.86	7	21.88	0.48
Last chemotherapy session					0.31
< 1 year	15	57.14	14	43.75	
≥ 1 year	13	42.86	18	56.25	

[*]The percentages may not add up to 100% due to combinations of chemotherapy [a]unpaired t-test (two-tailed) [b]Chi-square tests (two-tailed), or Fisher's exact tests, as appropriate. Body Mass Index (BMI); photobiomodulation (PBM); standard deviation (SD)

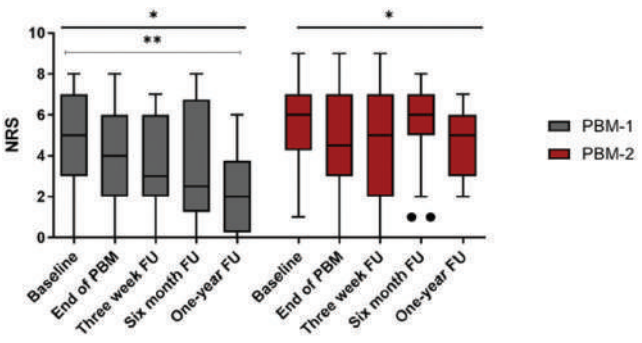

FIGURE 1: Pain scored on the Numeric Rating Scale (NRS). A higher score indicates a higher level of pain. Outliers are displayed as dots. Significance is shown as $^{*}p < 0.05$, $^{**}p < 0.01$. PBM, Photobiomodulation.

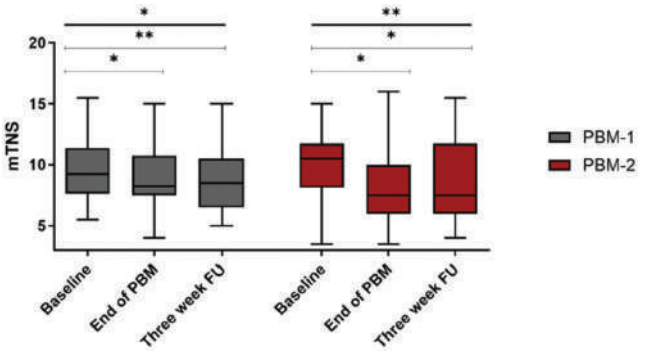

FIGURE 2: Modified Total Neuropathy Score (mTNS). A higher score indicates a more severe grade of peripheral neuropathy. Significance is shown as $^{*}p < 0.05$, $^{**}p < 0.01$. PBM, Photobiomodulation.

Conclusion: This trial shows that PBM can reduce the symptoms and pain associated with CIPN. A larger trial with a more extensive follow-up is necessary to support these findings.

Disclosure: This research is funded by Limburg Clinical Research Center, Kom op tegen Kanker (Stand up to Cancer), the Flemish cancer society, and the Limburgs Kankerfonds.

EPR-252 | Intraepidermal nerve fibre density in Val30Met aTTRv amyloidosis: Correlation with disease and amyloid deposition

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Background and Aims: Hereditary transthyretin amyloidosis (aTTRv amyloidosis) is characterized by a length-dependent polyneuropathy. Besides classical amyloid deposition, skin biopsies (SB) show changes in the intraepidermal nerve fibre density (IENFD). We aimed to study the value of IENFD in identifying aTTRv patients.

Methods: Retrospective collection of data from patients with the Val30Met mutation who underwent SB between 2019 and 2023. Clinical and neurophysiological data and the disease conversion status were retrieved.

Results: In total, 70 cases were identified (52.9% female), with a mean age at SB of 48.54 ±16.76 years. At the time of the SB, 22 were symptomatic (31.4%), 38 had doubtful symptoms (54.3%) and 10 were asymptomatic (14.3%). Thirteen cases (27.1%) with doubtful or no symptoms were considered affected by the disease during 4-year follow-up. Overall, patients (50.0%) had significantly lower distal IEFND compared to carriers (4.08 ±3.52 vs. 7.91 ±4.28) after adjusting for age and sex ($p = 0.002$). There was no association between IEFND and starting disease during follow-up in the group with doubtful or no symptoms. In asymptomatics, the distal/proximal IEFND ratio was significantly lower in patients that started the

disease (0.203 ±0.153 vs. 0.739 ±0.242, $p=0.018$). Amyloid deposits were present in 33 (47.1%) SB and associated with significantly lower IEFND both distally (3.88 ±3.65 vs. 7.78 ±4.08, $p<0.001$) and proximally (10.16 ±5.92 vs. 13.09 ±4.64, $p=0.041$). In the subset with doubtful symptoms and absent amyloid deposits, the two cases that became diseased had lower proximal IEFND (7.18 ±0.74 vs. 13.37 ±4.62, $p=0.038$).

Conclusion: Analysis of IEFND was not able to assert patients without explicit aTTR symptoms, while a clear association between amyloid deposition and IEFND reduction was seen.

Disclosure: The authors have nothing to disclose.

EPR-253 | Safety profile of subcutaneous efgartigimod PH20 from clinical trials in immunoglobulin G-mediated autoimmune diseases

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Background and Aims: Efgartigimod (EFG), a human immunoglobulin G (IgG) 1 Fc fragment, blocks the neonatal Fc receptor, selectively decreasing IgG levels. The safety profile of subcutaneous (SC) EFG PH20 (co-formulated with recombinant human hyaluronidase PH20) was assessed across generalized myasthenia gravis (gMG) and chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: EFG PH20 SC was assessed using cyclical dosing (4 once-weekly injections) in gMG (ADAPT-SC noninferiority study and ongoing open-label extension ADAPT-SC+ trial [data cut-off: 19 June 2023]) and weekly continuous dosing in CIDP (ADHERE [stage A: open-label; stage B: placebo-controlled] and ongoing open-label extension ADHERE+ trials [data cut-off: 15 June 2023]).

Results: EFG PH20 SC was well-tolerated and demonstrated a consistent safety profile, with similar rates of treatment-emergent adverse events (TEAEs) to placebo in ADHERE, across indications, and across routes of administration; a higher rate of injection site reactions (ISRs) was observed with EFG PH20 SC versus placebo in ADHERE (Table 1). Most TEAEs were mild to moderate in severity across studies. Discontinuation rates due to TEAEs were consistently low, ranging from 0% to 6.8% across studies. There was no increase in TEAE rates, including infections with repeated treatment. ISRs were mild to moderate in severity, and only 1 participant (in CIDP studies) discontinued EFG PH20 SC because of an ISR (Preferred term: Injection site rash). EFG PH20 SC did not reduce albumin or increase cholesterol levels.

TABLE 1:

Table 1 Incidence and event rates of adverse events for subcutaneous efgartigimod in ADAPT-SC, ADAPT-SC+, ADHERE and ADHERE+ trials, and intravenous efgartigimod in ADAPT-SC

Indication	Generalised myasthenia gravis			Chronic inflammatory demyelinating polyneuropathy			
Phase	Phase 3		Phase 3	Pivotal			Phase 2
Trial	ADAPT-SC (10 weeks, NCT04735432)		ADAPT-SC+ (53 years, NCT04818671)	ADHERE (80 weeks, NCT04281472)			ADHERE+ (52 years, NCT04280718)
Incidence, n (%) [event rate]	EFG PH20 SC (N=55; PYFU=10.73)	EFG IV (N=55; PYFU=10.53)	EFG PH20 SC (N=179; PYFU=193.4)	Stage A EFG PH20 SC (N=322; PYFU=46.9)	Stage B EFG PH20 SC (N=111; PYFU=56.7)	Stage B Placebo SC (N=110; PYFU=42.1)	EFG PH20 SC (N=228; PYFU=137.4)
Any TEAE	37 (67.3) [12.4]	28 (50.9) [7.6]	152 (84.9) [9.0]	204 (63.4) [13.4]	71 (64.0) [3.5]	62 (56.4) [3.1]	131 (57.5) [3.5]
Any SAE	8 (14.5) [0.9]	4 (7.3) [0.5]	33 (18.4) [0.3]	21 (6.5) [0.5]	6 (5.4) [0.1]	6 (5.5) [0.2]	21 (9.2) [0.5]
Any severe TEAE (or grade ≥3)	9 (16.4) [1.0]	4 (7.3) [0.5]	36 (20.1) [0.4]	25 (7.8) [0.6]	7 (6.3) [0.1]	7 (6.4) [0.2]	25 (11.0) [0.5]
Any treatment-related TEAE	24 (43.6) [4.9]	12 (21.8) [2.2]	96 (53.6) [4.1]	101 (31.4) [5.5]	27 (24.3) [1.1]	22 (20.0) [1.5]	54 (23.7) [0.9]
Discontinued due to TEAEs[a]	2 (3.6) [0.2]	0	4 (2.2) [0.03]	22 (6.8) [0.5]	3 (2.7) [0.05]	1 (0.9) [0.02]	9 (3.9) [0.09]
Any TEAEs of infections and infestations[b]	10 (18.2) [0.9]	9 (16.4) [0.9]	91 (50.8) [1.0]	44 (13.7) [3.2]	35 (31.5) [0.8]	37 (33.6) [1.3]	73 (32.0) [0.7]
Any TEAEs of injection site reactions[c]	21 (38.2) [1.9]	0	82 (45.8) [3.2]	62 (19.3) [2.6]	16 (14.4) [0.4]	7 (6.4) [0.2]	22 (9.6) [0.3]

AE, adverse event; EFG, efgartigimod; IV, intravenous; PH20, recombinant human hyaluronidase PH20; PYFU, patient-year(s) of follow-up; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.

[a]TEAEs grouped under Preferred Terms leading to EFG PH20 SC discontinuation were 'COVID-19' (n=1) and 'Myasthenia gravis' (n=1) in ADAPT-SC (EFG PH20 SC; 'Cardiac arrest' (n=1), 'COVID-19' (n=1), 'Renal cancer metastatic' (n=1), 'Myasthenia gravis crisis' (n=1) and 'Respiratory failure' (n=1) in ADAPT-SC+; 'Cardiac arrest' (n=1), 'Injection site rash' (n=1), 'COVID-19' (n=1), 'COVID-19 pneumonia' (n=1), 'Muscular weakness' (n=1), 'Chronic inflammatory demyelinating polyradiculoneuropathy' (n=15), 'Quadriparesis' (n=1) and 'Pruritus' (n=1) in ADHERE stage A; 'COVID-19 pneumonia' (n=1), 'Prostate cancer' (n=1) and 'Transitional cell carcinoma' (n=1) in ADHERE stage B EFG PH20 SC; 'Pneumonia' (n=1) in ADHERE stage B PBO SC; 'Lymphadenitis' (n=1), 'Eye movement disorder' (n=1), 'Asthenia' (n=1), 'Hepatic function abnormal' (n=1), 'COVID-19' (n=1), 'Chronic inflammatory demyelinating polyradiculoneuropathy' (n=4) and 'Cranial nerve disorder' (n=1) in ADHERE+.

[b]Infections and infestations are grouped under System Organ Class (Medical Dictionary for Regulatory Activities v. 24.1 for ADAPT-SC and ADAPT-SC+ and v. 25.1 for ADHERE and ADHERE+).

[c]Injection site reactions are defined as AEs in the Medical Dictionary for Regulatory Activities high-level term injection site reactions regardless of the time of AE onset relative to an injection.

Event rates were calculated as the number of events divided by the PYFU.

ADAPT-SC+ data cut-off: 19 June 2023; ADHERE+ data cut-off: 15 June 2023.

Conclusion: EFG PH20 SC was well-tolerated across indications and dosing regimens. Most TEAEs were mild to moderate in severity and did not increase in frequency with recurrent dosing.

Disclosure: PAvD: Annexon Biosciences, argenx, Grifols, Hansa Biopharma, Immunic Therapeutics, Prinses Beatrix Spierfonds, Octapharma, Roche, Sanofi, Sanquin. JLDB: Alexion, Alnylam, argenx, CSL Behring, Janssen, Sanofi Genzyme, UCB. JFH: AcademicCME, Ad Scientiam, Alexion, AstraZeneca Rare Disease, argenx, Biologix, Cartesian Therapeutics, Centers for Disease Control and Prevention, CheckRare CME, F. Hoffmann-LaRoche Ltd, Amgen, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Toleranzia AB, UCB, Zai Lab. TV: Alexion, argenx, Dianthus, Cartesian Therapeutics, Dianthus, Horizon/Viela Bio, ImmunAbs, Immunovant, Janssen/Momenta, Regeneron, Remegen, Sanofi, UCB/Ra. JAA: Akcea Therapeutics, Alexion, Alnylam, Annexon, argenx SE, CSL Behring, Grifols, Immuovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda. SA, MJ, PU, JTG, JP, and LL: Employees of argenx. RAL: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, Boehringer Ingelheim, CSL Behring, GBS/CIDP Foundation International, Grifols, Johnson & Johnson, Medscape, MGFA, Novartis, Peripheral Nerve Society, Pfizer, Roche, Sanofi, Takeda.

EPR-254 | Patisiran in ATTRv amyloidosis with polyneuropathy: "PatisiranItaly" multicenter observational study

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Background and Aims: Hereditary amyloid transthyretin amyloidosis with polyneuropathy (ATTRv-PN) is a multisystemic is a rare, inherited, progressive adult-onset disease, affecting the sensorimotor nerves and other organs. It is caused by mutations in the TTR gene, leading to misfolded monomers which aggregate generating amyloid fibrils. Patisiran is a small, double-stranded interfering RNA encapsulated in a lipid nanoparticle, able to penetrate into hepatocytes, where it selectively targets TTR mRNA, reducing TTR production. We report and discuss a multi-center real-life experience of patisiran in ATTRv-PN.

Methods: We enrolled patients with genetically confirmed diagnosis of ATTRv-PN, from 29 specialized centers from Italy. All subjects underwent neurologic evaluation, each obtaining a Polyneuropathy Disability (FAP) score, Neuropathy Impairment Score (NIS), quality-of-life assessment with the Norfolk Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) questionnaire and Compound Autonomic Dysfunction Test (CADT).

Results: One hundred seventy-five ATTRv patients (70% males) have been recruited. Most patients presented multisystemic involvement and only 15% presented isolated polyneuropathy. In 70% of patients, patisiran was the first treatment while in 30% it was switched from tafamidis or inotersen. Mean NIS values were stable during follow-up suggesting no progression of neuropathy. Patisiran was safe without any side effects in 90% patients. A significant positive correlation was demonstrated between the age at the start of patisiran and the severity of neuropathy assessed by NIS (R^2 =0.043) and quality of life assessed with Norfolk QOL-DN (R^2 =0.006).

Table 1. Demographics of ATTRv-PN patients

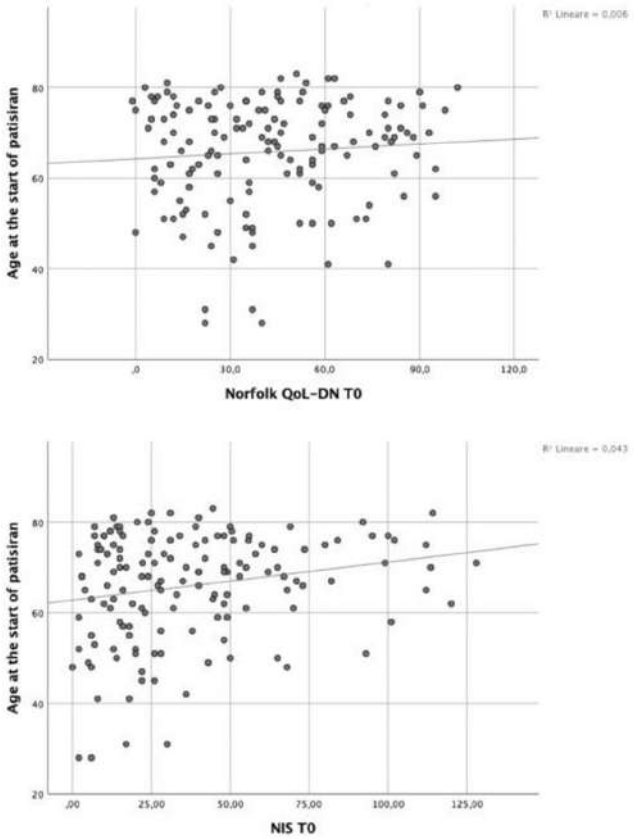
	ATTRv patients (n=175)
Age (years)	
Age at onset neuropathy (years)	62.9±13.1
Age at the start of patisiran (years)	65.9±11.9
Males	121 (70%)
FAP	FAP 1: 128 (74%)
	FAP 2: 47 (26%)
Follow-up	
<9 months	21 (12%)
9-18 months	82 (47%)
18-24 months	60 (34%)
>36 months	12 (7%)
Neuropathy Impairment Score (NIS)	
Baseline (T0)	38.6±30.3
9 months (T1)	39.2±32.5
18 months (T2)	39.2±31.1
Norfolk Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) questionnaire	
Baseline (T0)	43.8±26.5
9 months (T1)	44.3±27.2
18 months (T2)	41.8±25.9
Compound Autonomic Dysfunction Test (CADT)	
Baseline (T0)	16.9±8.3
9 months (T1)	16.7±9.4
18 months (T2)	18.7±8.7

Demographics of ATTRv-PN patients.

Table 2. Adverse event (AE) reported in 175 ATTRv-PN patients treated with patisiran

Adverse event (AE)	Frequency
AE (any type)	17 (9%)
Back pain	6 (3%)
Renal impairment	3 (2%)
Headache	2 (1%)
Rush	2 (1%)
Infusion site reaction	2 (1%)
Itching	1 (0.5%)
Intolerance to premedication	1 (0.5%)
Fatigue	1 (0.5%)
Abdominal pain	1 (0.5%)
AE leading to treatment discontinuation	0
AE leading to treatment interruption	0
Serious AE	0

Adverse event (AE) reported in 175 ATTRv-PN patients treated with patisiran.



A positive correlation was demonstrated between the age at the start of patisiran and the severity of neuropathy assessed by NIS and quality of life assessed with Norfolk QOL-DN.

Conclusion: Our data show that patisiran is effective and safe and that this drug stabilizes neurological symptoms, and QoL, of ATTRv amyloidosis patients.

Disclosure: Vincenzo Di Stefano received compensation for speaking from Alexion and Alnylam; he is SI in clinical trials for Alexion, Alnylam, Argenx, and Sanofi.

Motor neurone diseases

EPR-255 | Prediction of survival outcomes for patients with amyotrophic lateral sclerosis utilizing machine learning

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Background and Aims: ALS is a heterogeneous disorder for which survival prediction has been challenging. The European Network to Cure ALS (ENCALS) utilized the Royston–Parmar (RP) model to predict survival from symptom onset, using data from the diagnosis day. However, data from diagnosis days may not always be available. Hence, a model which predicts survival outcome from any clinical visit may be helpful to physicians and patients for individualized therapy.

Methods: We utilized demographic, clinical, and laboratory parameters from 11024 patient samples in the Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database to develop and validate both an ML Extreme Gradient Boosting (XGBoost) and RP model to predict 12-month survival from any clinical visit. Top predictive features for survival were identified using XGBoost. Refined XGBoost and RP models were trained utilizing the top 5 features.

Results: XGBoost demonstrated superior performance with an AUROC of 0.819 ±0.011 for 12-month forecasts, exceeding the RP's AUROC of 0.798 ±0.021. Top survival predictors identified by XGBoost included albumin level, onset location, ALSFRS-R slope, bicarbonate level, and basophil count. A refined XGBoost model using the top 5 features still performed robustly, with an AUROC of 0.762 ±0.012, compared to the refined RP model's 0.731 ±0.009.

Conclusion: We have developed a simple machine learning model that can accurately predict 12-month survival outcome from any clinical visit. Future studies would involve validating the model in more clinic patient cohorts. Key predictors identified by our ML model provide targets for further ALS research.

Disclosure: This abstract has been submitted to the annual meeting of the American Academy of Neurology.

EPR-256 | An observational cohort study on safety and efficacy in adult 5q SMA patients receiving risdiplam treatment

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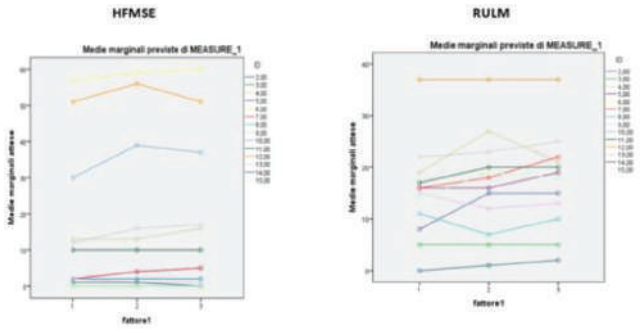
Background and Aims: Risdiplam is an orally administered molecule recently approved for the treatment of Spinal Muscular Atrophy (SMA). It increases functional SMN (survival motor neuron) protein by modifying pre- mRNA splicing of the gene SMN2. Aim of the study was to investigate safety, and efficacy of risdiplam in our adult cohort of SMA patients.

Methods: Inclusion criteria were clinical and molecular diagnosis of SMA2/SMA3; starting Risdiplam in adulthood; availability of clinical data and specific motor scale [Hammersmith Functional Motor Scale Expanded (HFMSE); Revised Upper Limb Module (RULM), six minute walking test (6MWT)] at treatment baseline (T0) and after 6 months (T6).

Results: We included 18 patients (9 SMA 2 and 9 SMA3), with a median age of 41 years at the first administration (IQR 37.7–48.6).

HFMSE significantly increased from T0 to T6 ($p=0.027$) and from T0 to T12 (p: 0.033). Moreover RULM showed a significant improvement at T12 ($p=0.016$). No changes in the 6MWT were detected in walking patients. Ten patients (55.6%) were classified as responders at T6, and 8 out of the 14 patients (71, 43.1%) were also classified as responders at T12. Among all demographic and clinical variables, the number of SMN2 copies was independently associated with clinical improvement at T6 ($p=0.023$) and T12 ($p=0.045$). No severe adverse events were reported.



Spaghetti plot show improvement from T0 to T6 and T12 on the HMFSE and RULM scales.

		N. of patients (%)	MEDIAN	IQR
AGE (YEARS)			42,7	37,7-48,6
AGE AT ONSET (MONTHS)			8,2	13,5-42
DISEASE DURATION (YEARS)			40,3	33,6-47,1
SEX	FEMALE	8 (44,4%)		
	MALE	10 (55,5%)		
SMA TYPE	SITTERS	14 (77,8%)		
	WALKERS	4 (22,22%)		
SMA COPIES	2	4 (11%)		
	3	14 (77,8%)		
	4	2 (11,1%)		
HMFSE 0	18		2	0,25-12,75
HMFSE 1	18		3	0,25-15,25
HMFSE 2	14		5	1,25-16,75
RULM 0	18		6,50	15,50-21,25
RULM 1	18		7,5	17,00-26,00
RULM 2	14		13,50	19,50-24,25

TABLE

Conclusion: our data highlight that the efficacy of Risdiplam is evident even in the first months of treatment, regardless of age/gender/functional clinical status at baseline and SMA type. Number of SMN2 copies influence positively clinical improvement.
Disclosure: Nothing to disclose.

EPR-257 | Impairment of brain "neurovascular coupling" in ALS: Correlations with cognitive abilities and prognosis

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Background and Aims: Alterations of brain-blood barrier, part of neurovascular unit (NVU), have been evidenced in Amyotrophic Lateral Sclerosis (ALS). We aim at exploring the potential NVC alterations across different resting state networks via the spatial combination of "cerebral blood flow" (CBF) and amplitude of low frequency fluctuations (ALFF) maps, respectively derived from arterial spin labeling (ASL) and blood oxygen level dependent (BOLD) RS-fMRI measurements, in a sample of ALS patients compared to healthy controls (HC). Additionally, we compared the NVC data at baseline in subsets of patients with different disease progression.
Methods: 51 ALS patients were screened by clinical and neuropsychological scales, and were classified a posteriori as very fast, fast, and slow progressors (VFPs, FPs, and SPs), according to change in the disability score over 12 months. 25 HCs were enrolled.
Results: No patient was affected by dementia, while 17 patients had cognitive impairment according to Strong Criteria. A statistically significant reduction of NVC (ALFF-CBF) was found in the default mode network (DMN) in ALS patients compared to HC. We found significant correlations between the NVC in the DMN and the executive function, memory, visuospatial ability and ALS-non-specific ECAS subscores. We identified significant differences in NVC at baseline in the DMN between VFPs and SPs groups.
Conclusion: Our findings suggest that significant changes in NVC occur outside the motor areas in ALS patients; NVC measures might represent a valuable tool to explore early signature of cognitive/extra-motor impairment in ALS. Moreover, NVC alterations in DMN could represent a predicter of faster clinical progression.
Disclosure: I have no disclosure.

EPR-258 | Characteristics of proteostasis changes in amyotrophic lateral sclerosis

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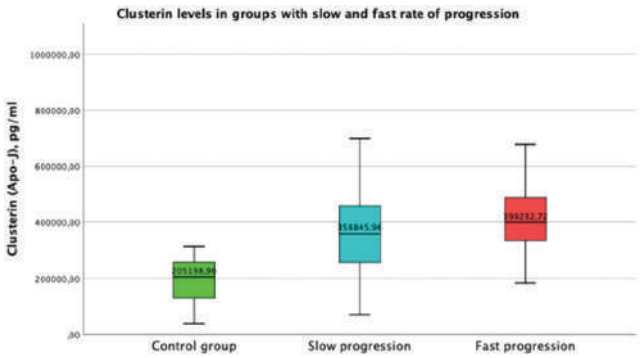
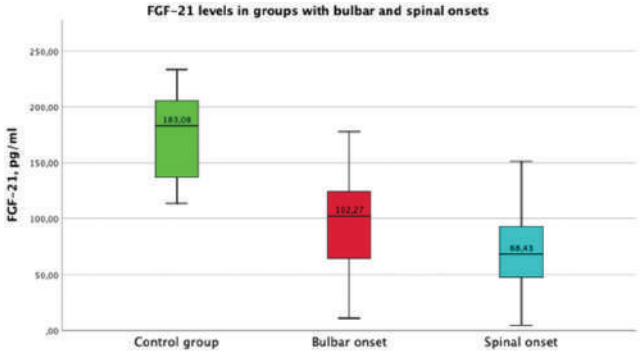
Background and Aims: Amyotrophic lateral sclerosis (ALS) is a fatal, rapidly progressive neurodegenerative disease. Increasing evidence suggests that disturbances in proteostasis play a significant role in the pathogenesis of ALS.

Methods: The study enrolled 100 patients diagnosed with ALS, while the control group consisted of 20 healthy volunteers. We performed clinical assessment with neurological examination and ALSFRS-R functional status evaluation. The concentrations of amyloid beta 1-40 and 1-42, FGF-21, Kallikrein-6, Neurogranin, Tau (total), Tau (pT181), Apolipoprotein E4, Clusterin and complement component C3 in cerebrospinal fluid were measured using the multiplex ELISA kit.

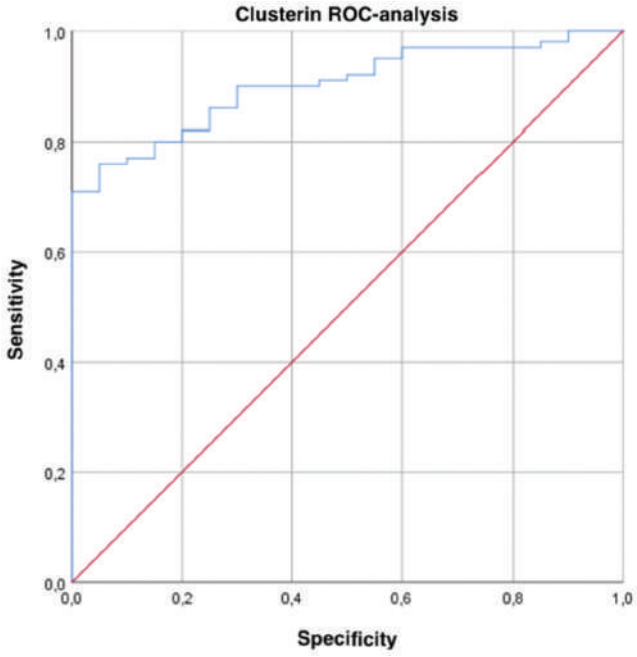
Results: Significant differences between the main and control groups ($p < 0.05$) were observed in the concentrations of Amyloid beta 1-40 and 1-42, FGF-21, Tau (total), Tau (pT181), Clusterin, S100B and complement C3. Multiple comparisons revealed significant difference in the levels of clusterin and apolipoprotein E4 between patients with slow and rapid rates of progression, with increased concentration in the group with rapid progression. It is known that clusterin involved in the elimination process of pathologically aggregated TDP-43 and SOD1. As a promising supplementary diagnostic biomarker clusterin demonstrated 76% and 95% of sensitivity and specificity relatively. FGF-21 levels significantly differ between patients with bulbar and spinal onsets and its concentration decreased in the case of spinal onset. In animal models it was shown that activation of the FGF21 pathway induces an effective anti-inflammatory response.



Clusterin levels in the groups with slow and fast rate of progression.



FGF-21 levels in the groups with bulbar and spinal onsets.



Clusterin ROC-analysis.

Conclusion: Investigating various aspects of proteostasis disruption in amyotrophic lateral sclerosis may provide future promising therapeutic opportunities and a potential diagnostic algorithm for assessing the progression of the neurodegenerative process.

Disclosure: Nothing to disclose.

EPR-259 | Parenteral nutrition in amyotrophic lateral sclerosis: An exploratory population-based study

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Background and Aims: Nutritional support is a crucial aspect in the management of amyotrophic lateral sclerosis (ALS). However, the realm of home parenteral nutrition (HPN) remains relatively unexplored in ALS research, and a thorough comparison with enteral nutrition (EN) regarding main health outcomes is lacking. This study aims to evaluate HPN within an ALS cohort.

Methods: We included 55 patients from the Turin ALS Centre diagnosed with probable, probable laboratory-supported or definite ALS between 2015 and 2022. Site of onset (bulbar – BO/spinal – SO), cognitive status (normal – CN/impaired – CI) and ventilatory support (none/not invasive – NIV/invasive – IV) were assessed.

Results: BO (50.9%), CI (58.2%) and ventilated (65.5%) patients were predominant. The mean interval between diagnosis and the initiation of HPN was 697 days, shorter in BO (614 days) and in CI (518 days). The mean survival (or time to IV) from the start of HPN was 120 days, shorter in BO (106 days) and in CI (104 days). The overall rate of

HPN-related complications was 43.6%, mainly consisting of local adverse events (66.7%).

Conclusion: The shorter survival in CI may primarily stem from suboptimal treatment compliance (e.g. NIV), yet the association with cognitive impairment may explain similar data in BO. Given the prevailing compromised status in our representative cohort, the mean overall survival observed with HPN, consistent with prior studies and comparable to that reported with EN plus respiratory insufficiency, may justify its utilization in advanced stages characterized by cognitive and respiratory impairment.

Disclosure: Nothing to disclose.

EPR-260 | Specific subcortical degeneration pattern is associated with bulbar-onset phenotype and social cognition deficits in ALS

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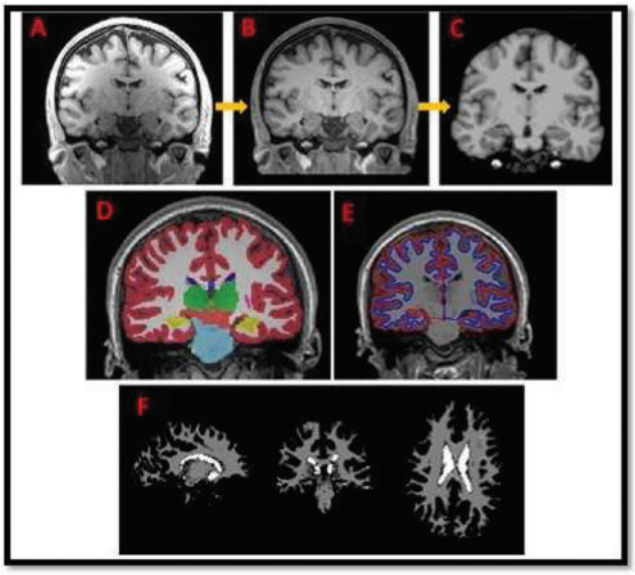
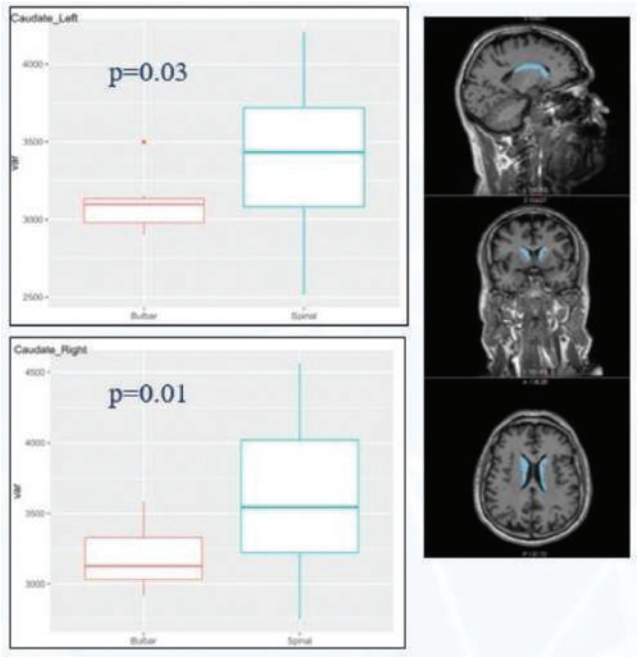
Background and Aims: Cognitive impairment is reported in up to 50% of ALS patients. Recent investigations suggest the presence of social cognition deficits, possibly unrelated to executive dysfunction. Only a few neuroimaging studies have attempted to correlate brain structural alterations to social cognition performance in ALS.

Methods: We enrolled 45 ALS patients. 20% had bulbar-onset. Disease severity was staged according to the King's Staging System (KSS, stage 0 = 1, stage 1 = 34%, stage 2 = 31%, stage 3 = 33%). All patients were tested with ECAS, Ekman and SET scale, and performed 3D T1-weighted sequences on 3T MRI. Imaging reconstruction and segmentation were performed with FreeSurfer. Clinical, neuropsychological and structural changes and their correlation with scores on social cognition tests were explored.



Representation of FreeSurfer pipeline steps for brain imaging parcellation and segmentation. (A) Raw T1-3D MRI; (B) intensity corrected; (C) removal of all non-brain areas; (D) automatic volume labelling; (E) White matter labelling; (F) segmentation.

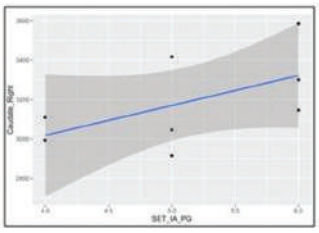
Results: Group comparison analysis showed worse results for Ekman ($p = 0.0375$) and SET-IA ($p = 0.0047$) in bulbar-onset and KSS-3 patients, and lack of correlation with executive dysfunction. The bulbar-onset group showed lower bilateral caudate volumes compared to spinal-onset patients (L: $p = 0.03$, R: $p = 0.01$). KSS-3 patients had reduced left caudate volume ($p = 0.01$) and left inferotemporal cortical thickness ($p = 0.04$). In the bulbar-onset subgroup, SET-IA score and right caudate volume were positively correlated, without reaching significance level possibly because of reduced sample size ($n = 8$, $r = 0.60$, $p = 0.54$).



Box plots of the bilateral caudate volumes according to disease type of onset (bulbar vs. spinal).

Bulbar (n=8) r coefficient	SAND			SET	Ekman				Imaging	
	denom	compr.	sem. assoc.	IA	GS	surprise	fear	sadness	Caudate_L	Caudate_R
SAND_ Denomination	1.00									
SAND_ Comprehension	-0.18	1.00								
SAND_ semantic association	-0.52	0.07	1.00							
SET_IA	-0.13	-0.44	0.18	1.00						
Ekman_GS_PG	0.55	0.20	0.85	0.08	1.00					
Ekman_surprise	0.69	0.37	0.54	-0.23	0.72	1.00				
Ekman_fear	-0.17	-0.24	-0.06	0.59	-0.22	0.68	1.00			
Ekman_sadness	-0.07	0.08	0.64	0.22	0.74	-0.35	0.11	1.00		
Caudate_Left	-0.22	0.10	0.17	0.25	0.18	-0.06	-0.17	-0.13	1.00	
Caudate_Right	-0.08	0.10	0.28	0.60	0.06	-0.06	-0.51	-0.13	0.64	1.00

	SET_IA p value
SAND_ Denomination	0.7573
SAND_ Comprehension	0.2797
SAND_ semantic association	0.6171
SET_IA	-
Ekman_GS_PG	0.8462
Ekman_ surprise	0.5868
Ekman_fear	0.0238
Ekman_ sadness	0.6079
Caudate_Left	0.5472
Caudate_Right	0.1122



Pearson correlation coefficients for all the areas and volumes considered (upper) and SET-IA corresponding p-values (lower) and graphic representation of the linear correlation between SET-IA raw score and the right caudate volume in bulbar subjects.

Conclusion: Social cognition and emotion recognition deficits are worse in bulbar-onset phenotype, in advanced disease stages, and are at least partly unrelated to executive dysfunctions. The possible correlation between the caudate volume and SET-IA score in bulbar patients provides preliminary evidence of a phenotype-specific subcortical degeneration pattern associated with social cognition deficits.

Disclosure: Nothing to disclose.

EPR-261 | Genetics screening in an Italian cohort of patients with ALS: The importance of early testing and its implication

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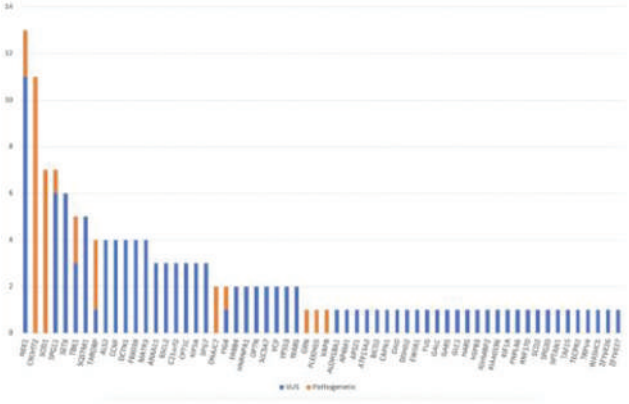
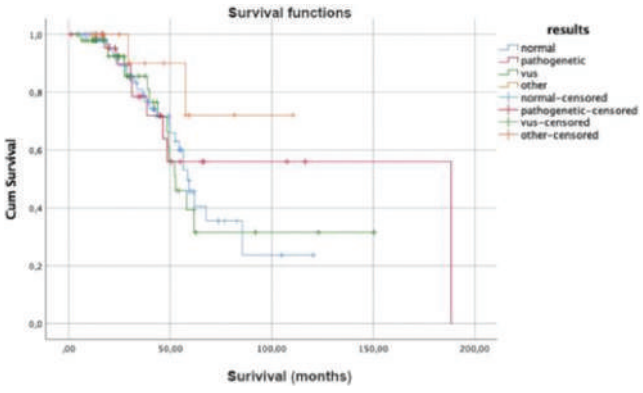
Background and Aims: Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease with an elusive etiology. The genetic connection is increasingly evident, even in patients with sporadic ALS. We allowed access to the genetic test to all patients attending our clinic to identify the prevalence and the role of genetic variations in the development of the disease and to identify patients with potentially treatable forms of the disease.

Methods: 194 patients with probable or definite ALS, were enrolled. A comprehensive genetic testing was performed, including sequencing all exons of the SOD1 gene and testing for repeat expansions in the C9orf72 gene. Whole Exome NGS Sequencing (WES) was performed, followed by an in silico multigene panel targeting neuromuscular diseases.

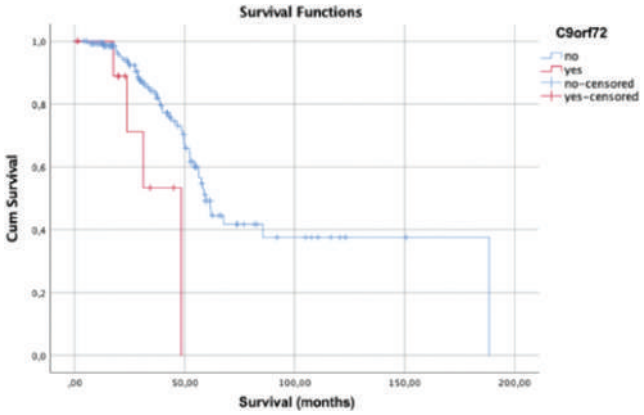
Results: Clinically significant pathogenetic variants were detected in 14.43% of cases. The highest prevalence of pathogenetic variants was observed in fALS patients, but a substantial proportion of sALS patients also displayed at least one mutation. The most observed pathogenetic mutation was the expansion of the C9orf72 gene, which was associated with a shorter survival. SOD1 mutations were found in 1.6% of fALS and 2.5% of sALS patients.



Distribution of mutated genes across our cohort, including pathogenic and variants of uncertain significance (VUS). Pathogenic and likely pathogenic variants are considered together.



No significant difference in survival among patients with and without genetic mutations (Log-rank p value = 0.448).



Patients with C9orf72 had a significative lower survival than patients without the mutation (log-rank *p* value of 0.013).

Conclusion: This study emphasizes the diverse genetic basis of ALS and advocates for integrating comprehensive genetic testing into diagnostic protocols. The evolving landscape of genetic therapies requires identifying all eligible patients transcending traditional familial boundaries. The presence of VUS highlights the multifaceted nature of ALS genetics, prompting further exploration of complex interactions among genetic variations, environmental factors, and disease development.

Disclosure: Nothing to disclose.

EPR-262 | Quantitative MRI study of paraspinal muscles in patients with ALS and correlation with neurophysiological data

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Background and Aims: Examining paraspinal muscles is crucial for diagnosing and staging Amyotrophic Lateral Sclerosis (ALS), typically accomplished through electromyography. This study aims to assess quantitative MRI of paraspinal muscles in ALS cohort and find the correlations between radiological and neurophysiological data.

Methods: Seventy-three subjects were enrolled at the IRCCS Mondino in Pavia. They were tested with quantitative muscular MRI, utilizing waterT2 (wT2) and Fat Fraction (FF) sequences, coupled with standard electromyography focusing on the paraspinal muscles. These examinations were conducted for specific muscles: Multifidus muscles, Longissimus thoracis muscles, Iliocostalis muscles and Iliopsoas muscles.

Results: The analysis of 55 muscle MRI did not show statistically significant difference in wT2 and FF values between right and left sides of the dorsal and lumbar portions of the paraspinal muscles; no statistically significant difference emerged after the stratification of patients based on the type of onset. Comparison between quantitative muscle MRI data and electrophysiological values did not reveal strong positive correlations.

Conclusion: This is the first study in which paraspinal muscles were evaluated in patients with ALS using quantitative muscle MRI techniques. Our results highlight a widespread and symmetric involvement of the paraspinal muscles, regardless of the onset site. Furthermore, quantitative muscular MRI have shown a greater sensitivity of electromyography in detecting muscular alterations present in the early stages of disease. Longitudinal data were not included as they are still being acquired.

Disclosure: None.

Peripheral nerve disorders

EPR-263 | Clinical evaluation of presymptomatic carriers of TTR mutations

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Background and Aims: The identification and monitoring of asymptomatic carriers is gaining importance after the therapeutic advances in hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN). However, there is not any consensus regarding genetic screening of family members of ATTR-PN and the diagnostic tools to monitor presymptomatic carriers of TTR mutations.

Methods: Presymptomatic p.Val50Met mutation carriers were included to the study. Individuals were evaluated by nerve conduction studies, DN4 neuropathic pain score, single fiber neuropathy questionnaire (SFN-SIQ), warm and cold sensation thresholds assessed by quantitative sensory testing (QST), and intraepidermal nerve fiber density (IENFD) annually until symptom onset.

Results: Thirteen members of five different families with a history of ATTRv-PN were included. The mean age was 40.6 (±11.9) years and three of them were male. The neurological examinations remained normal during follow-up in all carriers as well as the nerve conduction studies. Baseline DN4 score, SFN-SIQ, warm and cold sensation thresholds were normal in all individuals. Four carriers developed symptoms of small fiber neuropathy during a median follow-up of 2 (1–3) years. At symptom onset, warm and cold sensation

thresholds were increased and IENFD decreased to below normative values. In addition, IENFD decreased below normal values in four asymptomatic carriers despite normal clinical and other laboratory findings.

Conclusion: In our cohort, symptom onset of ATTRv-PN was concomitant with QST and IENFD abnormality. However, IENFD was below before symptom onset in four carriers. Our results underline the use of multiple diagnostic tools for the follow-up of presymptomatic ATTRv-PN carriers.

Disclosure: Nothing to disclose.

EPR-264 | Mobile health technologies in monitoring treatment response to immunoglobulins in CIDP: A pilot longitudinal study

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Background and Aims: Response to treatment in chronic inflammatory demyelinating polyneuropathy (CIDP) is defined by using disability and impairment scales, despite their limited accuracy in detecting minimal but significant changes in clinical settings. The aim of our study was to explore the potential role of mobile health technologies (MHT) in assessing treatment response in CIDP patients treated with I.V. immunoglobulins (Ig).

Methods: Seven patients with a diagnosis of CIDP according to EAN/PNS criteria treated with Ig and sixteen age- and sex-matched healthy controls (HC) were enrolled. Patients performed digital mobility assessments using MHT at drug administration and after 21 and 45 days. Differences between groups in postural transition, balance, turning, and gait MHT parameters were assessed using non-parametric tests. The comparison of the three time points was evaluated through repeated measures ANOVA.

Results: Compared to HC, CIDP patients showed greater jerks, longer step time and duration of turns, and lower peak angular velocity (all p values <0.02). At follow-up, an improvement in MHT parameters for time to rise from a chair ($p = 0.01$), duration of turns during the TUG test ($p = 0.04$), and jerks while standing on a widened base with eyes open ($p = 0.03$) was observed compared to baseline.

Conclusion: Mobile health technology was able to detect mobility alterations in CIDP and track the beneficial effects of Ig treatment. Therefore, MHT may be a useful tool to monitor patients with CIDP and their response to different management strategies.

Disclosure: Nothing to disclose.

EPR-265 | Diagnostic delay and burden of disease in chronic inflammatory demyelinating polyneuropathy: A real-world survey

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Background and Aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare condition of the peripheral nervous system characterized by progressive muscle weakness and impaired sensory function. The aim of this study was to describe the diagnostic pathway and disease burden experienced by CIDP patients in Europe.

Methods: Data were drawn from the Adelphi CIDP Disease Specific Programme™, a cross-sectional survey of neurologists in France, Germany, Italy, Spain, UK (September 2022–April 2023), treating at least two CIDP patients per typical month. Patients completed patient-reported outcome measures including the EuroQol-5 Dimension (EQ-5D-5L) and Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-Fatigue). This real-world data is limited by participating physicians' confirmation of the included patient's CIDP diagnosis.

Results: 83 physicians provided data for 542 patients with CIDP. Mean (SD) patient age was 54.0 (12.4) years; 62.2% were male. Median (IQR) time from symptom onset to CIDP diagnosis was 7.0 (3.8, 13.1) months; 36.7% of patients were initially misdiagnosed/suspected to have a different condition, most frequently Guillain-Barré syndrome. Maintenance treatment was prescribed to 85.4% of patients. Physicians were only partially satisfied with 57.9% of patients' treatment. 12.8% of patients had been hospitalized within the last 12 months, most frequently to treat a complication of CIDP. Patients reported a mean (SD) EQ-5D-5L health utility of 0.63 (0.24) (UK value sets) and FACIT-Fatigue of 34.8 (9.9).

Conclusion: These results highlight the challenges experienced by CIDP patients in Europe, pre-/post-diagnosis. Increased disease knowledge and awareness among physicians may improve diagnostic timelines and outcomes for CIDP patients.

Disclosure: Data collection was undertaken by Adelphi Real World as part of an independent survey, entitled the Adelphi Real World CIDP Disease Specific Programme. Janssen were one of multiple subscribers to the dataset. The study described here was funded by Janssen.

EPR-266 | Conceptualizing innovative approaches in the treatment of peripheral neuropathies

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Background and Aims: Effective therapies in hereditary and acquired peripheral neuropathies remain limited and focused on

disease symptom management. We describe an orally bioavailable, selective Histone deacetylase 6 inhibitor (HDAC6i) with potential to revert pathological hallmarks of Charcot-Marie-Tooth (CMT) disease and Chemotherapy-induced peripheral neuropathy (CIPN) through axonal regeneration and nerve function restoration.

Methods: HDAC6i AGT-100216 was profiled in a CMT1A C3 mice model, and in a curative mouse model of CIPN.

Results: In a CMT1A C3 mice model AGT-100216 exhibited high potency and selectivity on the HDAC6 enzyme resulting in a dose-dependent improvement of grip strength, compound muscle action potential (CMAP) and nerve conduction velocity. Increased acetylated alpha-tubulin, reduction of neurofilament light chain (NFL), improved axonal diameters and myelin g-ratios were also observed. In a curative CIPN model, AGT-100216 dose-dependently rescued sensory and motor function deficits, matching biomarker changes.

Conclusion: The discovery of a highly selective HDAC6 inhibitor AGT-216 with a potential of reverting axonal degeneration and restoring peripheral nerve function allows for further exploration of new paradigms in the treatment of PNS disorders. Confirming this inherent capacity of AGT-216 in future research in humans will allow for an innovative approach in the treatment of peripheral neuropathies.

Disclosure: Trad M. receives fees as a consulting part time Chief Medical Officer at Augustine Therapeutics; Prior R. receives consultancy fees from Augustine Therapeutics; Rombouts F., van Eyll J., Szyndralewiez C., Celanire S. Have no disclosures as they are full employees of Augustine Therapeutics.

EPR-267 | Whole genome sequencing in patients with clinically diagnosed Charcot-Marie-Tooth disease

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Background and Aims: Charcot-Marie-Tooth disease (CMT) is a genetically and clinically heterogeneous disorder characterized by progressive muscle weakness and sensory disturbances. Advances in genetic diagnosis have led to the identification of many genetic causes of CMT, but many patients clinically diagnosed with CMT do not have a genetic diagnosis. Whole-genome sequencing (WGS) is the most comprehensive next-generation sequencing assay because it can assess the entire extent of the human genome, including non-coding regions. In this study, we aimed to evaluate the diagnostic yield of WGS in CMT compared to whole-exome sequencing (WES).

Methods: WGS was conducted in 72 families with clinically diagnosed CMT where no genetic diagnosis was obtained from WES and 17p12 duplication screening. WGS was performed using the NovaSeq6000 platform, in accordance with the manufacturer's instructions.

Results: Among these families, 14 were diagnosed through WGS, resulting in a yield of 19.4%. The genotype-based analysis used in this study identified the cause of four cases and contributed the most to the diagnostic yield. The other cases included those due to better coverage of whole genome sequencing (two cases) and those due to structural or non-coding variants (one case each).

Conclusion: This study was the first to evaluate the additional diagnostic yield of WGS after performing WES in patients with clinically diagnosed CMT. A wider range of genes should be targeted in WGS using genotype-driven analysis. In addition to the well-known advantages of WGS compared with WES, such as structural variants and non-coding variants, better coverage even in the coding regions could be another important advantage of WGS.

Disclosure: Nothing to disclose.

EPR-268 | Clinical diversities of INF2 mutations in patients with Charcot-Marie-Tooth disease

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Background and Aims: Charcot-Marie-Tooth disease (CMT) is the most common inherited peripheral neuropathy. Patients with CMT occasionally exhibit complex clinical symptoms depending on genetic causes. As an example of the complex phenotypes, patients with mutations in the inverted formin-2 (INF2) gene have shown autosomal dominant Intermediate CMT type E (CMTDIE) with nephropathy of focal segmental glomerulosclerosis (FSGS). In this study, we aimed to identify INF2 mutations in patients with CMT and FSGS, and to define the clinical characteristics in affected patients.

Methods: The families with CMT or FSGS were examined for INF2 mutations. Clinical information was obtained using the standard methods. Nerve conduction study was used to assess the function of peripheral nervous system as an electrophysioological tool. Lower limb axial MRI scans of the bilateral thigh and calf muscles were reviewed.

Results: Four dominant missense INF2 mutations were identified as the underlying causes of CMT and/or FSGS. Four families with INF2 mutations showed different clinical symptoms. Two families had

symptoms of CMT and FSGS, while the others had symptoms of either CMT or FSGS. Moreover, different CMT types including CMT1 and CMTDIE were observed in families with INF2 mutations. The affected individuals with the two CMT types showed clearly different features in terms of onset age, muscle atrophy, nerve conduction, and functional disability.

Conclusion: We suggest that genotype-phenotype correlations may be more complex than we thought. This study expands the clinical spectrum of patients with INF2 mutations and will be helpful in the molecular diagnosis of CMT and FSGS.

Disclosure: Nothing to disclose.

EPR-269 | Efficacy and safety of efgartigimod PH20 in chronic inflammatory demyelinating polyneuropathy: Results of ADHERE/ADHERE+

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Background and Aims: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc fragment, blocks the neonatal Fc receptor, decreasing IgG recycling and reducing pathogenic IgG autoantibody levels. Multi-stage, double-blinded, placebo-controlled ADHERE, and ongoing open-label extension ADHERE+, assessed the efficacy and safety of efgartigimod PH20 subcutaneous (SC; coformulated with recombinant human hyaluronidase PH20) in chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: Enrolled participants with CIDP (treatment-naïve or on standard treatments withdrawn during run-in period) had active disease and received efgartigimod PH20 SC weekly (stage A). Responders were randomized (1:1) to weekly efgartigimod PH20 SC or placebo (stage B). Participants with clinical deterioration in stage B or those who completed ADHERE could enter ADHERE+ (efgartigimod once weekly). Primary outcomes were clinical improvement (stage A), efficacy (stage B) and safety (ADHERE+) (Figure 1).

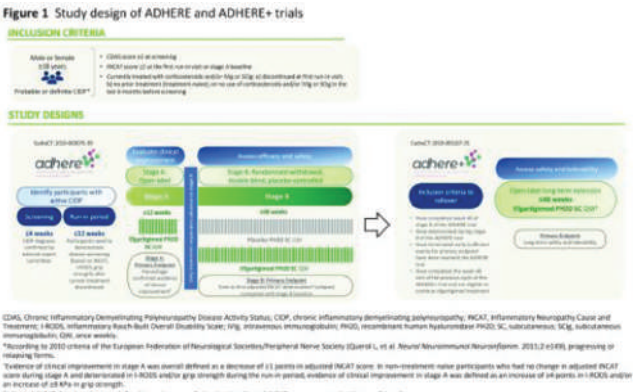

FIGURE 1

Results: In stage A, 214/322 (66.5%) participants demonstrated evidence of clinical improvement. In stage B, efgartigimod significantly reduced relapse risk (HR: 0.394; 95% CI: 0.253–0.614) versus placebo ($p = 0.00004$). Reduced risk of clinical deterioration was shown in participants regardless of prior CIDP therapy. Selected secondary outcomes are shown in Table 1. 99% of eligible participants entered ADHERE+. The safety profile of efgartigimod-treated participants was consistent over 137.42 total patient-years of follow-up for ADHERE+. Most treatment-emergent adverse events were mild/moderate; their incidence/severity did not increase in ADHERE+ (Table 2).

TABLE 1

Table 1 Key secondary efficacy endpoints in the ADHERE trial

	ADHERE		
	Stage A Efgartigimod PH20 SC (N=322)	Stage B Efgartigimod PH20 SC (N=111)	Stage B Placebo PH20 SC (N=110)
Mean (SD) change from baseline to last assessment*			
Adjusted INCAT score	−0.9 (1.71)	0.1 (1.08)	0.9 (1.98)
I-RODS score	7.7 (15.48)	0.8 (12.33)	−7.0 (19.10)
Mean grip strength (dominant hand), kPa	12.3 (18.68)	2.1 (13.29)	−8.2 (20.69)
Mean grip strength (non-dominant hand), kPa	11.2 (21.12)	2.0 (17.33)	−6.9 (21.30)
I-RODS deterioration of ≥4 points, n (%)		40 (36.0)	57 (51.8)
Hazard ratio (95% CI)		0.537 (0.354–0.814)	
Nominal *P* value		0.0034	
I-RODS improvement of ≥4 points, n (%)		50 (45.0)	40 (36.4)
Odds ratio (95% CI)		1.441 (0.814–2.567)	
Nominal *P* value		0.2294	

CI, confidence interval; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-built Overall Disability Scale; PH20, recombinant human hyaluronidase PH20 SC, subcutaneous; SD, standard deviation.
*For stage A, this was the change from stage A baseline to stage A last assessment, and for stage B, this was the change from stage B baseline to stage B last assessment.

TABLE 2

Table 2 Incidence and event rates of adverse events in ADHERE and ADHERE+ trials

	ADHERE			ADHERE+
Incidence, n (%) [event rate]	Stage A Efgartigimod PH20 SC (N=322; PYFU= 46.9)	Stage B Efgartigimod PH20 SC (N=111; PYFU= 56.7)	Stage B Placebo PH20 SC (N=110; PYFU= 42.1)	Efgartigimod PH20 SC (N=228; PYFU= 137.4)
≥1 TEAE	204 (63.4) [13.4]	71 (64.0) [3.5]	62 (56.4) [5.1]	131 (57.5) [3.5]
≥1 treatment-related TEAE*	101 (31.4) [5.5]	27 (24.3) [1.1]	22 (20.0) [1.5]	54 (23.7) [0.9]
≥1 SAE	21 (6.5) [0.5]	6 (5.4) [0.1]	6 (5.5) [0.2]	21 (9.2) [0.3]
≥1 treatment-related SAE*	4 (1.2) [0.09]	0	4 (3.6) [0.2]	3 (1.3) [0.03]
≥1 AE of Infections†	44 (13.7) [1.2]	35 (31.5) [0.8]	37 (33.6) [1.3]	73 (32.0) [0.7]
Discontinued due to TEAEs	22 (6.8) [0.5]	3 (2.7) [0.05]	1 (0.9) [0.02]	9 (3.9) [0.1]
Deaths‡	2 (0.6) [0.04]	0	1 (0.9) [0.02]	1 (0.4) [0.007]

AE, adverse event; PH20, recombinant human hyaluronidase PH20; PYFU, patient-year(s) of follow-up; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.
*Deemed treatment-related by the investigator.
†Infections and infestations are grouped under System Organ Class (Medical Dictionary for Regulatory Activities v. 25.1).
‡Deemed to be not related to efgartigimod PH20 SC by the investigator.
Event rates were calculated as the number of events divided by the PYFU.
ADHERE+ data cut-off: 15 June 2023.

Conclusion: ADHERE+ demonstrated long-term effectiveness of efgartigimod PH20 SC for the prevention of relapse. The safety profile of efgartigimod PH20 SC was similar between ADHERE and ADHERE+ and was consistent with the previously demonstrated safety profile of efgartigimod.

Disclosure: PAvD: Annexon Biosciences, argenx, Grifols, Hansa Biopharma, Immunic Therapeutics, Octapharma, Prinses Beatrix Spierfonds, Roche, Sanofi, Sanquin. JAA: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx SE, CSL Behring, Grifols, Immunovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda. IB, TD, YH, GLM, JL, MS, TC, and RY: None. CE: argenx, Biogen, GSK, UCB. JTG, EH, AT, PU, and BVH: Employees of argenx. KG: Alexion, argenx, UCB, Xeris Pharmaceuticals. CH: argenx, Biogen, Lupin, Roche, UCB. SK: Alexion, argenx, CSL Behring, Takeda. FL: Alexion, Bayer, Biogen, Fresenius, Grifols, Merck, Novartis, Roche, Teva Pharmaceuticals. MLi: argenx, CSL Behring, Kedrion, MedisonPharma/Alnylam, Pfizer, Sanofi, Sobi, Takeda. MLo: Employee of argenx when the studies were conducted. GLP: Biogen, Chromocell, CSL Behring, Home Biosciences, Janssen, Lilly, Sangamo Therapeutics, Vertex Pharmaceuticals, Zambon. LQ: Annexon Biosciences, Alnylam, argenx, Avilar Therapeutics, Biogen, CIBERER, CSL Behring, Dianthus, Fundació La Marató, GBS/CIDP Foundation International, Grifols, Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi Genzyme, UCB. RAL: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, Boehringer Ingelheim, CSL Behring, GBS/CIDP Foundation International, Grifols, Johnson & Johnson, Medscape, MGFA, Novartis, Peripheral Nerve Society, Pfizer, Roche, Sanofi, Takeda.

EPR-270 | Transthyretin amyloid deposition in ligamentum flavum in an Italian cohort of patients with lumbar spinal stenosis

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Background and Aims: Transthyretin amyloidosis (aTTR) is a disorder characterized by extracellular accumulation of misfolded transthyretin (TTR). As TTR deposition potentially occurs in every tissue, it also can lead to lumbar spinal stenosis (LSS), a clinical syndrome determined by hypertrophy of ligamentum flavum (LF) and narrowing of the lumbar spinal canal. Several studies report a strong association between LSS and TTR amyloid deposits in the LF. In this study, we prospectively investigated the frequency of TTR amyloid deposits in material obtained at LSS surgery performed at our Center.

Methods: LF specimens were provided from patients who underwent surgery for LSS in the Neurosurgery Department of Policlinico Gemelli, Rome, from June 2023. Demographic, clinical and radiological data were collected. Extensive pathological analysis to detect possible amyloid deposits was performed in all specimens.

Results: The study included 30 patients. Males/females ratio was 18/12. The mean age at the time of surgery was 64 ± 12.75 years. We detected amyloid deposits in 1/30 cases, which also resulted positive at immunohistochemistry with anti-TTR antibodies. Genetic investigations yielded a negative result for hereditary aTTR.

Conclusion: Lumbar canal stenosis is a common spinal condition in elderly patients. Although previous studies have shown a relevant frequence of amyloid deposits in LF hypertrophy, suggesting a possible role in LSS pathogenesis, in our cohort this occurrence was extremely rare. This result should be confirmed in different populations of the same non-endemic country in order to better define a possible geographic contribute to occurrence of amyloid deposits in LSS.

Disclosure: Nothing to disclose.

EPR-271 | **Clinical outcome measures and biomarkers in chronic inflammatory demyelinating neuropathy (CIDP): A literature review**

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Background and Aims: CIDP displays various clinical subtypes, and variability exists when assessing therapy and disease progression using clinical outcome assessments (COA). Biomarkers may be a novel way of establishing outcome and tracking progression in CIDP. This literature review aimed to identify COAs and biomarkers used, proposed, or studied to date in CIDP, and to attempt to inform future management.

Methods: A structured literature review was conducted to explore COAs and biomarkers in CIDP, covering publications from 2010-September 2023 and conference proceedings from 2020-September 2023, with older relevant publications also considered. COAs and biomarkers were mapped into groupings, based on type of assessment, which was then reviewed and validated by clinical experts for prioritization.

Results: Out of 1,863 publications screened, 778 were prioritized for mapping (Figure 1, Figure 2). Key COAs included the INCAT (Inflammatory Neuropathy Cause and Treatment) scale, RODS (Inflammatory Rasch Built Overall Disability Scale), MRC (Medical Research Council) sum scores, and grip strength. Disease-specific health-related quality of life measures were limited in number and lacked widespread use, while more generic COAs focused on specific, non-neuropathic, disease aspects. CIDP biomarker research is growing, with some demonstrating possible correlations with disease activity and therapeutic effects.

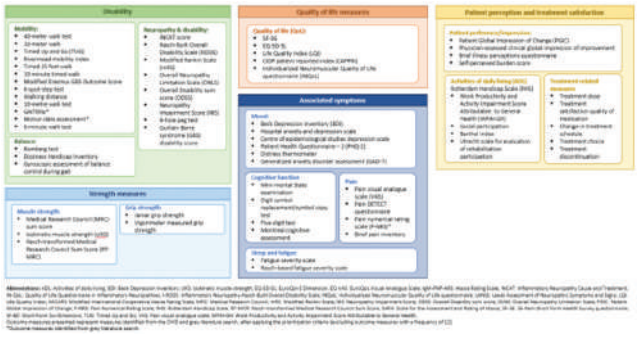

FIGURE 1: Clinical outcome assessments (COAs) mapping.

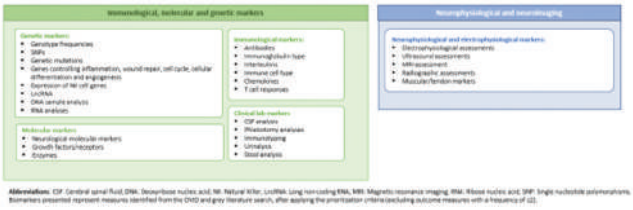

FIGURE 2: Biomarker mapping.

Conclusion: Commonly used COAs in CIDP are mostly specific to inflammatory neuropathy, rather than specifically to CIDP. All have documented limitations. Combining biomarkers with COAs may help to detect clinically meaningful changes in CIDP and aid therapeutic management. Further research is needed to determine the optimal integration of COAs and biomarkers for improved assessment and management of CIDP.

Disclosure: The study was funded by Janssen Pharmaceutical and provided Adelphi Values PROVE with funding for the review; Janssen employees GMB, CG, and WN, may possibly hold stock or stock options. YAR has received speaker/consultancy honoraria from LFB, Polyneuron, Argenx, Takeda, Janssen, Sanofi, Dianthus, has received educational sponsorships from LFB and CSL Behring and has obtained research grants from LFB. EN-O has received speaker/consultancy honoraria from Argenx, Takeda, CSL Behring, Dianthus, Janssen, Kedrion, LFB, Roche and has received a research grant from Takeda. Expert opinions were provided by two independent consultant neurologists.

Infectious diseases

EPR-272 | **The key role of neurological complications in infectious endocarditis: Frequency, diagnostic clue, and consequences**

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Background and Aims: Neurological complications (NC) are the most frequently observed in infectious endocarditis (IE). We aim to describe the spectrum of NC presented by inpatients with IE in our centre.

Methods: Retrospective observational study including all the cases of IE who displayed symptomatic NCs, attended at our institution between 2003 and 2023. We analysed for epidemiological, clinical, paraclinical, treatment and outcome differences among the different groups of NCs.

Results: Among 661 patients diagnosed of IE, 118 (17.8%) suffered any symptomatic NC (30.5% women, median age: 68 years old, IQR: 57–77). The most frequent diagnosis was ischaemic stroke (69.5%), followed by cerebral haemorrhage (28.9%), seizures (16.9%),

spondylodiscitis (11%) and meningitis (5.9%). *S. aureus* (30%) was the main causative microorganism, and *S. pneumoniae* was associated with meningitis ($p=0.01$). IE affected a prosthetic valve in 33.9% of cases, and surgical treatment was required in 44.1% of patients. In 47 cases (40.5%) the NC was the cause of patients' hospitalization, allowing the diagnosis of IE in 45 patients (38.1%). Median time between symptoms onset to antibiotic treatment was 4 days (IQR: 1.25–5), decreasing to 1 day in ischaemic stroke (IQR: 1–2). Cerebral haemorrhages presented an Or=4 for death (1.34–11.96, $p=0.01$) and an Or=4.89 (1.3–18.2, $p=0.01$) for unfavourable 90-day modified Rankin Scale score.

Conclusion: Cerebrovascular disorders were the most frequent NC in patients with IE. Clinical outcome seems to depend on the type of event, with a significant association of cerebral hemorrhages with higher rates of mortality.

Disclosure: None.

EPR-273 | Disseminated nocardiosis with cerebral lesions in immunocompetent patient

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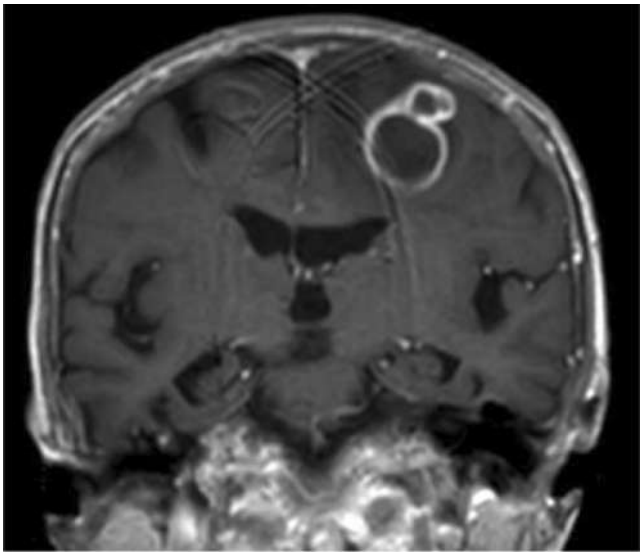
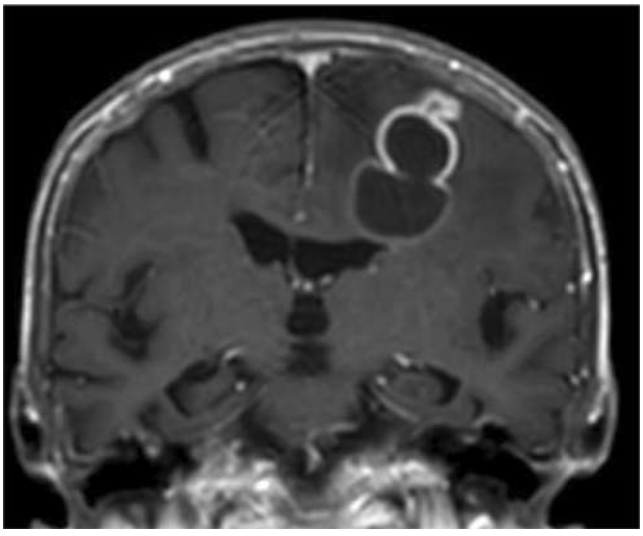
Background and Aims: Nocardiosis is an uncommon, life-threatening and opportunistic infection caused by an aerobic actinomycete in the genus Nocardia, an unusual gram-positive. The most common disease sites are the lungs, central nervous system (CNS) and skin. Parenchymal abscesses are typical hallmarks of CNS nocardiosis, which affects up to 40% of patients with systemic disease.

Methods: We report the case of an 86-year-old immunocompetent woman with a few months-history of progressive motor disorder with gait impairment and subsequent onset of altered mental status, difficulty in verbal expression, mild right hemiparesis and bilateral tonic-clonic seizures.

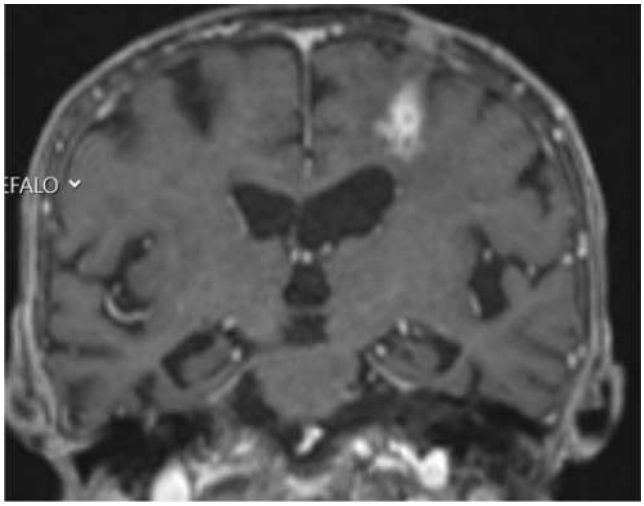
Results: Brain CT scan showed two left hemispheric lesions of suspected metastatic significance and whole-body CT scan revealed involvement of the lungs, left kidney and spleen. Brain MRI scan allowed the suspicion of abscesses, but the lumbar puncture pointed out just elevated CSF protein concentration and the blood infectious screening was negative. Because of worsening clinical conditions and difficulty in making a diagnosis, the patient underwent neurosurgical evacuation surgery: drained material was positive for Nocardia Cyriacigeorgica. Since the introduction of appropriate antibiotic therapy (imipenem and trimethoprim-sulfamethoxazole first, linezolid then plus a two-week course of amikacin), progressive improvement in radiological investigations and neurological status was observed until complete recovery.



Contrast-enhanced brain MRI T1-weighted sequence showing two ring enhancing lesions in the left frontal lobe (the smaller one consisting of at least three small confluent cysts).



First follow-up contrast-enhanced brain MRI showing in the T1-weighted sequence the appearance of a new colliquative lesion with incomplete capsule and slight enhancement after gadolinium.



Second follow-up contrast-enhanced brain MRI, performed after antibiotic therapy, showing in the T1-weighted sequence substantial reduction in volume of the left frontal lobe contrast enhancing lesions.

Conclusion: Nocardia has special tropism for CNS where it can present with symptoms suggesting a mass lesion without typical infectious signs, thus mimicking primary or metastatic brain neoplasm. Diagnosis usually requires an invasive procedure which, although questionable, allows to set up specific antibiotic therapy and to obtain restitutio ad integrum.

Disclosure: The authors declare that they have no conflict of interest.

EPR-274 | Newer insights into clinical features and neuroradiology in rabies encephalitis: A prospective study from north India

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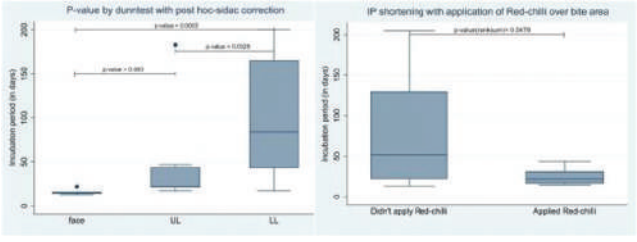
Background and Aims: Rabies is the most lethal infectious disease, with ~100% case fatality. It is highly neglected disease thus there is limited literature available, mostly via retrospective studies.This prospective study aims to narrow the gap.

Methods: 31 patients were enrolled in this prospective observational study over a period of 22-months.Detailed clinical history was obtained and patients were managed with Milwaukee protocol. Contrast-enhanced MRI brain was done for 21 patients. CSF, saliva, nape of neck skin biopsy samples were obtained for diagnosis.

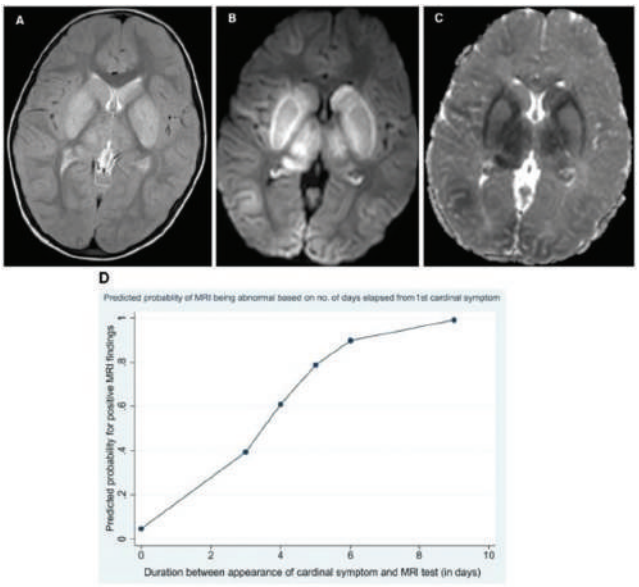
Results: Only 61% took adequate wound care. 48% initiated PEP, but only 26% received RIG; despite availability of adequate infrastructure. Adherence to vaccination schedule was poor, with only 13.3% completing full course. Median incubation period was 29 days, with variations depending upon the type of rabies, site of the bite, and the application of irritant red chili on the wound. The study revealed a spectrum of findings related to autonomic dysfunction-variability in heart rate (90%), blood pressure (90%), and temperature (81%); hypersalivation (61%), hyperhidrosis, spontaneous ejaculations (29%), neurogenic pulmonary edema (19%), etc. MRI revealed dorsal brainstem (90%), peri-aqueductal-grey (72.7%), basal ganglia (63.6%) and cervical spinal-cord (72.2%) being most commonly affected regions. Antemortem diagnosis revealed the following positivity rate–nape of neck skin biopsy IHC (40%), saliva-PCR (23.8%), skin biopsy PCR (20%), and CSF-PCR (4.3%). Postmortem brain-biopsy-PCR had 100% positivity.

Clinical features at presentation	ENCEPHALITIC (n = 27)	PARALYTIC (n = 4)	TOTAL (n = 31)
Pharyngeal muscle hyperactivity	**27 (100%)**	**1 (25%)**	**28 (90%)**
Hydrophobia	27 (100%)	1 (25%)	28 (90%)
Inability to swallow liquids	25 (93%)	1 (25%)	26 (84%)
Inability to swallow solids	24 (89%)	1 (25%)	25 (80%)
Aerophobia	23 (85%)	0	23 (80%)
Inspiratory spasms	22 (81%)	0	22 (80%)
Autonomic dysfunction			
Hypersalivation	18 (67%)	1 (25%)	19 (61%)
Spontaneous ejaculation	9 (33%)	0	9 (29%)
Increased Sweating	8 (30%)	0	8 (26%)
Increased oro-nasal secretions	8 (30%)	1 (25%)	9 (29%)
Piloerection	6 (22%)	2 (50%)	8 (26%)
Neurogenic pulmonary edema	6 (22%)	0	6 (19%)
Photophobia	**13 (48%)**	**0**	**13 (42%)**
Phonophobia	**10 (37%)**	**0**	**10 (32%)**
Bite site sensory-motor symp	**12 (44%)**	**1 (25%)**	**13 (41%)**
Sensory symptoms	11 (92%)		11 (35.5%)
Positive sensory symp (Paraesthesia)	1 ()	0	1 (3.2%)
Negative sensory symp (Numbness)	10 ()	0	10 (32.2%)
Motor symptoms	6 (50%)	1 (25%)	7 (22.5%)
Neuro-psychiatric manifestations	**27 (100%)**	**2 (50%)**	**29 (93.5%)**
Anxiety	27 (100%)	1 (25%)	28 (90%)
Delusions	0	1 (25%)	1 (3.2%)
Hallucinations	1 (3.7%)	0	1 (3.2%)
Delirium/ AMS	6 (22.2%)	4 (100%)	10 (32.2%)
Increased/ irrelevant talkativeness	5 (18.5%)	0	5 (16%)
Personality or behavioural changes	11 (40.7%)	1 (25%)	12 (30%)
Low mood	2 (7.4%)	1 (25%)	3 (10%)
Feeling of impending doom	18 (67%)	0	18 (58%)
Agitation outbursts	16 (59%)	0	16 (52%)
Abusive	12 (44%)	0	12 (39%)
Tending to run away from bed	4 (15%)	0	4 (13%)
Hypersexuality	1 (4%)	0	1 (3.2%)

Clinical features of rabies encephalitis at the time of presentation.



Incubation period based on (A) the site of bite and (B) application of the irritant, red chilli.



MRI images of a patient (A) T2 TSE showing hyperintensities in bilateral basal ganglia & thalamus; & corresponding (B) DWI & (C) ADC Images; (D) Univariable logistic regression to estimate predicted probability of appearance of MRI abnormality after 1st symptom.

Conclusion: The study highlights autonomic dysfunction as major clinical syndrome of rabies encephalitis, the most striking features include repeated unprovoked spontaneous ejaculations, neurogenic-pulmonary-edema and rapid variability in heartrate and bloodpressure. Neuroradiology highlighted specific pattern of involvement which can aid in ante-mortem diagnosis. Moreover, it also reveals that MRI may be absolutely normal during the early stages of disease even when the patient is E1VTM1, which highlights the important fact that the MRI changes take time to develop.

Disclosure: Nothing to disclose.

EPR-275 | Concurrent longitudinal extensive transverse myelitis and leptomeningitis in West Nile virus

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Department of Neurology, Lahey Hospital and Medical Center, Burlington, MA, USA

Background and Aims: Here we report a rare case with concurrent longitudinal extensive transverse myelitis (LETM) and leptomeningitis due to West Nile virus (WNV) infection.

Methods: Case Report.

Results: A 47-year-old man initially presented with a 6-day progressive, intermittent low-grade fever, headache, diplopia, malaise, myalgia, lower back pain, and difficulty walking that developed to progressive asymmetric paralysis. Initial lab work was notable for mild lactic acidosis and hyperCKemia. Brain MRI with contrast demonstrated small foci of leptomeningeal enhancement in the cerebellum, pons, medulla and right CN VI at the cisternal segment. MRI of the spine was remarkable for edema in the spinal cord extending from T10 to L1 with diffuse enlargement of the cord contour at T11 to L1 and subtle enhancement of nerve roots within the thecal sac and cauda equina regions. The patient responded favorably to 5-day intravenous immunoglobulin therapy (total dose, 2 g/kg).

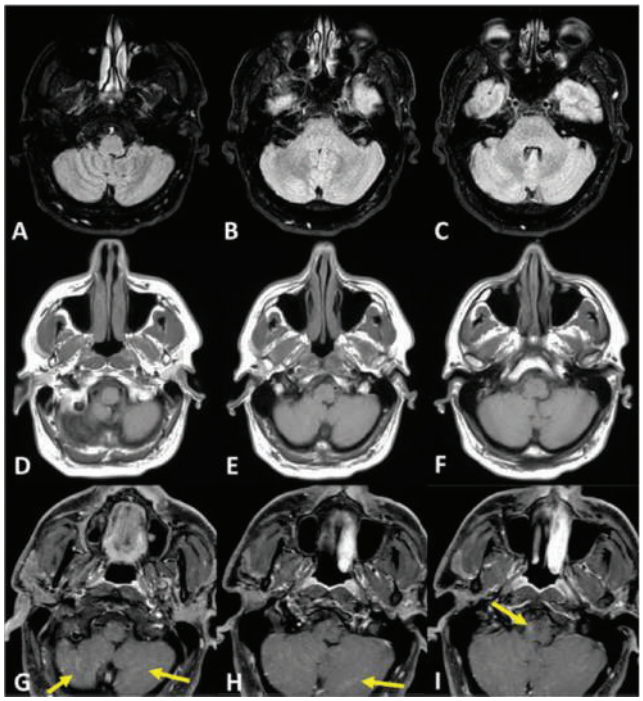

FIGURE 1: Axial FLAIR (A–C), axial T1 pre- (D–F) and post-contrast (G–I) brain magnetic resonance imaging (MRI) from day 2 of hospitalization.

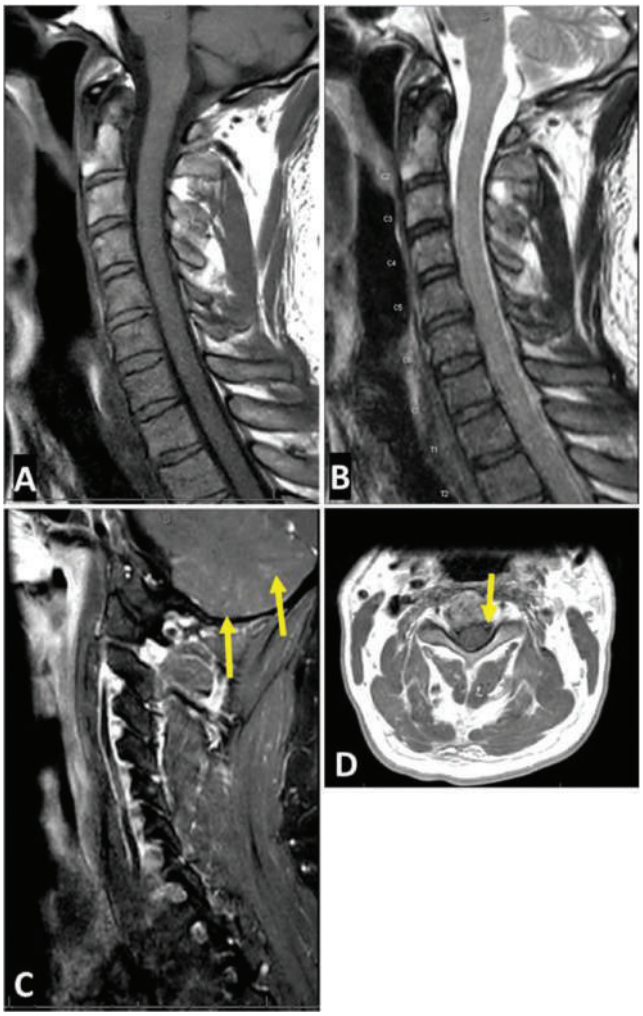

FIGURE 2: Sagittal T2 (A), T1 pre- (B) and post-contrast (C), as well as axial T1 post-contrast (D) MRI cervical spine from day 2 of hospitalization.

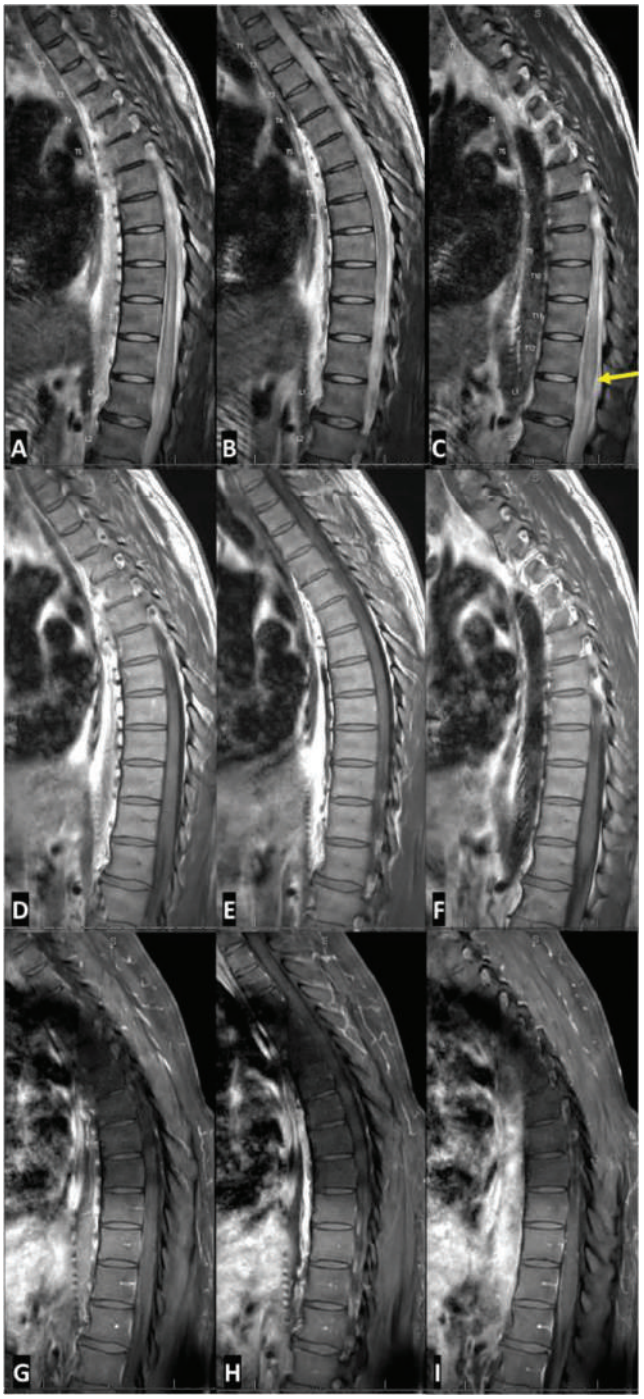

FIGURE 3: Sagittal T2 (A–C), T1 pre- (D–F) and post-contrast (G–I) MRI thoracic spine from day 2 of hospitalization.

Conclusion: Clinically, this case highlights the ill-defined and non-specific nature of the presentation of West Nile neuroinvasive disease. It can pose a diagnostic challenge for clinicians and, if unrecognized, is associated with significant morbidity and mortality in older and compromised individuals.

Disclosure: Nothing to disclose.

EPR-276 | Characteristics and prognostic factors of bacterial meningitis in the intensive care unit: A prospective cohort study

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Amsterdam UMC, Location AMC, Department of Neurology

Background and Aims: Patients with bacterial meningitis can be severely ill necessitating intensive care unit (ICU) treatment.
Methods: We prospectively assessed clinical features and outcome of adults (age >16 years) with community-acquired bacterial meningitis included in the MeninGene study, that were initially admitted to the ICU. We identified independent predictors for initial ICU admission and for unfavourable outcome by multivariable logistic regression.
Results: A total of 2709 episodes of bacterial meningitis were included, of which 1369 (51%) were initially admitted to the ICU. We observed a decrease in proportion of patients being admitted to the ICU during the Covid-19 pandemic in 2020 (decreased to 39%, $p=0.004$). Median age of the 1369 patients initially admitted to the ICU was 61 years (IQR 49–69), and the rates of unfavourable outcome (47%) and mortality (22%) were high. During the Covid-19 pandemic, we observed a trend towards an increase in unfavourable outcome. Prognostic factors predictive for initial ICU admission were younger age, immunocompromised state, male sex, factors associated with pneumococcal meningitis, and those indicative of systemic compromise. Independent predictors for unfavourable outcome in the initial ICU cohort were advanced age, admittance to an academic hospital, cranial nerve palsies or seizures on admission, low leukocyte count in blood, high C-reactive protein in blood, low CSF:blood glucose ratio, listerial meningitis, need for mechanical ventilation, circulatory shock and persistent fever.
Conclusion: The majority of patients with community-acquired bacterial meningitis is admitted to the ICU, and the unfavourable outcome and mortality rates of these patients remains high.

EPR-277 | Primary CNS Whipple disease: Clinical case, systematic review and diagnostic recommendations of a fatal condition

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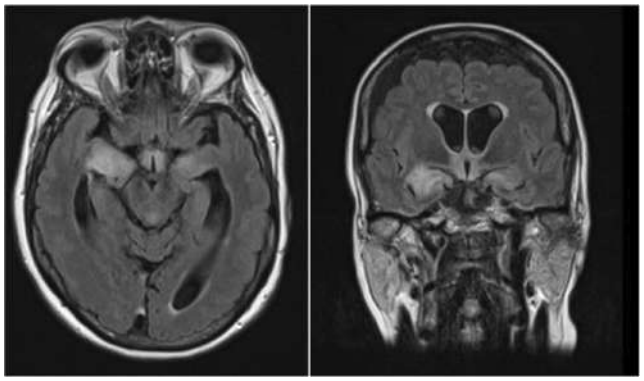
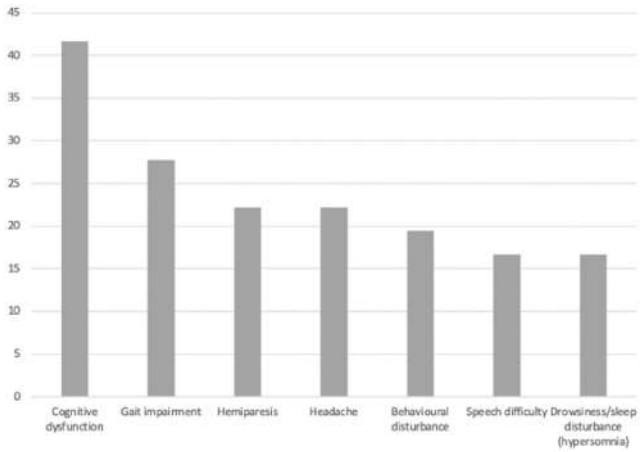
Background and Aims: Whipple disease is a rare multi-systemic disease involving the nervous system in 15%–43% of cases. Few cases of pCNS WD have been reported and no diagnostic recommendations for this potentially fatal, yet treatable condition are available. We conducted a systematic review on pCNS WD in order to guide clinicians through its diagnosis.
Methods: We report a representative case report and systematic literature review via PubMed was performed. Cases with previous arthritis, diarrhea or abdominal pain were excluded.
Results: A 64 year old woman presented with left arm numbness followed by hypersomnia and slowly progressive cognitive impairment. MRI showed bilateral temporal lobe enhancement. CSF results were normal, with negative T. whipplei PCR. Brain biopsy revealed typical PAS+ histiocytes and positive T. whipplei PCR. The patient was treated with ceftriaxone and co-trimoxazole with full recovery. In our review 35 cases of pCNS WD were included. The most common clinical presentation at onset was cognitive impairment (42%), followed by ataxia (28%), headache (22%), hemi-or paraparesis (22%), behavioral alterations (19%), and sleep disturbances (17%). In 17% of cases the clinical presentation is acute. CSF WBC elevation was reported in 29% of cases, protein elevation in 43% of cases. Although specific, T. whipplei PCR has a relatively low sensibility (71%).



Bitemporal and hippocampal FLAIR hyperintensities.



Initial clinical presentation of pCNS WD.

Conclusion: This is the largest dataset of pCNS WD so far. This disease has an extremely variable presentation. Importantly, CSF analysis might result negative. Because of low sensibility of T. whipplei PCR, in cases of high clinical suspicion brain biopsy is indicated early in the disease course.

Disclosure: No disclosure.

EPR-278 | Target enriched metagenomics in cerebrospinal fluid of patients with a central nervous system infection

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Background and Aims: Metagenomic next-generation sequencing (mNGS) is a promising diagnostic tool for recognizing a broad spectrum of pathogens in clinical samples. Adding a target enrichment step might increase sensitivity of pathogen detection in samples with a low pathogen load, as is often the case in cerebrospinal fluid (CSF). We conducted a study on the performance of mNGS with targeted enrichment for pathogen detection in CSF.

Methods: Patients with a microbiologically confirmed CNS infection were included from two prospective cohort studies from The Netherlands. The index test, targeted mNGS using the Respiratory Pathogen ID/AMR Enrichment Panel Kit (RPIP), was performed using the isolated DNA from the CSF and resulting data was analyzed with the RPIP Data Analysis Solution in BaseSpace Sequence Hub (Illumina). Results from the regular diagnostics were considered the reference standard.

Results: We performed targeted metagenomics on 43 CSF samples: 15 of patients with bacterial, 20 with viral and 6 with fungal CNS infections. Positive agreement was achieved in 28 of 41 (68%) microbiologically confirmed samples. In 7 (17%) samples an incorrect pathogen was detected and in 6 (15%) cases no reads or pathogen was detected. The yield of targeted mNGS differed per pathogen, ranging from 89% for Varicella Zoster virus and 29% for Epstein–Barr virus.

Conclusion: Targeted mNGS was in concordance with regular diagnostics in 68% of CNS infections, but yield differed greatly between pathogens. Further fine-tuning of the methods is needed to improve test characteristics prior to implementation in clinical practice.

Disclosure: Nothing to disclose.

EPR-279 | Cerebrospinal fluid metabolome in adults suspected of a central nervous system infection: A study of diagnostic accuracy

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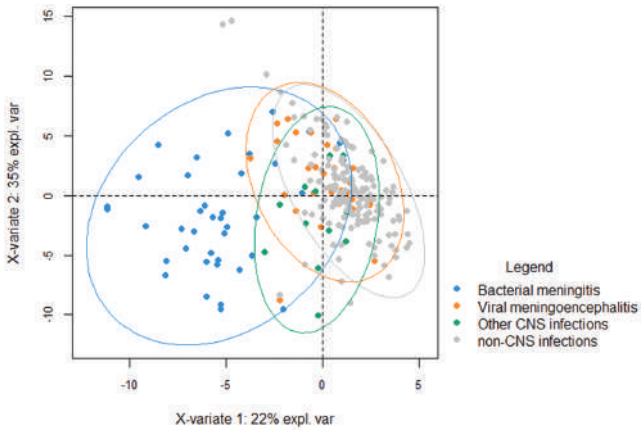
Background and Aims: To assess the diagnostic accuracy of metabolites in the cerebrospinal fluid (CSF) for the diagnosis of central nervous system (CNS) infections.

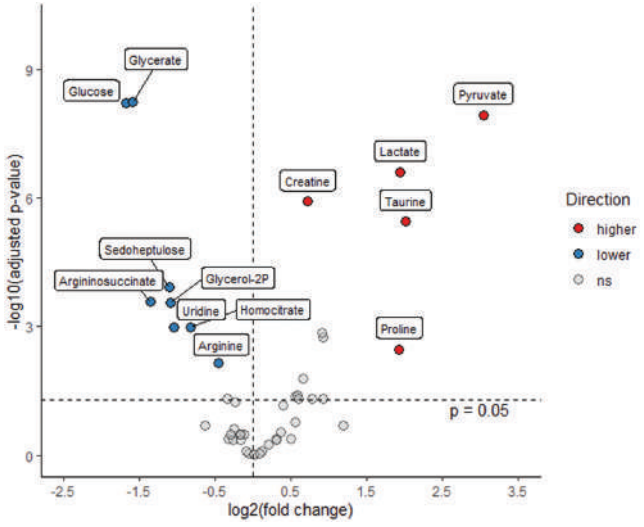
Methods: CSF samples were derived from two prospective cohort studies in The Netherlands that included patients ≥16 years suspected of a CNS infection whom underwent a diagnostic lumbar puncture. Semi-targeted high-performance liquid chromatography with tandem mass spectrometry was used to detect metabolites in 235 randomly selected patients. Metabolite quantification was the index test; final clinical diagnosis was the reference standard.

Results: Of the 235 patients, 82 (35%) had a CNS infection. A total of 39 of 235 (17%) were diagnosed with bacterial meningitis, 31 (13%) with viral meningoencephalitis and 12 (5%) with other CNS infections. Patients without a CNS infection were diagnosed with CNS inflammatory diseases in 17 of 153 (7%) cases, other neurologic diseases in 74 (31%) or systemic infections in 62 (26%). A distinct metabolite profile was observed in patients with bacterial meningitis which was driven by 17 (26%) of 66 metabolites detected in CSF (Figure 1 and 2). Pyruvate, lactate and glycerate showed high diagnostic accuracy for the diagnosis of bacterial meningitis, especially when compared to viral meningoencephalitis, with an area under the

curve of respectively 0.94 (95% confidence interval [CI] 0.88–0.94), 0.93 (95% CI 0.86–0.93) and 0.92 (95% CI 0.86–0.92).



Partial least squares-discriminant analysis of the CSF metabolome in patients suspected of a central nervous system infection. Colors indicate the clinical diagnosis.



Volcano plot of individual metabolites in CSF for bacterial meningitis versus viral meningoencephalitis. Significant metabolites with a VIP (variable importance in the projection) score >1 are labelled, ns = not significant.

Conclusion: CSF metabolites have a high diagnostic accuracy for the diagnosis of bacterial meningitis in patients suspected of a CNS infection. This finding highlights the potential of CSF metabolite testing in clinical practice.

Disclosure: Nothing to disclose.

EPR-280 | Boutonneuse fever associated with CNS vasculitis: A case report

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Background and Aims: Boutonneuse fever is a disease caused by Rickettsia Conorii, endemic of the Mediterranean area. It usually presents with a rash, fever and a characteristic necrotic eschar. Focal neurological manifestations are unusual. We describe such a case, presenting with acute oculomotor symptoms secondary to CNS vasculitis.

Methods: 43-year-old male with acute bifrontal oppressive headache, nausea, vertigo, binocular diplopia and oscillopsia, in the context of fever of 38.7°C and a skin lesion on the right forearm. Physical examination: horizontal-rotatory nystagmus on dextroversion of the right eye and upbeat vertical nystagmus with restricted adduction and exotropia of the left eye, generalized maculopapular exanthema and a necrotic eschar.

Results: Elevated blood inflammatory markers. Negative blood cultures. Serology of Rickettsia Conorii IgG+ (titers 1/64) and IgM+. Normal total-body CAT scan. CSF analysis: normal cytobiochemistry; negative PCR and serology. Skin biopsy and exudate: positive PCR for Rickettsia. Normal transthoracic echocardiography. Brain MRI with contrast and vascular study: Five hyperintense lesions in T2 and FLAIR sequences with diffusion restriction and hypointensity in ADC map, located in corpus callosum, periventricular and subcortical white matter and left medial midbrain, without enhancement. Vascular study showed no large vessel occlusion. CNS vasculitis secondary to Rickettsiosis was diagnosed. After starting Doxycycline 100 mg/12 h IV, fever and exanthema resolved in 24 h. At discharge the patient presented only left internuclear ophthalmoplegia.

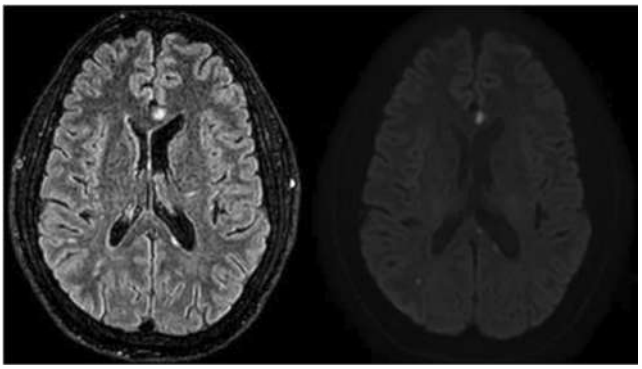

IMAGE 1: Brain MRI in FLAIR T2-Weigted sequence (left) and DWI (right) showing ischemic lesions in splenium, periventricular and subcortical white matter.

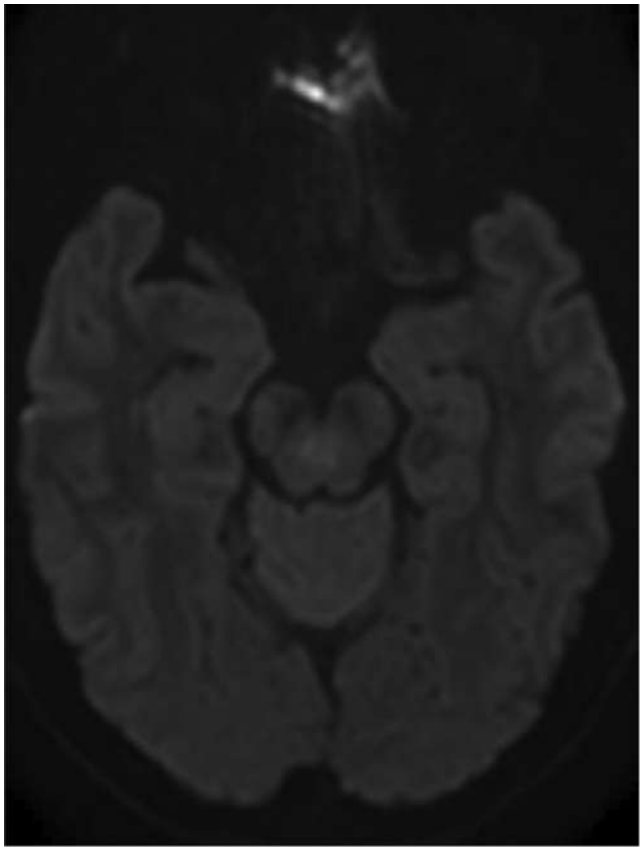

IMAGE 2: Brain MRI in DWI showing restricted diffusion in midbrain region.

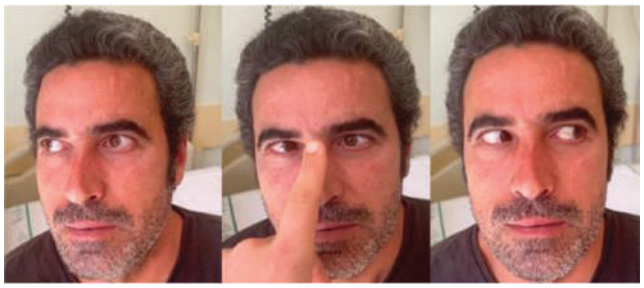

IMAGE 3: Internuclear Ophthalmoplegia evidenced by restricted adduction of left eye and rotational nistagmus of right eye during right side gaze; with conserved convergence.

Conclusion: In cases of neurological symptoms, fever and exanthema CNS vasculitis secondary to Rickettsiosis should be considered, especially in endemic areas such as the mediterranean basin, and treat it early with Doxycycline.

Disclosure: Nothing to disclose.

Neuroimmunology 3

EPR-281 | Watchful-waiting approach in an international multicenter incident case series of patients with MOGAD

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Background and Aims: Given the variable risk of relapse and generally good response to acute treatment, watchful-waiting may be a potential long-term management approach for some patients with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).

Methods: This is an international, case series. We identified MOGAD patients who (1) fulfilled the 2023 International MOGAD criteria; (2) presented to the participating institutions with the first clinical attack; and (3) had >3 years of follow-up. We compared chronic steroid-sparing immunotherapy versus watchful-waiting after the onset attack and determine the proportion of relapsing disease and worsening disability.

Results: Among 81 incident cases of MOGAD, the median age of onset was 31 years, and 57% were female. After the onset attack, 65 (80%) underwent watchful-waiting. Forty-one (63%) watchful-waiting patients had relapsing disease with a median number of 3 (IQR 2–5) relapses. At the last visit, 7/64 (11%) watchful-waiting patients had poor disability outcomes from the onset attack and 4/64 (6%) from relapses. Acute treatment delay was longer for the onset attack than for relapses ($p=0.001$). Twenty-five (38%) patients later received chronic immunotherapy: 12/41 (29%) after a second attack, 11/24 (46%) after a third attack, and two after at least 4 attacks. Annualized relapse rate (ARR) was lower among relapsing patients who underwent watchful-waiting throughout their disease (0.2) compared to those who later received chronic immunotherapy (0.3, $p=0.039$).

Conclusion: Watchful-waiting is a potential long-term management option for MOGAD patients with good recovery and lower ARR given timely access to acute treatment. Future prospective studies are warranted.

Disclosure: Nothing to disclose.

EPR-282 | A retrospective multicenter study in MuSK myasthenia gravis patients with and without general immunosuppression

A. De Rosa[1]; I. Koneczny[2]; M. Mané-damas[2]; S. Zong[2]; S. De Haas[2]; S. Huda[3]; M. Maestri[1]; M. Guida[1]; P. Van Damme[4]; J. Damoiseaux[5]; P. Molenaar[2]; A. Fichtenbaum[6]; T. Perkmann[6]; M. De Baets[2]; K. Lazaridis[7]; V. Zouvelou[8]; S. Tzartos[7]; R. Ricciardi[1]; M. Losen[2]; P. Martinez-Martinez[2]

[1]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy; [2]Research group neuroinflammation and autoimmunity, Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; [3]Neurosciences Group, Nuffield Department of Clinical Neurosciences, Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, UK; [4]Neurology Department, University Hospital, Leuven, Belgium; [5]Central Diagnostic Laboratory, Maastricht University Medical Center, Maastricht, The Netherlands; [6]Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Vienna, Austria; [7]Department of Immunology, Hellenic Pasteur Institute, Athens, Greece; [8]1st Neurology Department, National and Kapodistrian University of Athens, Greece

Background and Aims: Muscle-specific kinase (MuSK)- myasthenia gravis (MG) is caused by pathogenic autoantibodies against MuSK that correlate with disease severity and are predominantly of the IgG4 subclass. Immunosuppressants are the first-line treatment but their effect on IgG4 and MuSK IgG4 levels has not been fully investigated.

Methods: We analysed the clinical data and sera from 52 MuSK-MG patients from Italy, The Netherlands, Greece and Belgium, and 43 AChR-MG patients from Italy, that were receiving prednisone, azathioprine, cyclosporine, intravenous immunoglobulin, combinations thereof or no immunosuppression, and sera from 45 age- and sex-matched non-disease controls from The Netherlands. We analysed the disease severity, and measured concentrations of MuSK IgG4, MuSK IgG, total IgG4 and total IgG in the sera by ELISA, RIA and nephelometry.

Results: We observed that MuSK-MG patients showed a robust clinical improvement and reduction of MuSK IgG after therapy, and that MuSK IgG4 concentrations, but not total IgG4 concentrations, correlated with clinical severity. MuSK IgG levels and MuSK IgG4 concentrations were reduced after immunosuppression in 4/5 individuals with before-after data, but data from non-linked patients showed no significant difference. MuSK-MG patients improved within the first four years after disease onset, but longer disease duration (>4 years) did not lead to further clinical improvement or MuSK IgG4 reduction.

Conclusion: Based on our observations, we conclude that MuSK-MG patients improve clinically with general immunosuppression but may require further treatment to reach remission. Inter-assay variability may hide individual changes of MuSK IgG4 levels; therefore longitudinal testing of individual patients may be clinically more useful than single measurements.

Disclosure: Nothing to disclose.

EPR-283 | Anti-MuSK antibody resurgence precedes exacerbation

C. Elmas Tunc[1]; R. Weng[2]; F. Zimprich[2]; R. Höftberger[1]; I. Koneczny[1]

[1]Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Vienna, Austria; [2]Department of Neurology, Medical University of Vienna, Vienna, Austria

Background and Aims: Myasthenia Gravis (MG) is an autoimmune disease of the neuromuscular junction, where a subset of patients exhibit predominantly IgG4 antibodies against muscle-specific kinase (MuSK). Considered immunologically inert and anti-inflammatory, pathogenicity of IgG4 is unusual. As a typical IgG4 autoimmune disease, MuSK-MG has distinct clinical features and differs in treatment response. This study aims to investigate IgG subclass profile changes in MuSK-MG patients across disease states and treatments to assess their prognostic potential.

Methods: Sixteen MuSK-MG patients (10 female, 6 male) contributed 55 serum samples to KINbiobank. The disease severity was assessed using the Myasthenia Gravis Foundation of America (MGFA)

classification at sample collection. Anti-MuSK seropositivity was established with cell-based assays, employing semiquantitative scoring (0–4 points). The IgG subclass profiles were analyzed with flow cytometry, defining high (>75th%) and low (<25th%) levels.

Results: IgG subclass analysis showed a predominance of IgG4 (mean 89%), followed by IgG1 (mean 5%). IgG4 levels correlated with CBA and MGFA scores. IgG4 levels during exacerbation were significantly higher than during remission ($p=0.0001$). Lower IgG4 levels were associated with favourable clinical outcomes (minimal residual symptoms or remission), while high levels preceeded exacerbations. Post-rituximab treatment, IgG4 levels decreased in the first month, remaining low for 6–10 months before a resurgence (>20%).

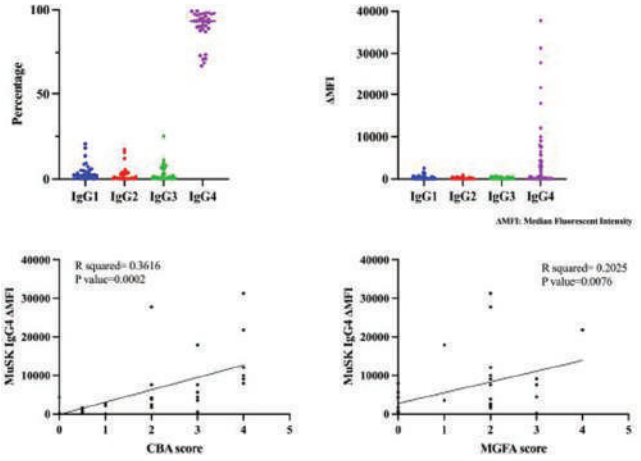

FIGURE 1: IgG subclass profiles showed IgG4 predominance, IgG4 correlated with CBA and MGFA scores (MFI: median fluorescence intensity).

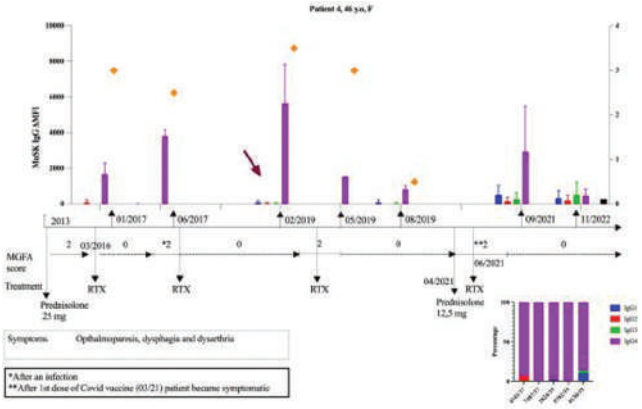

FIGURE 2: IgG subclass profile of a 42 y.o. female patient, arrow showing high IgG4 levels during remission period, followed by exacerbation (RTX: rituximab).

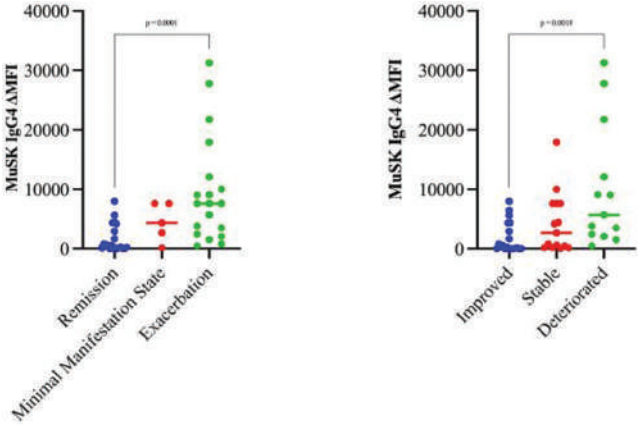

FIGURE 3: IgG4 levels were significantly higher during clinical deterioration and exacerbation.

Conclusion: IgG subclass profiles showed IgG4 predominance which correlated with the clinical severity. IgG4 levels decreased after treatment, while sustained high levels and resurgence may indicate exacerbation and worse clinical outcome. Our results suggest possible prognostic value of MuSK-IgG4 levels.

Disclosure: Author C.E.T. received EAN Research Training Grant in 2023.

EPR-284 | Performance of the 2023 MOGAD diagnostic criteria in children and adults

E. Fonseca[1]; G. Olive-Cirera[1]; E. Martínez-Hernández[1]; J. Cabrera-Maqueda[1]; M. Guasp[1]; L. Naranjo[2]; R. Ruiz-García[2]; E. Caballero[1]; S. Llufriu[1]; Y. Blanco[1]; A. Saiz[1]; J. Dalmau[1]; M. Sepulveda[1]; T. Armangué[3]

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Background and Aims: The recently reported MOGAD criteria perform well in adults but have not been assessed in children. We determined their performance in two large cohorts of adults and children, considering the acute and remission phases of the disease.

Methods: This prospective observational study includes patients of all ages whose serum or CSF harbored MOG-IgG determined with a live cell-based assay. We assessed core syndromes, MOG-IgG titers, and supportive features. Patients tested within 3 months of symptom onset (acute phase) or afterward (remission) were considered separately.

Results: 257 patients (133 children) were included (median age 15 years [IQR 6–38], 54% female). Among 202 assessed during an acute attack; 158 (78%) had high MOG-IgG titers, 36 (18%) low titers, and 8 (4%) antibodies only in CSF. No differences were identified

between patients with high and low titers, but those with low titers were more likely to have an alternative diagnosis at last follow-up (2/36 [6%] vs. 0/158, $p=0.012$). Supportive features were present in 230/257 (89%) patients, without differences regarding age, MOG-IgG titers, and core syndromes except for optic neuritis in adults which assessment was limited by the lack of systematic orbital MRI. Overall, the criteria performed better during the acute phase than during remission (190 [94%] vs. 49 [89%] well-classified patients, $p=0.038$) and in patients harboring MOG-IgG in serum versus those with MOG-IgG only in CSF (187 [96%] vs. 3 [38%], $p<0.00001$).

Conclusion: MOGAD criteria performed similarly well in children and adults. The best performance was obtained when applied during the acute phase of the disease.

Disclosure: Nothing.

EPR-285 | Predictive serological biomarkers of disease outcome in myasthenia gravis

F. Beretta[1]; E. Schiavo[1]; G. Spagni[2,3]; S. Falso[2]; S. Cornacchini[1]; M. Verza[1]; L. Palazzo[1]; L. Massacesi[1]; A. Evoli[2]; V. Damato[1]

[1]*Department of Neurosciences, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy;* [2]*Department of Neuroscienze, Università Cattolica del Sacro Cuore, Rome, Italy;* [3]*German Center for Neurodegenerative Diseases (DZNE) Berlin, Berlin, Germany*

Background and Aims: Myasthenia gravis (MG) is an autoimmune disorder caused by antibodies targeting the neuromuscular junction. Most patients have autoantibodies against the acetylcholine receptor (AChR) which can bind specifically to either the adult or the fetal AChR isoform. To date, there are no reliable predictive biomarkers of MG clinical outcome. We investigated whether antibody reactivity for the adult-AChR or the fetal-AChR isoform correlated with MG clinical outcome.

Methods: We conducted a cross-sectional study on 174 patients with a confirmed MG diagnosis and positive radioimmunoassay for AChR-antibodies. Antibody reactivity against the adult-AChR versus the fetal-AChR isoforms was assessed by live cell based assay on flow cytometry. Clinical outcome was assessed through the "patient acceptable symptom state" (PASS-question) and the post-intervention status (PIS).

Results: We found a significantly lower adult/fetal AChR immunoreactivity ratio in patients who answered "yes" to the PASS-question compared to those whose answer was "no" ($p=0.039$, Mann–Whitney test) showing that patients with good clinical outcome (PASS = yes) have antibodies mostly binding to fetal-AChR. This finding was confirmed by testing the adult/fetal ratio in patients in minimal manifestation or better ("MM or better") versus those who were still symptomatic ($p=0.001$, Mann–Whitney test). The adult/fetal AChR immunoreactivity ratio was significantly lower in patients in complete stable remission versus those in MM status ($p=0.04$, Mann–Whitney test). No significant differences in the A/F ratio were found when comparing ocular and generalized MG.

Conclusion: The adult/fetal AChR immunoreactivity ratio may constitute a biological marker predictive of AChR-MG outcome and should be investigated in larger prospective studies.

Disclosure: Work supported by: (1) #NEXTGENERATIONEU (NGEU) and funded by the Ministry of University and Research (MUR), National Recovery and Resilience Plan (NRRP), project MNESYS (PE0000006) – A Multiscale integrated approach to the study of the nervous system in health and disease (DN. 1553 11.10.2022); (2) Myasthenia Gravis Rare Disease Network–MGNet, a member of the Rare Disease Clinical Research Network Consortium (RDCRN) NIH U54 NS115054. All RDCRN consortia are supported by the network's Data Management and Coordinating Center (DMCC) (U2CTR002818). Funding support for the DMCC is provided by the National Center for Advancing Translational Sciences (NCATS) and the National Institute of Neurological Disorders and Stroke (NINDS).

EPR-286 | Defining molecular and cellular pathways of paraneoplastic antigen expression

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Background and Aims: Classical paraneoplastic antigens are intracellular proteins with diverse functions typically expressed in both tumors and neuronal cells. Tumor immunosurveillance leads to cross-reactive T-cells and autoantibodies that cause damage to neuronal cells expressing the tumor antigen. It is unclear why from numerous tumor antigens only a few trigger aberrant immune responses leading to autoimmunity. To address this question, we used carcinogenesis cellular models to explore the mechanism driving paraneoplastic antigen.

Methods: We employed a genetically induced cellular model (Hahn, 1999, Nature. 400, 464) which comprises the following: a. BJ, normal human fibroblasts or epithelial cells b. BJ-E, cells genetically modified to lack telomerase c. BJ-LE, cells expressing SV-40 antigens and inactivated p53 and d. BJ-LER, cells with activated hRAS oncogene. Cell lines represent progressive stages of carcinogenesis of either a fibroblast or epithelial lineage.

Results: We performed Western Blot using cell-line derived proteins and sera from patients harboring anti-Hu, Yo, Ri, Ma2, SOX-1, Tr/DNER and amphiphysin antibodies. In the fibroblast-derived model, we detected binding of anti-Ri and anti-amphiphysin antibodies (from 3/15 patients tested) according to the stage of carcinogenesis.

In the epithelial-derived model, we detected binding of anti-Hu and anti-Yo antibodies, again on a stage-dependent pattern. Results were validated using qPCR. We are currently testing our cell lines with immunofluorescence to determine sub-cellular localization of binding.

The carcinogensis model (A) and representative Ri antigen expression data (B).

Conclusion: Our preliminary results support that our cellular models are fitting to study the mechanisms that drive expression of paraneoplastic antigens. Pending experiments aim to unveil post-translational modifications that affect antigen-antibody binding avidity and transcriptional activators or suppressors.

Disclosure: Nothing to disclose.

EPR-287 | Phenotypic adaptation of surveilling T cells at the borders of the human central nervous system

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Background and Aims: Immune surveillance by T cells is indispensable for maintenance of a healthy central nervous system (CNS), yet infiltrating T cells can also contribute to inflammatory diseases. It is unknown how and where human perivascular white matter (WM) T cells acquire their characteristic brain tissue-resident memory (TRM) phenotype. We investigated the phenotypic profiles and transcriptional programs of human CD4+ and CD8+ T cells in several CNS compartments.

Methods: Of consecutive Netherlands Brainbank fresh autopsies, CD4+ and CD8+ T cells were isolated from paired peripheral blood (PB), border organs (choroid plexus and leptomeninges), cerebrospinal fluid (CSF), and WM. Cells were analyzed with flow cytometry. FACS-sorted T cells from PB, CSF, and WM T cells were analyzed with RNA-bulk sequencing.

Results: Compared to PB, CD4+ and CD8+ T cells in border organs were enriched for CD45RAloCD45R0hi memory T cells. In border organs, T cells were characterized by a high expression of brain TRM-associated integrins (CD49a, CD103), chemokine receptors (CCR2, CCR5, CXCR3), and surface markers (CD20) yet preserve their tissue egress-associated CD69lo phenotype. CSF T cells displayed an enrichment of TRM-associated markers and transcripts including high CD69 expression and lack of tissue egress mediators (S1PR1). Compared to CSF, WM T cells expressed less surface markers and transcripts associated with recent activation (HLA-DR, CD25) and co-stimulation (CD28).

Conclusion: CNS-surveilling T cells show enrichment for brain TRM-associated phenotypic characteristics at the border organs and further display a TRM-phenotype within the CSF. These data provide insights to modulate CNS immune-surveillance for the benefit of patients with neurological diseases.

Disclosure: No disclosures relevant to this manuscript.

EPR-288 | Patient-derived monoclonal antibodies as a tool to study CASPR2-autoantibody encephalitis

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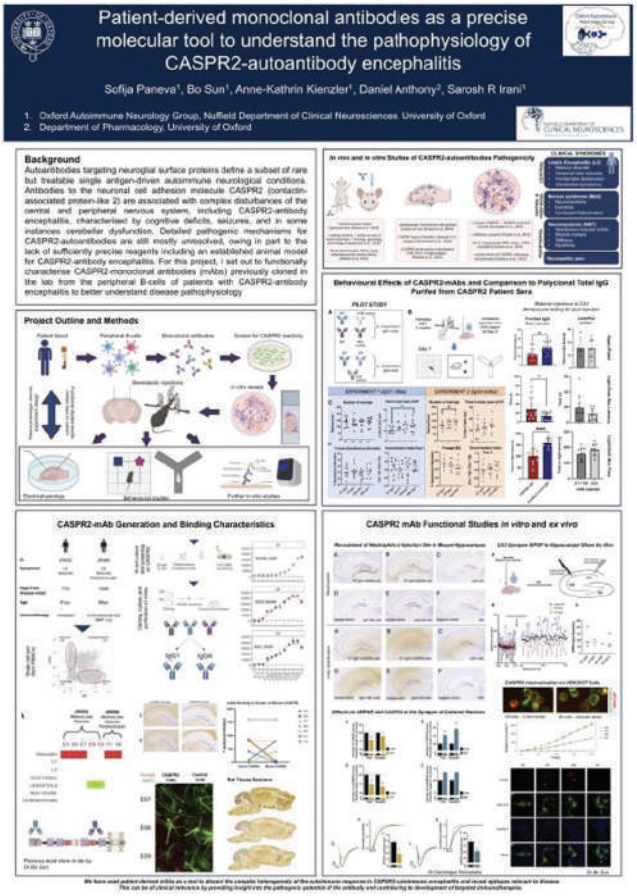
Background and Aims: Antibodies to the neuronal cell adhesion molecule CASPR2 are associated with complex disturbances of the central and peripheral nervous system, but. detailed pathogenic mechanisms for CASPR2-autoantibodies are still mostly unresolved.

Methods: We functionally characterize CASPR2-monoclonal antibodies (mAbs) cloned from peripheral B-cells of patients with CASPR2-autoantibody encephalitis. Cloning was done using a bulk B-cell culture method, followed by screening for human and moue CASPR2 reactivity, target affinity and internalisation assays, and staining on neurons and rodent tissue, Antibody effects were assessed via electrophysiology on cultured neurons and stereotaxic injection into mouse hippocampi.

Results: mAbs targeting the discoidin and the L3/EGF2/L4 domains of CASPR2 were generated. Three out of seven (3/7) mAbs bound to hippocampal neurons in culture and to rat and mouse tissue sections. Two were found to be high-affinity binders while one was a low-affinity binder. The mAbs induced CASPR2 internalisation on HEK293T cells, reduced AMPAR and CASPR2 levels at the synapse of cultured neurons, and recruited neutrophils upon injection in

mouse hippocampus. A low affinity discoidin-mAb reduced rearing in the open field, whereas a high-affinity L3/EGF2/L4-mAb produced an anxiety-like phenotype in mice. Co-injection of multiple mAbs failed to produce behavioural deficits, in contrast to injection of IgG from CASPR2-reactive sera.



Poster showing results.

Conclusion: We demonstrate for the first time the effects of patient-derived CASPR2-mAbs across multiple experimental paradigms, offering an unprecedented view into diesase pathophysiology.

Disclosure: None.

Sleep-wake disorders

EPR-289 | Sex affects REM sleep behavior disorder identification: Clinical data, screening questionnaires and REM without atonia

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Background and Aims: Accurate REM sleep behavior disorder (RBD) diagnosis is essential due to the risk of injuries, and as isolated-RBD is an early alpha-synucleinopathy. Although RBD is more frequently reported in men, epidemiological studies reported similar prevalence in both sexes, suggesting underdiagnosis in women. We investigated sex differences in RBD identification.

Methods: In this bicentric prospective study, 300 subjects (159 men, 141 women) referred to sleep center for the first time, completed three RBD screening questionnaires: RBD-screening- questionnaire (RBDSQ), RBD-single-question (RBD1Q), and Innsbruck-RBD-Inventory (RBD-I) before sleep-expert interview, and underwent 8-h-video-polysomnography (V-PSG) to confirm/exclude RBD. Clinical history, questionnaires, and RWA were compared between men and women.

Results: Among RBD patients ($N=30$ (10.0%): women = 12 (8.5%), men = 18 (11.3%)), women were less likely to have bed partners ($p=0.002$) and to report abnormal sleep behaviors ($p=0.006$). Only for men, being above the published cut-off for all three RBD questionnaires was associated with RBD diagnosis (RBD1Q: Log odds ratio (LOR) 95% CI 2.837 (1.716–4.347), $p<0.001$; RBDSQ: LOR 3.076 (1.671–5.362), $p=0.003$; RBD-I: LOR 3.076 (1.671–5.362), $p=0.003$). For women, only being above the RBD-I was associated with RBD diagnosis, $p=0.023$. Women had a higher RWA-SINBAR-index ($p=0.035$) and lower flexor digitorum superficialis activity ($p=0.003$). RWA scores had higher RBD identification performance for women compared to the questionnaires (AUC >0.82 for all variables).

Conclusion: This study demonstrated sex-related variability in RBD screening questionnaires, probably related to sex-specific differences in RBD awareness, likely affecting referral to V-PSG. These findings emphasize the need for sex-specific approaches for RBD screening and diagnosis.

Disclosure: Nothing to disclose. Acknowledgements: We are thankful to Mr. Heinz Hackner for accurate V-PSG scoring and technical support.

EPR-290 | Effects of acute exposure to altitude on restless legs syndrome

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Background and Aims: Restless Legs Syndrome (RLS) pathogenesis involves several factors. Some studies suggested a role of hypoxia, supported by an upregulation of the vascular endothelial growth factor in leg muscles of RLS patients and higher RLS prevalence in high altitude (HA) regions. We aimed to investigate the effect of acute HA exposure in RLS versus healthy subjects.
Methods: Fifty-six individuals, 28 with RLS and 28 matched healthy-controls were included. For two nights, 1-h Suggested-Immobilization-Test (SIT) was followed by 8-h polysomnography in an altitude chamber. In randomized, double-blinded order, one night was spent in normobaric hypoxia corresponding to 3000 m above sea-level, while the other night was spent at Innsbruck altitude (574 m). During SIT, PLM during wakefulness (PLMW) and subjective symptoms were recorded every 15 min, utilizing a visual analog scale. Sleep stages and associated events were scored according to AASM criteria.
Results: Fifty-six participants aged 45.1 ± 10.8 years were included, 51.8% female. At both altitudes, RLS patients had more discomfort and urge to move during SIT at any time point, versus controls ($p < 0.01$). Only in RLS patients, the urge to move during SIT was higher after 30 and 45 min at 3000 m versus 574 m ($p = 0.048$, $p = 0.031$). PLMW during SIT and PLM during sleep (PLMS) did not change with HA exposure. Only men had an increased PLMS index at 3000 m, $p = 0.032$.
Conclusion: In RLS patients, the urge to move the legs during SIT is stronger at HA. In men with RLS the PLMS index increases at high-altitude. These data support a role of hypoxia in the pathogenesis of RLS.
Disclosure: Nothing to disclose. We are thankful to the Swedish RLS Foundation for supporting this study, and to Nikolaus Prinz, Katrina Lehner, and Timon Schwarz-Wissel for helping to conduct the polysomnographies.

EPR-291 | Frailty in isolated REM sleep behavior disorder (iRBD): Prevalence and clinical characterization

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Background and Aims: This study aims to investigate prevalence and associated features of frailty in iRBD. Frailty significantly affects the well-being of the elderly population. The interaction between frailty and Parkinson's disease (PD) is complex and bidirectional, since PD is a potential contributor to frailty in the elderly. In turn, iRBD, representing a prodromal stage of PD, potentially amplifies the risk and severity of frailty.
Methods: 35 iRBD patients (33 males, 2 females, age 70.77 ± 9.6 years) underwent a comprehensive clinical and instrumental phenotyping. In particular, each patient underwent assessment of frailty through the SHARE-FI scale, and clinical scales: MMSE, UPDRS part III, UPSIT-40, SCOPA-AUT, RBD-HK, PSQI, ESS, HADS-A, HADS-D, BDI, EQ-5D; Schellong Test and neuroimaging studies (DATSCAN, FDG-PET).
Results: 8 patients (22.9%) resulted to be fragile. Statistically significant correlations were found between frailty and MMSE corrected score ($p = 0.046$), UPDRS part III ($p = 0.05$), UPSIT-40 ($p = 0.012$) and BDI score ($p = 0.002$). HADS-A was pathologic in 57.1% fragile patients versus 14.8% non-fragile patients ($p = 0.019$); BDI in 62.5% versus 22.2% ($p = 0.031$), alteration in dopaminergic reuptake (DAT-scan) in 87.5% versus 39.1% ($p = 0.018$) and brain glucose metabolism (FDG-PET) in 62.5% versus 21.7% ($p = 0.034$).
Conclusion: Frailty is frequent in prodromal PD (1/5 of the patients) and it is associated with worse cognitive and motor performances, with depression, anxiety and functional imaging of the brain. Clinicians should be aware of frailty in iRBD, although further studies should clarify its effective clinical consequences.
Disclosure: Nothing to disclose.

EPR-292 | COVID-19 associated sleep disorders and the role of inflammation in the pathogenesis

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Background and Aims: Insomnia is a common sleep disorder in Covid-19 patients. Previous research has demonstrated that

extreme elevations in IL-1β-NF-α can impair sleep. Based on these findings, we hypothesized that COVID-19 and insomnia cooperation developing on an inflammatory background.

Methods: Patients diagnosed with insomnia were included in the study; those who still had insomnia 3 months after being diagnosed with covid-19 acute infection and who were diagnosed with insomnia as a result of insomnia diagnostic criteria. Three groups were formed for the study: (1) COVID-19 patient with insomnia (CWI), (2) COVID-19 patient without insomnia (CWoI), (3) Healthy control (HC) were designed. Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Beck Anxiety Inventory (BAI), Insomnia Severity Index (ISI) were applied. BDNF, IL-6, TNF-α, IL-1β, IL-10, MMP-9 levels were measured in the volunteers' blood.

Results: A total of 96 participants were recruited. Group 1:33 patients, group 2:31 patients, group 3:32 volunteers. BDNF ($p < 0.001$), IL-6 ($p < 0.001$), TNF-α ($p < 0.001$) ($p < 0.036$), IL-1β ($p < 0.001$), IL-10 ($p < 0.001$) values were shown a significant difference in insomnia patients compared to CWoI and HC. Insomnia patients were increased cytokine levels than the other groups. Therewithal CWoI were increased cytokine levels than the HC. MMP-9 levels were shown a significant difference between control group and covid patients ($p < 0.001$). ESS, PSQI, BAI, ISI scores were shown a significant difference in CWI compared to CWoI and HC ($p < 0.001$).

Conclusion: Patients who developed insomnia after covid 19 had increased inflammatory cytokines and PUKI, BAI, ESS, ISI scores compared to CWoI and HC. Based on the data obtained, it was demonstrated that the basis of insomnia is inflammatory pathogenesis.

Disclosure: Nothing to disclose.

EPR-293 | Variability of REM sleep without atonia in consecutive polysomnographies of patients with hypersomnia

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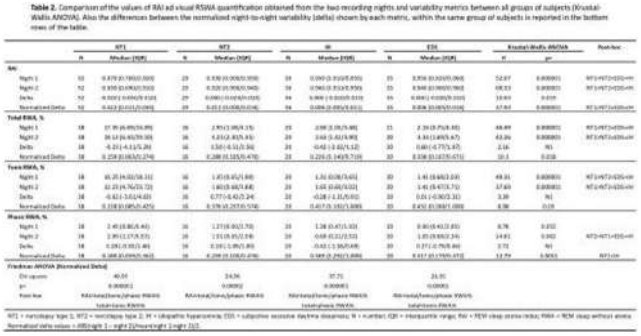
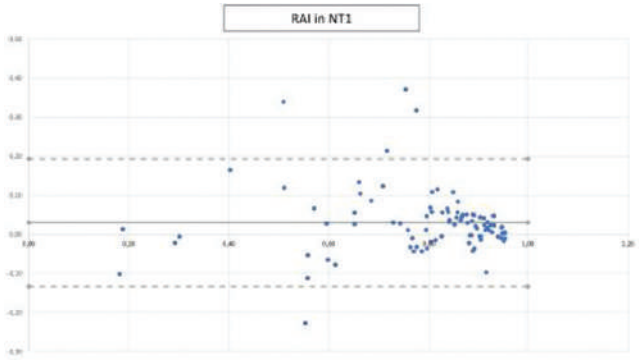
Background and Aims: To explore inter-night variability of motor dyscontrol during REM sleep in patients with central disorder of hypersomnolence (CDH).

Methods: Two consecutive overnight polysomnographies (PSG) of 250 adults with suspected CDH (92 NT1; 29 narcolepsy type 2; 36 idiopathic hypersomnia; 93 other diagnoses) were analyzed. Chin REM atonia was quantified with the automatic REM atonia index (RAI), and visually, in a subgroup of 111 patients, with percentage of REM sleep without atonia (RSWA%) according to American Academy of Sleep Medicine manual. The variability of RAI and RSWA between the two nocturnal PSG was assessed stratified by diagnosis, and the normalized inter-night variabilities of the different measures were compared.

Results: In patients with NT1 RAI resulted more frequently altered (63% with RAI <0.9 on night 1) than in other groups (<27% with RAI <0.9 on night 1), $p < 0.001$, and the rates of patients with altered values remained stable across the two nights in all groups. RAI significantly decreased from night 1 to night 2 in NT1 only (from 0.87 (IQR 0.76–0.92) to 0.83 (IQR 0.69–0.91), $p < 0.001$), whereas it did not vary in other groups. Normalized inter-night variability was lower for RAI than for visual RSWA in all groups ($p < 0.001$).



Comparison of the values of RAI ad visual RSWA quantification obtained from the two recording nights and variability metrics between all groups of subjects (Kruskal–Wallis ANOVA). Also the differences between the normalized night-to-night variability (delta)



Bland-Altman plot: agreement between night1/night2 in NT1.

Conclusion: Motor dyscontrol during REM sleep is a distinctive feature of NT1, and it is stable across different nights. RSWA could provide a potential utility in the diagnosis and characterization of NT1, especially if computed with automatic algorithms that appeared less variable than the visual scoring method in all disorders of hypersomnolence.

Disclosure: Nothing to disclose.

EPR-294 | Unattended home-video-PSG monitoring in 325 patients with sleep disorders: Hazards and values of diagnosis

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Background and Aims: Polysomnography (PSG) recorded in a sleep lab is the International gold standard for the diagnosis of sleep disorders. The cardio-respiratory home monitoring is scientifically validated for in the suspicion of OSAS. However, this approach does not detect all sleep disorders or coexistent multiple sleep disorders. The objective of the study is to evaluate the feasibility of the unattended Home-Video-PSG monitoring for all sleep disorders.

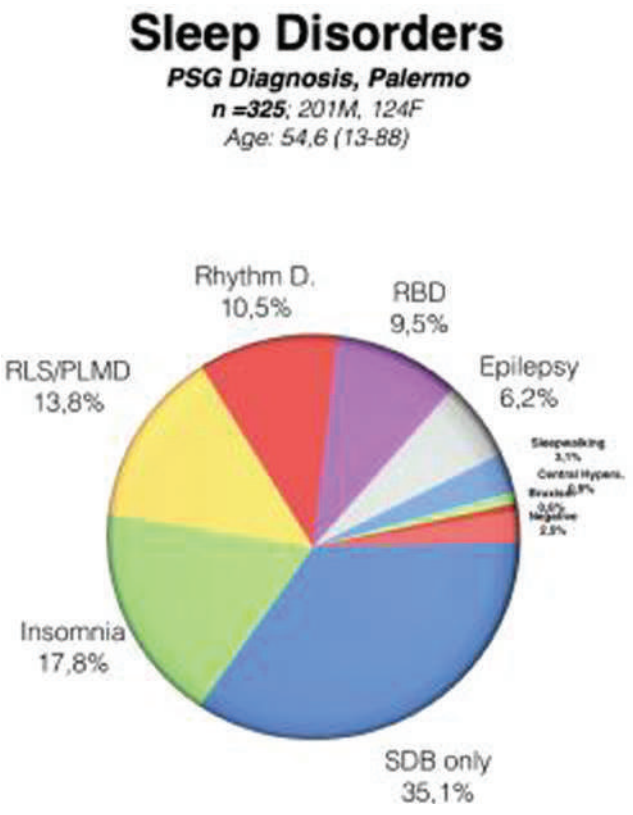
Methods: All the adult collaborating outpatients with a Sleep Disorder afferent to the Sleep Lab of the "Clinical Course" Neurophysiology Unit of Palermo between the years 2018–2019 were consecutively enrolled. Placement of all electrodes and sensors always took place in the lab and the recording was carried out at the patients' home without supervision.

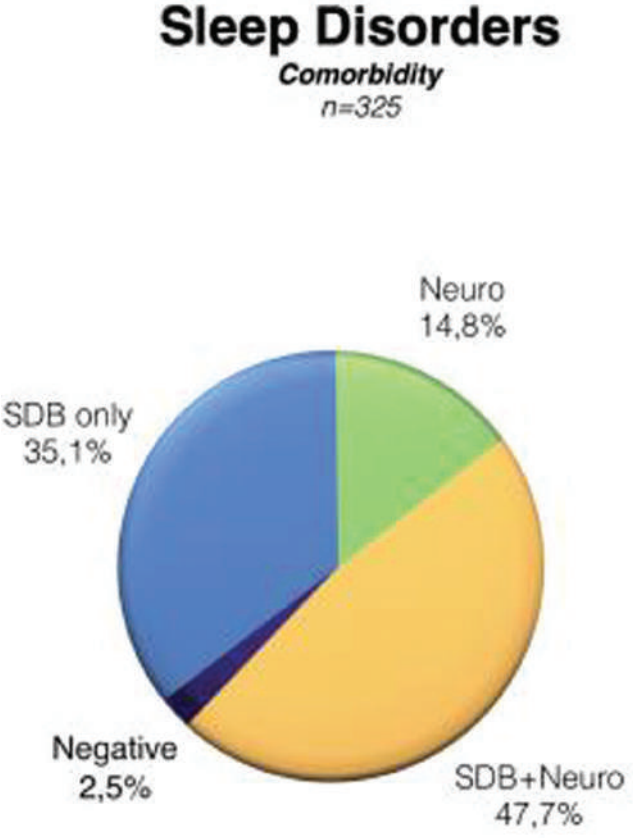
Results: We recruited 325 patients (201 males, mean age 54.6, range 13–88). The final diagnoses were isolated sleep-disordered breathing (SDB) (35.1%), isolated neurological sleep disorders (14.8%), combined neurological-SDB (47.7%) and negative (2.5%). The video recording was confirmatory in 69.4% of cases, integrative or diagnostic in 18.2% and negative in 12.4%. In 4.1% of the videotaped cases the patient was out of the frame, in 31.1% the patient was partially recorded. Unsuccessful recordings were 7.3%; 8.6% had artifacts on the neurological channels; 4.6% presented cardio-respiratory pitfalls.

Figure 1	Negative n=6 2,5%	SDB n=114 35,1%	Neuro n=48 14,8%	SDB + Neuro n=155 47,7%	TOT n=325 100%	ANOVA F	Sign. p
Age (Years)	34,5 ± 24,8	50,7 ± 19,2 #	40,8 ± 17,8 °	59,8 ± 15,3 §	54,6 ± 17,3	19,868	**0,000**
AHI	1,5 ± 1,5	30,1 ± 25,1 #	1,1 ± 1,1 °	19,9 ± 19,7 §	20,8 ± 22,8	25,137	**0,000**
BMI (Kg/m²)	28,6 ± 9,0	33,0 ± 9,0 #	24,6 ± 6,0 °	31,6 ± 7,4	31,0 ± 8,3	13,169	**0,000**
SpO2 (%)	95,2 ± 1,8	92,0 ± 4,2 #	94,6 ± 1,5 °	91,9 ± 7,3	92,4 ± 5,7	3,682	**0,012**
T90 (%)	9,0 ± 0,8	19,3 ± 25,5 #	1,1 ± 2,7 °	13,6 ± 22,1 §	13,8 ± 22,7	8,798	**0,000**
LM in PLM	2,7 ± 1,9	5,6 ± 9,0	8,2 ± 13,8	14,2 ± 20,9 §	10,6 ± 17,4	3,145	**0,027**
TRT (min)	463,1 ± 26,3	460,7 ± 74,4	484,0 ± 64,2	463,2 ± 69,0	465,4 ± 69,8	1,174	0,320
WASO (min)	21,9 ± 20,3	49,2 ± 41,4	44,5 ± 46,6 °	60,0 ± 43,2 §	53,1 ± 43,3	3,018	**0,030**
TST (min)	426,2 ± 20,6	395,0 ± 86,6 #	424,5 ± 75,1 °	387,4 ± 71,7	396,5 ± 77,9	2,706	**0,046**
SL (min)	14,9 ± 17,8	12,1 ± 13,4	14,9 ± 16,12	15,6 ± 15,9	14,3 ± 15,1	1,014	0,387
SE (%)	92,1 ± 2,4	86,7 ± 9,1	87,6 ± 10,0 °	83,8 ± 10,3 §	85,5 ± 9,9	3,378	**0,019**
N Awa.	7,0 ± 5,7	11,3 ± 7,4	10,0 ± 7,4 °	14,0 ± 9,6 §	12,3 ± 8,6	3,493	**0,016**
N3 (%)	22,7 ± 6,6	20,7 ± 10,0 #	24,2 ± 6,4	21,3 ± 8,5	21,5 ± 8,8	2,927	**0,034**
REM (%)	21,8 ± 3,8	18,1 ± 6,5	17,8 ± 7,0	16,5 ± 6,6	17,4 ± 6,7	2,055	0,107

Demographics and sleep parameters of the studied population expressed as mean and standard deviation; ANOVA for group comparisons, $p < 0.05$ as significant in bold. Post- hoc LSD sign. diff.: # SDB versus Neuro;° Neuro versus SDB+Neuro; § SDB versus SDB+Neuro.

Sleep disorders: PSG diagnosis, Palermo (Italy) *n* =325; 201M, 124F Age: 54.6 (13–88).





Sleep disorders: Comorbidity $n = 325$.

Conclusion: Despite the technical difficulties and possible artifacts, video-PSG offers the opportunity for the evaluation of complex pathologies, being diagnostic in nocturnal seizures, behavioral/agitation disorders during sleep and parasomnias; in movement disorders it helps in diagnostic confirmation; it also provides additional information on respiratory disorders associated with neurological disorders.

Disclosure: We declare no conflict of interests.

EPR-295 | The clinical and socioeconomic consequences of insomnia: An umbrella systematic review

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Background and Aims: Insomnia – defined by disturbed sleep initiation and -maintenance and impairment of daytime functioning despite adequate opportunity and circumstances for sleep – is the most common sleep disorder among adults. Good quality sleep is one of the determinants to preserve brain health. The aim of this umbrella systematic review is to assess the role of insomnia as risk factor for many health and socio-economic consequences in the general population.

Methods: Cohort studies and systematic reviews of these studies were eligible for inclusion if including general population, considering insomnia as possible risk factor and death, cognitive impairment, stroke, mental disorders, social and economic consequences as outcomes. This systematic review was registered with PROSPERO database (CRD42021285454).

Results: Preliminary data are available for death, cognitive impairment, and work injuries. Three systematic reviews did not find insomnia as risk factor for death. One systematic review found two components of insomnia associated with death (difficulty falling asleep – DFA – HR 1.13, 95% CI 1.03–1.23; non-restorative sleep HR 1.23, 1.07–1.42). Two systemic reviews with meta-analysis found insomnia as risk factor for dementia (any cause OR 1.53, 1.07–2.18; RR 1.27, 1.16–1.39). One systemic review found two components of insomnia as risk factors for work injuries (DFA OR 1.29, 1.07–1.55; non-restorative sleep OR 1.40, 1.05–1.86).

Conclusion: Insomnia seems to be a risk factor for dementia and work injuries in general population. Less clear data are available on mortality. When completed, this systematic review will show the current knowledge on insomnia as risk factor for clinical and socioeconomic consequences.

Disclosure: Nothing to disclose.

EPR-296 | Exploring REM sleep behavior disorder across pathologies: A cinematic and emotional journey through clinical phenotypes

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Background and Aims: Loss of muscle atonia during REM sleep behavior disorder (RBD) results in movements mimicking dream content. RDB manifests early in 60%–100% of patients with synucleinopathy. Additionally, it affects 10%–15% of patients with narcolepsy, and often presents as idiopathic (RBDi) with a substantial proportion later diagnosed as synucleinopathy. These pathologies have their own semiological frameworks. However, scarce data exist to differentiate specific RBDs between these diseases. Our hypothesis posits distinctive patterns of RBD (movement types, kinetics, emotional valence…) across narcolepsy, synucleinopathies, RBDi and other disorders (e.g., autoimmune encephalitis).

Methods: We applied a new classification on RBDs to visually compare their movements (elementary, violent, scenic…), their topography (legs, hands, face…), and their emotional valence (negative, positive, neutral) in patients belonging to each group, who underwent a polysomnography (2014–2024) in Toulouse University Hospital. We added objective markers detected by a semi-automating tracking of RBD movements using a deep learning algorithm.

Results: Sixty patients, including 16 patients with synucleinopathy, 26 RBDi, 10 narcoleptics, and 8 with other disorders have been included. According to first results, in a subgroup of 38 patients, RBD is more violent in RBDi and narcolepsy, more scenic in synucleinopathies. Narcolepsy-associated RBD tended to exhibit a positive emotional valence, while it is negative in RBDi and synucleinopathies. A deep learning algorithm is currently being trained on RDB videos to confirm these distinctive profiles.

Conclusion: Our results highlight identifying pathology-specific patterns holds significant clinical importance, positioning RBD as a potential diagnostic marker. This is especially relevant for identifying the conversion from RBDi to synucleinopathy.

Disclosure: Nothing to disclose.

EPR-297 | Disorders of arousal motor patterns in isolated RBD patients: A video-polysomnography analysis of 48 patients

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Background and Aims: Disorders of Arousal (DoA) and REM sleep behaviour disorder (RBD) are sleep parasomnias arousing from NREM and REM sleep, respectively. DoA episodes can be classified from simple to complex patterns (Loddo et al., Sleep Medicine, 2017). RBD consists of dream-enactment episodes, however, during video-polysomnography, these patients mostly show simple jerks, very distinct from DoA patterns, which include mainly truncal/axial movements. Our aim was to search for these patterns on our cohort of iRBD patients.

Methods: We reviewed all video-polysomnographies from our cohort of 48 iRBD patients, consecutively recorded at the Bologna Sleep Centre between 2011 and 2023. All recordings were examined by one observer, blinded to clinical history, in search for DoA patterns, according to Loddo et al. Each episode was characterized by sleep stage, sleep cycle, triggers, onset, DoA pattern (type of movement, duration, progression).

Results: Our sample comprised 37 (77%) males, median age of 71.8 years-old. We identified 32 DoA patterns in 18 patients (38%). The most observed pattern was simple arousal movements – head flexion/extension with/without limb movement or partial trunk flexion/extension – accounting for 29 (91%) events. Rising arousal movements – trunk flexion followed by sitting – were observed in three events. 22 events (69%) arose from REM sleep and 10 from NREM sleep.

Conclusion: DoA patterns can be found in some patients with iRBD and may expand the current description of sleep-related motor patterns in iRBD patients, inciting more studies. A further correlation with clinical data could explain the significance of these patterns and their prognostic implications.

Disclosure: Nothing to disclose.

Neuroimaging 1

EPR-298 | Neuronal remodeling in migraine patients correlates with disease activity

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Background and Aims: Migraine represents one of the most prevalent neurological conditions worldwide. There is evidence for reduced gray matter (GM) and white matter (WM) volume with an increased incidence of white matter lesions (WML) in migraine patients, particularly in those with aura. Advanced MRI techniques allow us to evaluate the underlying microstructural substrate and glymphatic system function.

Methods: Using a Connectome scanner, we utilized the diffusion weighted imaging (DWI) models TractCaliber and Soma and Neurite Density Imaging (SANDI) to characterize the microstructure of GM and WM in 17 patients with migraine with aura and 17 matched healthy controls (HC). All patients completed a clinical questionnaire on disease activity. We assessed glymphatic system activity with diffusion-tensor image analysis along the perivascular space (DTI-ALPS).

Results: The GM of migraine patients exhibits reduced neuronal density with an increase in soma radius of the remaining cells, in both cortex and deep GM structures. WM shows evidence of axonal loss with increased axonal diameter, also in WM that appears normal on conventional MRI. WM TractCaliber CSF volume fraction correlates with disease duration in years ($r = 0.5$ and $p = 0.04$). There is no difference in glymphatic activity between migraine patients and HC.

Conclusion: High-gradient diffusion MRI shows occult changes in the microstructural integrity of GM and WM in migraine patients, which correlates with migraine duration. Our findings suggest that migraine is associated with neuronal remodeling, which may contribute to increased cerebral vulnerability in patients.

Disclosure: Melanie Li, Laleh Eskandarian, Kyla Gaudet have nothing to disclose. Susie Huang has NIH grants R01NS118187 and P41EB030006. Katharina Eikermann-Haerter has Ralph Schlaeger Award (MGH).

EPR-299 | Diagnostic accuracy of computed tomography in detection of carotid plaque characteristics: A systematic review

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Background and Aims: Beyond the stenosis degree, the carotid plaque morphology assessed by noninvasive imaging may improve the stroke risk stratification. This study aimed to assess the accuracy of computed tomography (CT) to detect the carotid plaque characteristics compared to histology in patients with symptomatic and asymptomatic carotid plaques, conducting a systematic review.

Methods: We registered the protocol in PROSPERO (ID CRD4202232969) and searched Medline Ovid, Embase.com, Cochrane Library, and Web of Science for diagnostic accuracy of CT in specific carotid plaque characteristic imaging compared to histology, without any search limitation.

Results: Of 8,168 studies, 20 studies that evaluated seven specific plaque characteristics were included in our systematic review. The best diagnostic accuracy was found for the detection of ulceration (sensitivity 39.4%–100%, specificity 74%–100%), followed by calcification (sensitivity 72.7%–100%, specificity 35.7%–100%), lipid-rich necrotic core (sensitivity 63.2%–95.6%, specificity 60%–100%), and intraplaque hemorrhage (sensitivity 61.5%–100%, specificity 20%–99.5%). Only a few studies evaluated specifically vulnerable, mixed, and fibrous plaque. Novel CT techniques promise more accuracy and patient safety in carotid plaque features imaging.

Conclusion: CT allows for highly accurate detection of carotid plaque features, in particular ulceration and calcification, followed by the lipid-rich necrotic core and intraplaque hemorrhage. These results underline the role of routine CT examinations not only to assess the stenosis degree but also plaque morphology and individual patient stroke risk to better guide management.

Disclosure: Nothing to disclose.

EPR-300 | Abstract withdrawn

EPR-301 | Exploring the relation among choroid plexus enlargement, glymphatic dysfunction and brain damage in multiple sclerosis

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Background and Aims: Choroid plexus (CP) regulates immunological functions and cerebrospinal fluid (CSF) production within the CNS. In multiple sclerosis (MS), CP enlargement is associated with higher inflammatory activity and more severe brain damage. We investigated whether the associations of CP enlargement with white matter (WM) lesions and brain volumes is mediated by glymphatic system dysfunction.

Methods: Brain 3T MRI scans were obtained from 146 MS patients and 72 age- and sex-matched healthy controls (HC). We quantified the diffusion along the perivascular space (DTI-ALPS) index as a proxy of glymphatic function, and normalized (n) CP volume using a fully automatic method on brain three-dimensional T1-weighted and FLAIR MRI sequences.

Results: Compared to HC, MS patients showed significantly higher WM lesion and nCP volumes ($p < 0.001$), together with significantly lower DTI-ALPS index, normalized brain, thalamic, and cortical volumes ($p \leq 0.048$). In MS patients, higher nCP volume correlated with lower DTI-ALPS index (standardized-$\beta = -0.332$, $p < 0.001$). Both measures were significantly associated with higher brain, periventricular and juxtacortical WM lesion volumes (nCP volume: standardized-β range = 0.291; 0.332, $p < 0.001$; DTI-ALPS index: standardized-β range = −0.229; −0.315, $p \leq 0.005$), as well as with lower normalized brain, thalamic and cortical volumes (nCP volume: standardized-β range = −0.238; −0.364, $p \leq 0.003$; DTI-ALPS index: standardized-β range = 0.233; 0.351, $p \leq 0.001$). DTI-ALPS index partially mediated the associations of normalized CP with WM lesion volumes (standardized-β range = 0.073; 0.115) and brain volumetric measures (standardized-β range = −0.075; −0.125).

Conclusion: In MS, enlarged nCP may contribute to structural brain damage accumulation, particularly in regions close to the CSF, possibly through the promotion of a chronic pro-inflammatory state and the occurrence of glymphatic system dysfunction.

Disclosure: P Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He has received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM).E Pagani,

M Rubin, G Corazzolla have nothing to disclose. M Margoni reports grants and personal fees from Sanofi Genzyme, Merck Serono, Novartis and Almiral. M. Filippi received compensation for consulting or speaking activities from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPR-302 | Increased resting state functional connectivity after cognitive rehabilitation in progressive MS: CogEx study results

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Background and Aims: CogEx (ClinicalTrials.gov, NCT03679468) was a trial determining effectiveness of cognitive rehabilitation (CR) and aerobic exercise (EX) in progressive multiple sclerosis (PMS). We present resting-state (RS) functional connectivity (FC) findings.

Methods: Participants were randomized (1:1:1:1) to "CR-plus-EX", "CR-plus-sham-EX (EX-S)", "EX-plus-sham-CR (CR-S)", and "CR-S-plus-EX-S" and attended 12-week intervention. Physical/cognitive assessments were performed at baseline, immediately after intervention (week-12) and 6 months post-intervention (month-9). MRI sub-study participants underwent RS-fMRI to estimate RS FC in the main cognitive networks.

Results: 104 PMS participated in the MRI sub-study ("CR-plus-EX": $n=25$; "CR-plus-EX-S": $n=28$; "CR-S-plus-EX": $n=25$; "CR-S-plus-EX-S": $n=26$); 87 (83%) completed baseline and week-12 RS-fMRI. At week-12 and month-9, no differences were found among interventions for symbol-digit modalities test (SDMT) correct responses, nor SDMT, California verbal learning test (CVLT) and brief visuospatial memory test *Z*-scores (p = range 0.12–0.94). Time-by-treatment interactions of voxel-wise RS FC changes at week-12 versus baseline indicated increased RS FC in most analyzed networks ($p<0.001$, uncorrected) in "CR-plus-EX" and "CR-plus-EX-S" patients, and decreased RS FC over time in "CR-S-plus-EX" and "CR-S-plus-EX-S" patients ($p<0.05$, corrected). Whole-network RS FC of salience (SN, $p=0.07$) and default-mode network (DMN, $p=0.08$) exhibited similar trends, becoming significant (SN: $p=0.01$; DMN: $p=0.02$) when comparing all patients performing CR versus CR-S. In CR patients, increased DMN RS FC at week-12 versus baseline showed trend correlation with increased CVLT Z-score ($r=0.27$, $p=0.06$).

Conclusion: CR modulated RS FC in cognitive networks of PMS. Funding. Funded by the MS Society of Canada (grant #EGID3185). Ancillary funding from CMSC, Danish MS Society, and National MS Society.

Disclosure: Nothing to disclose.

EPR-303 | Unveiling the power of nerve ultrasonography in Guillain–Barre syndrome diagnosis

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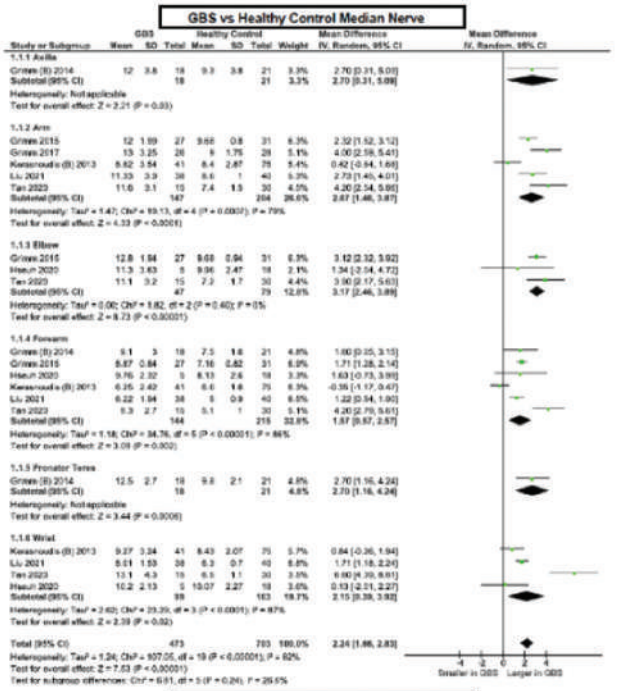
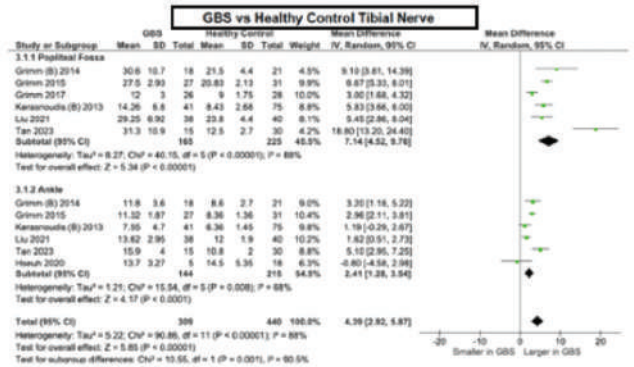
Background and Aims: Guillain–Barré syndrome (GBS) is an inflammatory disorder of the peripheral nervous system. Distinguishing

GBS from chronic inflammatory demyelinating polyneuropathy (CIDP) can be challenging. Nerve ultrasonography emerged as a non-invasive diagnostic tool that provides quantitative information about nerve morphology. This study aims to compare the cross-sectional areas (CSAs) of upper and lower limb nerves in GBS patients with healthy individuals, CIDP patients, and axonal neuropathy patients.

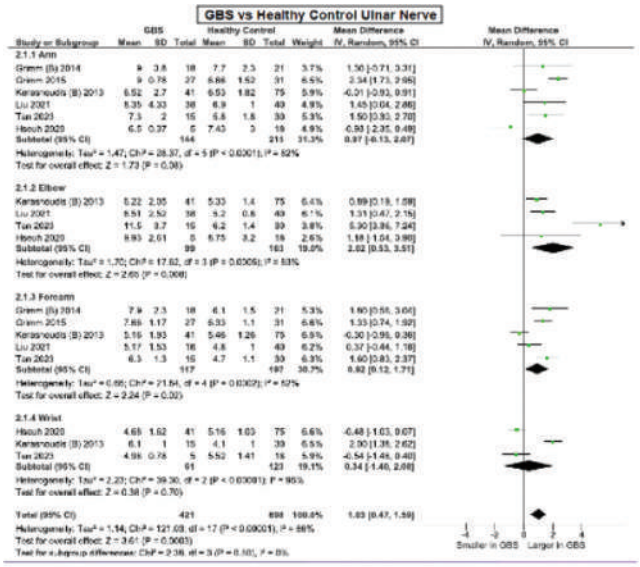
Methods: We performed a systematic search of Medline (PubMed), Scopus, Embase, and Web of Science up to May 24, 2023. After article selection and screening, we performed a quality assessment. Furthermore, a statistical analysis and subgroup analysis were performed.

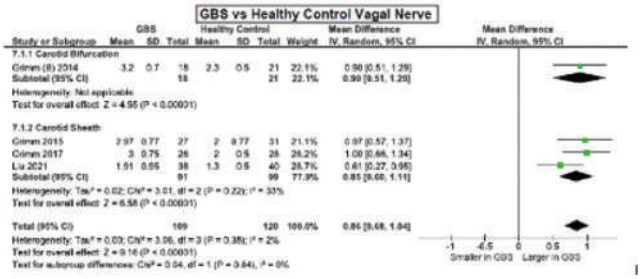
Results: 12 studies included 624 participants, yielding 6284 nerve CSA measurements. The median, radial, ulnar, tibial, sural, fibular, and vagus nerves were found to be significantly larger in GBS patients than in healthy controls. Whereas the median, ulnar, sural, and fibular nerves were found to be significantly smaller in GBS patients than in CIDP patients. Additionally, reference values for peripheral nerve CSAs at different anatomical sites were reported for GBS patients.



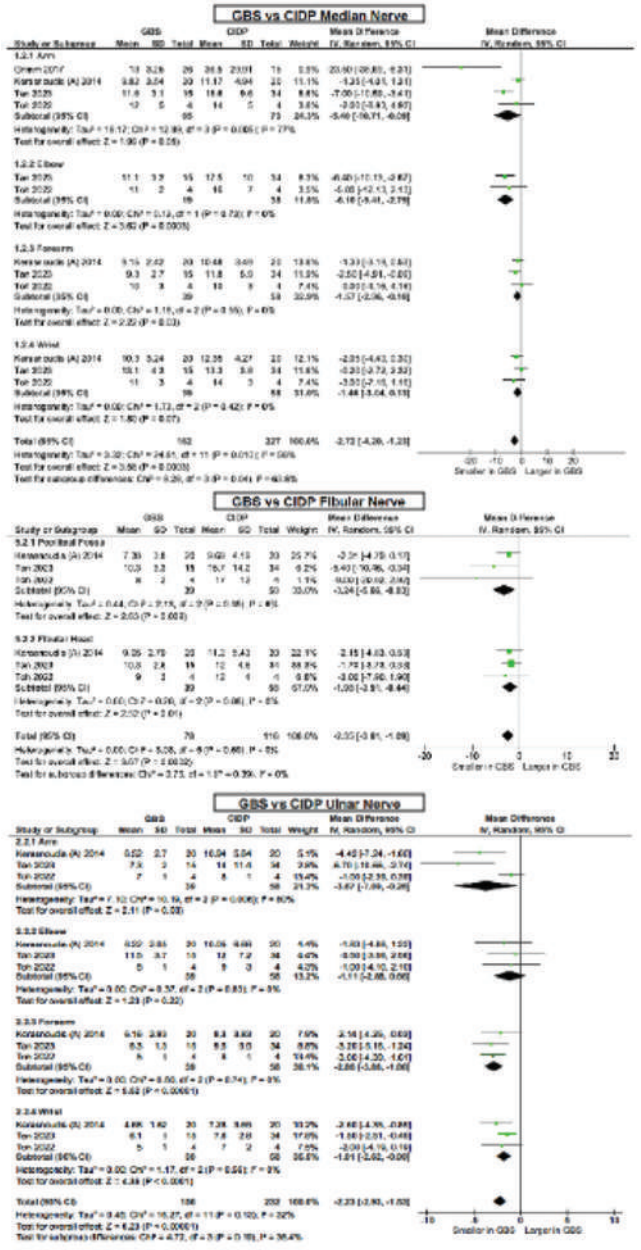


Mean difference in median and tibial nerves CSAs between GBS patients and healthy controls.





Mean difference in the ulnar and vagal nerves CSAs between GBS patients and controls.



Mean difference in median, ulnar & fibular nerves CSAs between GBS patients and CIDP patients.

Conclusion: Measuring the CSA of the tibial nerve at the level of the popliteal fossa, the median and ulnar nerves at the elbow level and the cervical nerve roots can aid in the diagnosis of GBS. However, measuring the CSA of the median at proximal sites, ulnar at distal sites and fibular nerve can help in distinguishing GBS from CIPD.

Disclosure: Nothing to disclose.

EPR-304 | The "swallow tail sign" in the diagnosis of dementia with Lewy bodies: A systematic review and meta-analysis

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Background and Aims: Loss of dorsolateral nigral hyperintensity (DNH) on susceptibility-weighted imaging (SWI) has proven useful in Parkinson's disease. We aim to quantitatively synthesize evidence regarding diagnostic accuracy of DNH loss on SWI for the differential diagnosis of dementia with Lewy bodies (DLB), an a-synuclein-related pathology, from other dementias, investigating the role of MRI, a first-line imaging modality, in early disease detection.

Methods: We searched MEDLINE, Scopus, Web of Science and Cochrane Library using the terms "lewy body dementia", "swallow tail sign", "dorsolateral nigral hyperintensity", "nigrosome-1, "SWI". We included English-written peer-reviewed diagnostic accuracy studies that compared SWI to a reference standard. QUADAS-2 was used for quality assessment.

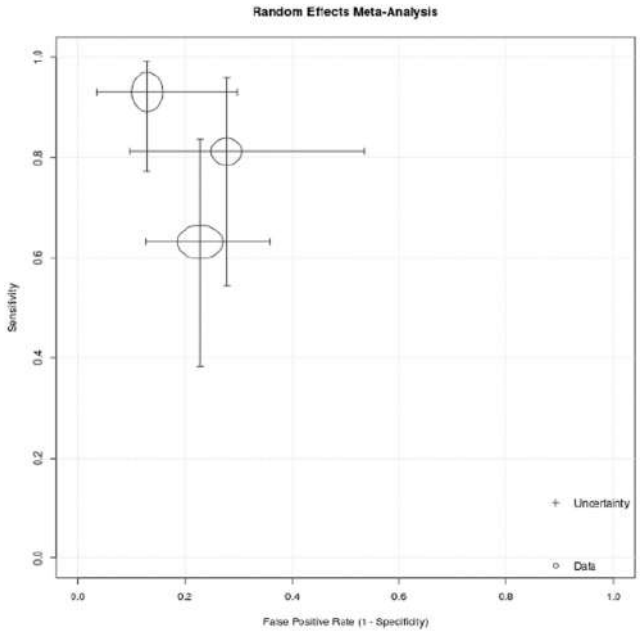
Results: Among 363 search results, three studies were eligible. The overall quality of the included studies was considered adequately high. In total 227 patients were included, 63 with DLB, 164 with other pathologies (Alzheimer disease, frontotemporal dementia, mild cognitive impairment). Meta-analysis of mixed 1.5 and 3T data with a univariate random-effects logistic regression model resulted in pooled sensitivity, specificity and DOR of 0.82 [0.62; 0.92], 0.79 [0.70; 0.86] and 16.26 ([3.3276; 79.4702], $p=0.0006$), respectively. Subgroup analysis of 3T scans showed pooled sensitivity, specificity and DOR of 0.82 [0.61; 0.93], 0.82 [0.72; 0.89] and 18.36 ([4.24; 79.46], $p<0.0001$), respectively.

Table 1: Study characteristics

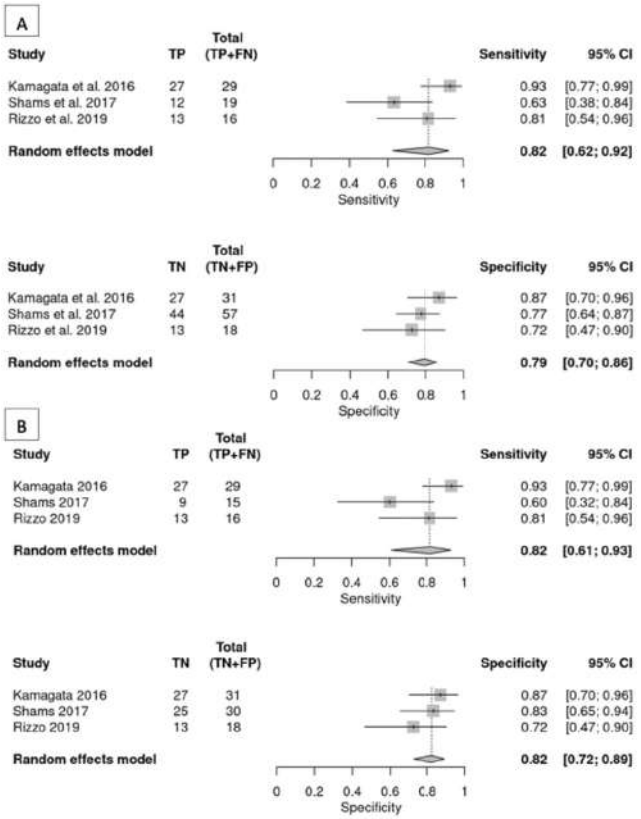
	MRI scan characteristics				Reliability			Second index test	Reference standard
	Field strength	Sequence	Section thickness	Duration (seconds)	Intra-rater	Inter-rater (k)	Rater's experience in years, mean (SD)		
Kamagata 2016	3T	SWI	2mm	108s	NR	0.84	5.5 (0.7)	DaT-SPECT	Clinical diagnosis (Consensus DLB criteria 2005)
Shams 2017	1.5T (n = 31) 3T (n = 45)	SWI	1.5-1.6mm (n = 36) 2mm (n = 40)	NR	NR	0.4	12.5 (4.9)	No	Clinical diagnosis (Consensus DLB criteria 2005)
Rizzo 2019	3T	SWI	1.6mm	180s	NR	0.71	NR	No	Clinical diagnosis (Consensus DLB criteria 2005)

MRI: magnetic resonance imaging; SWI susceptibility weighted imaging; DaT-SPECT: Dopamine transporter single-photon emission computed tomography' DLB: Dementia with lewy bodies

Study characteristics.



Summary receiver operating characteristic (SROC) curve of primary studies using both 1.5 and 3T. Confidence intervals for each study are presented.



Forest plot of pooled sensitivity and specificity of mixed 1.5T and 3T field strength (A) and using only 3T data from each study (B).

Conclusion: Our results suggest the possible use of STS loss on SWI as a biomarker for DLB detection. Further evaluation of standardized protocols is needed, with direct comparison to other indicative and supportive DBL biomarkers.

Disclosure: Nothing to disclose.

EPR-305 | Brain and spinal cord lesion distribution criteria for differentiation of MS, NMOSD and MOGAD

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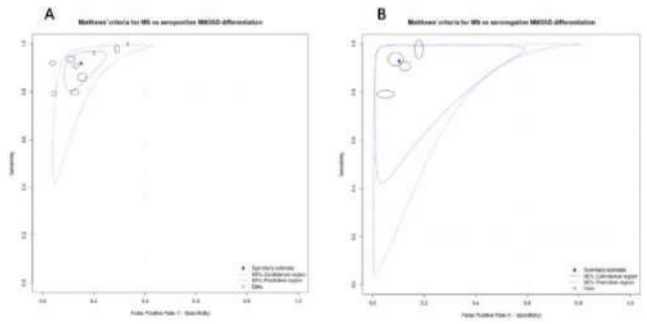
Background and Aims: Multiple sclerosis (MS), Neuromyelitis optica spectrum disorder (NMOSD) and Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) can present with similar clinical attacks and radiological characteristics on Magnetic Resonance Imaging (MRI), causing diagnostic confusion and delay of appropriate treatment initiation, especially in cases of uninformative or unavailable serologic tests. We conducted a systematic review and diagnostic accuracy meta-analysis on the MRI lesion distribution criteria, that have been proposed for disease differentiation.

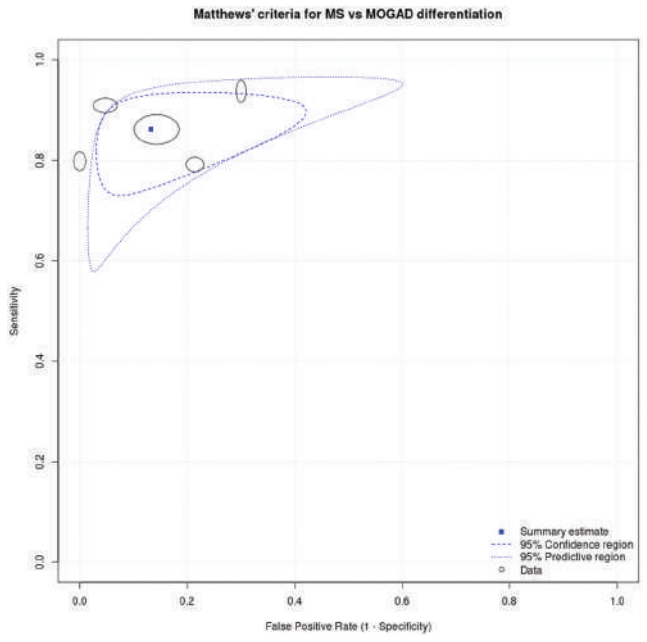
Methods: Our review complies with the PRISMA statement. We searched MEDLINE, SCOPUS, Web of Science, ProQuest and Google Scholar and included English-written peer-reviewed diagnostic accuracy studies. We used QUADAS-2 for quality assessment. We quantitatively synthesized evidence using hierarchical logistic regression models.

Results: Among 313 search results, eleven studies of adequate to high quality (2041 patients; MS, 1037; NMOSD, 862; MOGAD; 142) were eligible. Matthews' brain MRI criteria demonstrated pooled sensitivity and specificity of 0.92 [0.86; 0.96] and 0.85 [0.79; 0.90] for MS versus AQP4-positive-NMOSD, 0.93 [0.84; 0.97] and 0.90 [0.80; 0.95] for MS versus AQP4-negative-NMOSD, 0.86 [0.81; 0.90] and 0.87 [0.76; 0.93] for MS versus MOGAD. The addition of spinal cord MRI raised both sensitivity and specificity (up to 1.00 and 0.87) in one study. Cacciaguerra's brain-spinal cord criteria for NMOSD versus MS differentiation showed pooled sensitivity and specificity of 0.96 [0.76; 0.99] and 0.84 [0.73; 0.92], respectively.

Forest plots of sensitivity and specificity of the Matthews criteria diagnostic accuracy meta-analysis for MS versus seropositive NMOSD.



Graphical representation (summary receiver-operating characteristic model curve) of the Matthews criteria diagnostic accuracy meta-analysis for MS versus seropositive NMOSD (A) and seronegative NMOSD (B) differentiation.



Graphical representation (summary receiver-operating characteristic model curve) of the Matthews criteria diagnostic accuracy meta-analysis for MS versus MOGAD differentiation.

Conclusion: Atypical NMOSD and MOGAD often satisfy MS diagnostic criteria leading to misdiagnosis. Brain and spinal cord distribution criteria are easily applicable and can accurately help distinguish between the three entities.

Disclosure: Nothing to disclose.

EPR-306 | In vivo γ-aminobutyric acid alterations as a biomarker of the therapeutic effect of MRI-negative temporal lobe epilepsy

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Background and Aims: The effectiveness of magnetic resonance imaging (MRI)-negative temporal lobe epilepsy (TLE) treatment depends on accurate localization of the epileptogenic brain region and timely adjustment of the therapeutic schedule. Imaging biomarkers are particularly important because they are noninvasive and real-time. Therefore, we used proton magnetic resonance spectroscopy (1H-MRS) to investigate the associations between γ-Aminobutyric acid (GABA) alteration in the epileptogenic regions indicated by interictal video electroencephalography (EEG) and therapeutic effects in MRI-negative TLE to search for significant biomarkers.

Methods: Overall, 40 patients (17 women) were enrolled in this study. Routine 1H-MRS and MEshcher–GArwood Point RESolved Spectroscopy sequences were acquired. Moreover, we followed up with the patients to obtain reexamination data from seven patients (three women) with an interval of at least 3 months and analyzed the correlation between the increasing index of tonic–clonic seizure frequency and the increasing index of GABA in the region of interest.

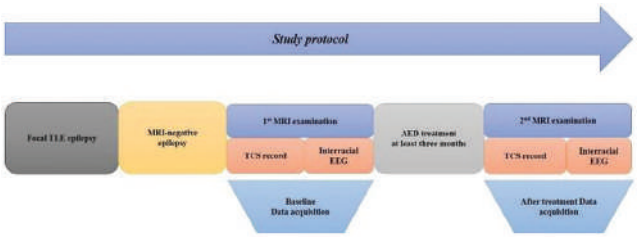
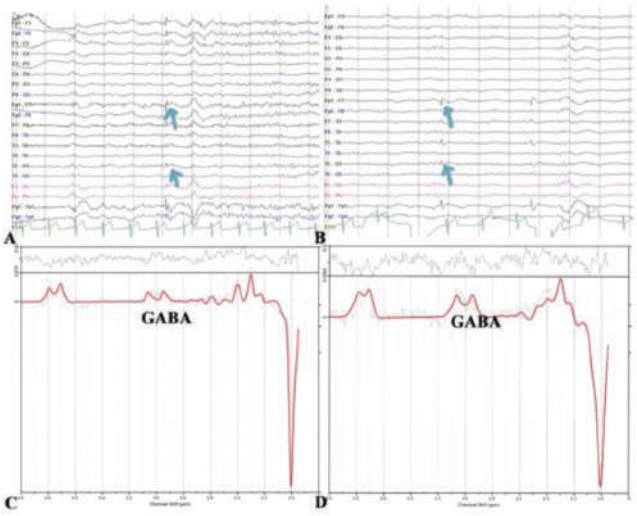
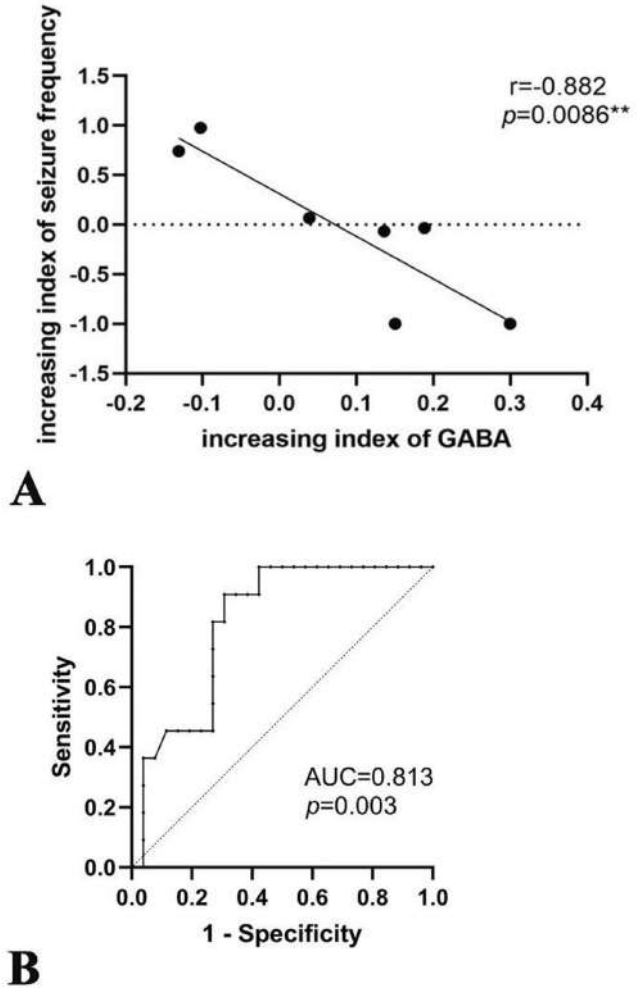


Diagram of the study protocol. The study protocol according to the procedure is presented schematically.

Results: We found that GABA levels is significantly lower on the epileptic side (2.355 ±0.883) than on the contralateral side (2.693 ±0.723, $p=0.033$*) on the mesial temporal lobe cortex (MTLC) of the patients. In the prospective drug effect monitoring analysis, a significant negative correlation was found between the increasing index of GABA values and the increasing index of seizure frequency in epileptogenic MTLC ($r=-0.882$, $p=0.008$**).



(a) and (b) show the initial and after treatment EEG respectively, and seizure waves frequency decreased; (c) shows the GABA peaks in the initial examination, and (d) shows the increased GABA peaks in the same voxel after treatment.



(a) Correlation between the increasing index of GABA and increasing index of seizure frequency in epileptic MTLC. (b) Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic efficacy of epileptic MTLC GABA levels in patients.

Conclusion: GABA level in the MTLC will be a specific and effective biomarker for therapeutic effect monitoring in MRI-negative TLE.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Epilepsy 3

EPR-307 | "An Artificial intelligence (AI)-driven retrospective study to predict depression in patients with epilepsy"

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Background and Aims: Literature suggests a bi-directional relationship between epilepsy and the development of depressive symptoms. However, little is known about the exact mechanisms underlying this relationship, which could involve a combination of many factors. Machine learning (ML) can identify complex patterns within systems of many variables, allowing detection of unexpected associations, generation of new testable hypotheses, as well as support clinical decision making through its predictive power. This study aims to leverage ML to identify predictors of depression onset in patients with epilepsy.

Methods: A tree-based risk prediction model was trained on data from 50,000 epilepsy patients recorded between 2010 and 2023 in German Electronic Medical Records. Recorded diagnoses, prescriptions, and other outcomes (visits, hospitalisations, referrals) were used as input features. Explainable AI identified important features for prediction.

Results: The model correctly identified 62% of patients with epilepsy developing depression, with a precision 70% better than random screening. Age, gender, usage patterns of medical care and use of anti-depressants were found to be potentially associated with onset of depression.

Conclusion: Model results were aligned with the literature, confirming applicability of the approach, with interesting findings for further exploration. This analysis is part of a multi-country AI-driven database study that will address how comorbid epilepsy and depression affect patient management, treatment choices and clinical outcomes. Knowledge on features relevant for onset of depression in patients with epilepsy could be helpful for early diagnoses and improved treatment choices.

Disclosure: Angelini is the sponsor and funded IQVIA to conduct the study.

EPR-308 | Epicranial stimulation for drug-resistant epilepsy at Ghent University Hospital, Belgium

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Background and Aims: Epicranial stimulation is a novel minimally invasive treatment option for drug-resistant epilepsy. The EASEE ® System (Epicranial Application of Stimulation Electrodes for Epilepsy) was implanted in the first Belgian patient in February 2020.
Methods: After a 1- month baseline period, the EASEE® System was implanted epicranially above the seizure onset zone. Focal cortical stimulation was delivered using both high-frequency and direct current components performed via electrode arrays. We evaluated the safety and efficacy of the EASEE ® System up to 3 years follow-up.
Results: The monthly seizure frequency decreased from 75 seizures at baseline to 70, 56, 33 and 27 seizures after 4 months, 8 months, 2 years and 3 years follow-up respectively. The beck depression inventory decreased from 19 at baseline to 13, 12 and 10 after 8 months, 2 years and 3 years follow-up. The Epitrack cognitive screening score increased from 20 at baseline to 30, 32 and 28 after 8 months, 2 years and 3 years follow-up. Adverse events were pain at the incision site and paresthesia behind the left ear, both mild and transient.
Conclusion: Treatment with the EASEE® System was well tolerated and associated with an effective reduction in seizure frequency. Additionally, positive effects on mood and cognition were reported. Similar to other neurostimulation therapies, there seems to be an increased effect over time. The EASEE® System may offer a promising treatment option for patients with a predominant epileptic focus who are not suitable candidates for epilepsy surgery.
Disclosure: This patient was included in the EASEE II trial by Precisis.

EPR-309 | The efficacy of vagus nerve stimulation in adults with drug-resistant epilepsy beyond seizure count

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Background and Aims: Vagus nerve stimulation (VNS) represents a therapeutic option for people with drug-resistant epilepsy who are not eligible to curative surgery, resulting in a >50% seizure reduction in 45%–65% of cases. This study aims to assess the impact of VNS on seizure burden, as indicated both by frequency and severity, across different seizure types.
Methods: Seizure frequency and severity were evaluated at 1-year post-implantation (T1) and at the last follow-up (FU) (T2). Seizure occurrence was categorized into frequency groups (multidaily-daily-weekly-monthly-annually), and severity was assessed based on patients' reports.
Results: At our center, 91 individuals (53-males, 38-females) with epilepsy of different etiology (structural-47%; genetic-14%), of whom 45% with an encephalopathy, underwent VNS treatment. We observed an overall reduction in seizure frequency in 46% of cases at T1 and in 63% at T2 (mean FU = 95 months). 66% of patients reported a reduction in seizure intensity at both T1 and T2. Generalized/focal-to-bilateral Tonic-Clonic seizures (TCS) disappeared in 37% of patients at T2 and decreased in an additional 46% (T1)–51% (T2). Clusters and seizures-associated falls decreased in 71% (T1)–69% (T2), and 54% (T1)–42% (T2) of patients, respectively. Although adverse effects were common (45%), they were mostly transient and mild (hoarseness/cough).
Conclusion: In our population, VNS proves to be a safe procedure improving seizure control, especially for the most threatening ones: TCS, falls, and seizure-clusters. Developing outcome measures that include seizure type and severity might offer a more comprehensive quantification of VNS efficacy than counting seizures, which, as a single measure, poorly represents the quality of life in people with refractory epilepsy.
Disclosure: Dr Mostacci and Professor Tinuper report research funding to their Institution from LIVANOVA.

EPR-310 | Intraoperative seizures: Does everything end in the operating room?

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Background and Aims: Intraoperative seizures (IOSs) occur in about 2.9%–54.3% of glioma surgery, often considered as provoked events without a clear clinical impact. Notwithstanding, less is known about the effect of IOSs on seizure and clinical outcome. Our aim is to assess the possible role of IOSs on short- and long-term epileptological and clinical outcome in patients with tumor-related epilepsy (TRE).
Methods: This is a retrospective, monocentric study of 155 patients affected by glioma and TRE who underwent surgery. Seizure and clinical outcome were evaluated considering Engel class, Karnofsky Performance Status scale and modified Rankin Scale, at 12 and 24 months of follow-up.

Results: Thirty-nine subjects (25.16%) presented with IOSs. Focal cognitive seizures were the prevalent seizures type (20.9%). In the 89.74% of cases, seizures occurred during awake surgery without changing in the anesthesiologic protocol. Comparing patients with versus without IOSs, any significant difference was found in term of development risk of early post-operative seizures (POSs) ($p=0.453$). IOSs occurrence did not influence both epileptological and clinical outcome at 12 ($p=0.595$; $p=0.348$; $p=0.559$) and 24 months ($p=0.544$; $p=0.750$; $p=0.410$). Otherwise, the development of early POSs was associated with a worse epileptological and clinical outcome at 1 ($p=0.020$; $p=0.05$) and 2 years ($p=0.023$; $p=0.05$; $p=0.04$).

Conclusion: IOSs seem to be possibly harmful during surgery, not influencing short- and long-term seizure control and clinical outcome, unlike early POSs that present a higher impact.

Disclosure: Nothing to disclose. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

EPR-311 | Barriers in access to care for persons living with epilepsy in rural Rwanda

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Background and Aims: Epilepsy is a common neurological condition with nearly 80% of 70 million persons with epilepsy (PwE) worldwide living in low- and middle-income countries. In Rwanda the prevalence varies between 29 and 73/1000 population and the treatment gap is >75%.

Methods: The Rwandan Organisation Against Epilepsy (ROAE) screened for epilepsy in 48 villages in the Rulindo District, north of Kigali in October 2021. PwE completed the Limoges questionnaire, socio-demographic data, reasons for treatment non-adherence and QOLIE10.

Results: Epilepsy screening was performed by community health workers. Epilepsy diagnosis was confirmed by neurologists in 146 PwE. Eighty-three were newly diagnosed. Mean age of seizure onset was 16.1 years. The male:female ratio was 1.00:1.24. More than 67% of PwE aged ≥20 years were single. Farming was the most frequent reported profession (37.7%). Half of the PwE expressed seizure recurrence worry, more frequently reported by women compared to men. A reduced or absent mood was reported by 83% (downheartedness). Nearly 60% reported poor QoL. Important barriers to access to care were misunderstanding of the disease (27.4%), ignorance (21.0%), lack of household finances (10.5%) and stigma, despair and hopelessness resulting in demotivation (13.7%).

Conclusion: This field study highlights an urgent need for increased education and awareness among caregivers and families in rural communities as only a limited number of PwE were identified in a routine screening programme. Significant educational efforts are needed to improve epilepsy care, knowledge, and attitudes.

Disclosure: None.

EPR-312 | Clinical characteristics and treatment approach of established new-onset status epilepticus (eNOSE)

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Background and Aims: Status epilepticus (SE) can occur in patients without a previous epilepsy diagnosis, a condition identified as "new-onset status epilepticus" (NOSE). Treatment with benzodiazepine may fail in NOSE termination, requiring anti-seizure medication (ASM) employment. In this context, the term "established NOSE" (eNOSE) is generally employed. This study aims to describe the main clinical characteristics of a large sample of patients suffering from eNOSE comparing the ASM efficacy and exploring the risk factors associated with ASM treatment unresponsiveness and E-NOSE associated mortality.

Methods: Adult patients with eNOSE were retrospectively selected between January 2016 and December 2022. Demographics and clinical data as well as diagnostic work-up and treatment were reviewed. We considered effective the last ASM introduced or increased in dose before the eNOSE termination.

Results: 123 patients were included (age: 67.9 ± 17.3). eNOSE acute etiology was mostly reported. In the overall cohort, phenytoin showed the highest response rate. In the pairwise comparisons, valproate was superior to levetiracetam ($p=0.02$), but not to lacosamide ($p=0.65$). Phenytoin had a significantly higher resolution rate compared to levetiracetam ($p=0.0005$) but not to lacosamide ($p=0.16$). Thirty patients were refractory to ASM treatment. No predictors of refractoriness were identified. Thirty-nine patients died. Age and GCS were identified as eNOSE-related mortality risk factors.

Conclusion: eNOSE frequently shows an acute etiology with several associated semiologies. Phenytoin shows the higher effectiveness in eNOSE management, even if lacosamide, valproate and levetiracetam can represent further therapeutic options. Age and GCS represent the main risk factor of eNOSE-associated mortality.

Disclosure: Nothing to disclose.

EPR-313 | Status epilepticus in elderly: An Italian multicenter, retrospective, real-world study

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Background and Aims: Status Epilepticus (SE) is a neurological emergency with a mortality risk around 20%. SE onset can be observed in all ages, including elderly. Clinical hallmarks as well as the therapeutic approaches of SE in elderly have not been exhaustively explored in the current literature
Methods: in this retrospective, multi-center, real-world study, patients aged >75 have been selected from two third-level epilepsy centers between 2011 and 2023. Demographics, clinical as well as SE four axis characteristics (i.e., age, semiology, etiology and EEG correlates) and therapeutic intervention were collected. GCS, STESS, EMSE and CARING scales were evaluated as outcome predictors
Results: 87 patients (age: 83 ±6, 28 male) were included. Non-convulsive SE with acute etiology was mainly described. Patients were treated with 2.7 ±1.5 drugs. First-line treatment consisted of diazepam (mean dose: 10.4 ±3.3 mg) in most of patients followed by levetiracetam (mean dose: 1815.8 ±931.1 mg). Among the ASM, levetiracetam, valproic acid, phenytoin and lacosamide were mostly administered. Thirty-three patients developed a refractory SE and 32 patients died for SE. Compared to survivors, patients who died for SE showed an increased prevalence of cardiological comorbidities ($p=0.03$). Refractoriness was not a predictor of mortality ($r=0.21$). STESS ($p=0.002$), EMSE ($p=0.01$) and CARING ($p=0.01$) scales resulted as good outcome predictors tools
Conclusion: SE is associated with a great mortality in elderly. Treatment strategies generally consist of benzodiazepine and ASM. Anesthetics are less employed. Commonly used prognostic scales have a good reliability. CARING scale may be employed in elderly patients as outcome predictor tool.
Disclosure: Nothing to disclose.

EPR-314 | Markers of oxidative stress in patients with drug-resistant and drug-sensitive focal epilepsy

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Background and Aims: Epilepsy affects over 70 million individuals globally, thus representing a prevalent neurological disorder. Current anti-seizure medications, while symptomatically effective, lack preventive efficacy against epileptogenesis. Approximately 30% of patients develop pharmacoresistance, wherein poorly understood mechanisms thwart therapy. Recent research highlights neuroinflammation and oxidative stress as pivotal in epileptogenesis and pharmacoresistance. This study explores the role of oxidative stress in epilepsy, aiming to unravel its mechanisms, assess drug resistance, and consider therapeutic implications.
Methods: A cohort of 100 focal epilepsy patients was analyzed, stratified by therapy response and epileptogenic focus. Plasma levels of oxidative stress biomarkers (AOPP, FRAP, thiols) were quantified and compared with 100 age- and gender-matched healthy controls.
Results: Patients displayed significantly elevated AOPP ($p<0.001$) and reduced thiols ($p<0.001$) compared to controls, while differences in FRAP were nonsignificant ($p>0.05$). Multivariate analysis confirmed group significance for AOPP and thiols, irrespective of age and gender. Additionally, drug-resistant patients exhibited lower thiols levels than drug-sensitive subjects ($p=0.039$) after adjusting for confounding variables. Thiols also showed lower levels in temporal epilepsy compared to extratemporal epilepsy, regardless of age or gender ($p=0.005$). Lastly, therapy sensitivity and focal epilepsy type, simultaneously considered and normalized by age and gender, showed a significant and independent impact on thiols levels ($p=0.026$ and $p=0.029$, respectively).
Conclusion: Our findings highlight the pivotal role of oxidative stress in epileptogenesis and drug resistance. The observed antioxidant capacity decrease, especially in resistant cases and temporal lobe epilepsy, suggests potential therapeutic avenues. Ongoing research may refine early detection and personalized interventions for improved patient outcomes.
Disclosure: Nothing to disclose.

EPR-315 | Descriptive analysis of prehospital seizure management protocols – We need standardized guidelines

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Background and Aims: No common European clinical practice guidelines on prehospital seizure management exists. Today most patients are transported to hospital for seizure treatment with great variation in which prehospital treatment is provided. Only 33% of all SE patients receive the recommended benzodiazepine as first anti-seizure medication (ASM). The specialist healthcare in Norway is organized into four Regional Health Authorities, comprising 18 local Emergency Medical Services (EMS). Patients with seizures constitutes a significant group in acute neurology. Norway lacks national guidelines for the prehospital management of seizures. The aim of this study is to assess the current prehospital seizure control protocols in the EMSs in Norway, and comparisons to recent evidence for acute management.

Methods: A descriptive analysis of protocols used by EMSs in Norway and compare the findings to recent evidence on prehospital treatment. Analysis will be done on drug of choice, dosages used, route of medication administered, number of additional rescue doses permitted, requirements for glucose testing prior to medication and requirement for registration of type of seizures and seizure duration.
Results: We identified 18 local protocols for seizure management in the Norwegian ambulance service. The protocols vary in terms of medication of choice, administration method, dosage, recommendation regarding first- and second-line therapy choices.
Conclusion: There are disparities in the prehospital seizure management protocols within the Norwegian healthcare system, a system comparable to other European countries. To shorten time to seizure control we should agree on standardized guidelines for prehospital treatment.
Disclosure: Nothing to disclose.

Pain

EPR-316 | Brain imaging predictors of pain catastrophizing in chronic pain

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Background and Aims: The chronic pain development is associated with maladaptive cognitive and emotional disorders, the basis of which can be the pain catastrophizing. We hypothesize that in addition to lifestyle, comorbidities and others, there are structural changes in the brain that contribute to pain catastrophizing. Objective: to study cognitive and emotional components of pain catastrophizing and its predisposing MRI morphometric features in patients with chronic pain
Methods: 28 patients with chronic primary and secondary musculoskeletal pain were tested using the Four-Dimensional Symptom Questionnaire (4DSQ), MoCAtest, the Visual Analogue Scale (VAS) and the Pain Catastrophizing Scale (PCS). Additionally to standardized MRI morphometry, we manually segmented the periaqueductal grey (PAG) with an assessment of its signal intensity.
Results: 15 patients with total PCS score above 35 were included in the first group, and 13 patients with a score below 25 comprised the second group. Group 1 had a more pronounced pain intensity and a higher score on the 4DSQ, both total and on all subscales, compared to Group 2. Despite the lack of differences in the MoCA total, attention and recall were more impaired in the 1st group. MRI morphometry identified an increase in volume of the fronto-limbic circuit structures as well as PAG density in the first group (Table 1).

TABLE 1: Comparative assessment of patients of the first and second groups.

Parameters	1st Group n = 15	2nd Group n = 13
	Median (IQR)	
Age, years	49 (44 – 56)	50 (44 – 54)
Men / Women	9/6	7/6
Disease duration (months)	19 (10 – 28)	22 (12 – 26)
Visual Analogue Scale	7 (6 – 8)	4 (4 – 6) *
MoCA total	27 (26 – 29)	28 (27 -30)*
Attention	4 (3 – 5)	6 (5 – 6) *
Recall	3 (3 – 4)	5 (4 – 5) *
4DSQ total	75 (66 – 88)	40 (33 – 51) *
Distress	27 (20 – 34)	20 (16 – 26) *
Depression	8 (6 – 11)	4 (3 – 7) *
Anxiety	11 (6 – 13)	6 (5 – 9) *
Somatization	28 (24 – 30)	13 (10 – 18) *
Pain Catastrophizing Scale total	41 (37 - 48)	20 (17 – 23) *
MRI morphometry		
Medial orbitofrontal cortex	5768 (5567 – 5985)	5415 (5230 – 5453) *
Anterior cingulate cortex	980 (845 – 1047)	893 (754 – 997) *
Amygdala	1424 (1363 – 1579)	1254 (1184 – 1368) *
PAG density	73,3 (67,3 – 78,8)	62,5 (58,9 - 74,6) *

MoCA - Montreal Cognitive Assessment
* - p ≤ 0,05 - Significant differences between the 1st and 2nd group (Mann-Whitney test)

Conclusion: The Identified changes in the structures of the cortico-limbic loops with PAG density reorganization contribute to the enhance of nociceptive inputs. These changes can be considered as a preexisting pain catastrophizing marker in people with chronic pain, and should be taken into account in psychotherapeutic procedures.
Disclosure: Nothing to disclose.

EPR-317 | Contribution of the cannabinoid receptors to the antinociceptive actions of mesenchymal stem cells in neuropathic pain

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Background and Aims: Mesenchymal stem cells (MSCs) have the ability to alleviate neuropathic pain (NP) and this may be linked to cannabinoid receptors. Our objective was to investigate the impact of cannabinoid receptors on the MSC-induced antinociception in experimental peripheral NP.
Methods: We induced NP in Wistar rats through sciatic nerve injury. On the 7th day post-surgery, animals received a consistent dose of adipose tissue-derived MSCs. To explore the influence of cannabinoid receptors, we utilized selective agonists and antagonists (anandamide and AM251 for the CB1 receptor, AM1241, and AM630 for the CB2 receptor). These ligands were either added to the MSC culture or locally injected around the nerve injury area before MSCs. Additionally, we tested combinations of these ligands. The analgesic effect of MSCs was evaluated over a 90-day period.
Results: Anandamide, when added to the culture of cells, enhances their ability to alleviate pain. Stimulation of CB2 receptors on MSC has a weaker impact on pain relief. Blockade of CB1 receptors

weakens the analgesic effect. Surprisingly, it completely disables the alleviation of thermal hyperalgesia when anandamide is injected before MSCs. This fact underscores the critical role of CB1 receptors in this process. A similar trend was observed when a combination of locally injected AM1241 and MSCs preincubated with AM630 was used. When a CB1 or CB2 receptor antagonist was injected locally, and then MSCs preincubated with agonists were transplanted, the analgesic effect gradually declined.

Conclusion: Obtained data suggests that the therapeutic impact of MSCs on pain relief is contingent upon cannabinoid receptor activity.

Disclosure: Nothing to disclose.

EPR-318 | The multimodal rehabilitation of complex regional pain syndrome – A nonrandomized controlled trial

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Background and Aims: To investigate whether Multimodal Rehabilitation Program (MRP) affects the change in visual-spatial abilities, especially attention, information processing speed and visual-spatial learning, severity of depression, and coping with pain strategies.

Methods: The study was conducted, with a 4-week rehabilitation program that included: individual physiotherapy, manual and physical therapy, and psychological intervention such as psychoeducation, relaxation, and Graded Motor Imagery therapy. The study was a 2-arm parallel: twenty CRPS participants with MRP intervention and twenty healthy control group matched to the CRPS group according to demographic variables. Before and after, the MRP participants in the CRPS group had visual-spatial, attention abilities, severity of depression, and pain-coping strategy assessment. The healthy control group had the same assessment without intervention before two measurements.

Results: In the post-test compared to the pre-test, the participants with CRPS obtained a significantly high score in visual-spatial learning ($p < 0.01$) and visual information processing speed ($p = 0.01$). They made significantly fewer omission types of mistakes in visual working memory ($p = 0.01$). After MRP compared to the pre-test, the CRPS participants declared a decrease in the severity of depression ($p = 0.04$) and more often used task-oriented coping with pain strategy than before the rehabilitation program ($p = 0.02$).

Conclusion: After a 4-week MRP, the following outcomes were obtained: an increase in visual-spatial learning, visual information processing speed, a decrease in severity of depression and a change in the pain-coping strategies – which became more adaptive.

Disclosure: Nothing to disclose.

EPR-319 | Sensory phenotyping in trigeminal neuralgia

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Background and Aims: Trigeminal neuralgia (TN) is characterized by recurrent paroxysmal episodes of unilateral facial pain in the distribution of one or more branches of the fifth cranial nerve. Beside paroxysmal pain, about 50% of patients experience a concomitant continuous pain, which may be underlied by distinct pathogenetic mechanisms. The aim of the present study is to investigate sensory phenotypes characterizing the presence of concomitant continuous pain in TN.

Methods: The main inclusion criterion was a definite diagnosis of primary TN according to ICHD-3. Each patient underwent 3T MRI scans with sequences dedicated to the study of neurovascular compression, and Quantitative Sensory Testing examination according to the German Research Network on Neuropathic Pain 3 protocol, carried out on both sides of the face.

Results: We enrolled 52 patients with definite TN, including 29 patients (56%) with concomitant continuous pain and 23 with purely paroxysmal pain (44%). All QST parameters had normal mean *Z*-scores values on both sides of the face. CDT was significantly lower in the affected side ($p = 0.02$) in the group of patients with concomitant continuos pain. The correlation analysis between the volume of the affected root and WUR showed a significant negative correlation ($p = 0.01$).

Conclusion: Our findings suggest that concomitant continuous pain in TN may be related to small nerve fibers loss, possibly triggering abnormal activity in denervated trigeminal second-order neurons.

Disclosure: Nothing to disclose.

EPR-320 | Effects of non-pharmacological and non-invasive interventions on chronic deafferentation pain: A meta-analysis

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Background and Aims: Deafferentation pain (DP), resulting from damage to the peripheral nervous system, poses a clinical challenge. Pharmacological and invasive approaches often fall short, leading to exploration of alternative therapies like mirror therapy and sensory discrimination training. However, existing studies assess interventions separately for conditions like brachial plexus avulsion (BPA), spinal cord injury (SCI), amputation, or complex regional pain syndrome type II (CRPS II), despite similar pain descriptions. Previous reviews focused on single therapies, lacking comparisons between interventions. This meta-analysis evaluates non-pharmacological,

non-invasive interventions for DP to enhance understanding and guide the development of effective interventions.

Methods: In June 2023, MEDLINE, Web Of Science, PsycINFO, Cochrane CENTRAL, and PubMed were searched for controlled studies evaluating the effects of non-pharmacological and non-invasive interventions on pain intensities in adult patients with chronic DP after SCI, amputation, BPA, or CRPS II. Two reviewers independently screened studies, and network meta-analysis was performed to compare intervention effects. The full protocol is available on PROSPERO (CRD42023431497).

Results: 27 studies evaluating 24 interventions reached qualitative synthesis. Repetitive transcranial magnetic stimulation showed the highest effects for both SCI and amputees. Heterogeneity among studies was high, and certainty of evidence was low. No studies on CRPS II and only 2 studies on BPA evaluated the interventions of interest.

Conclusion: Similar underlying pain mechanisms in considered conditions suggest that interventions promising for DP after SCI and amputation may apply to BPA and CRPS II, where corresponding therapies are yet unexplored. However, higher methodological quality studies are needed for all four conditions.

Disclosure: Nothing to disclose.

EPR-321 | Multicolumn spinal cord stimulation for chronic back and leg pain in patients with failed back surgery syndrome

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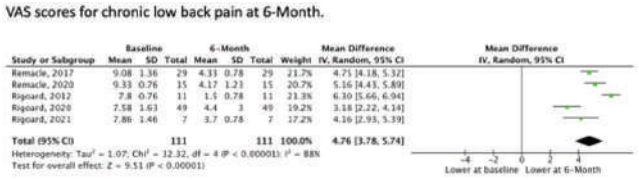
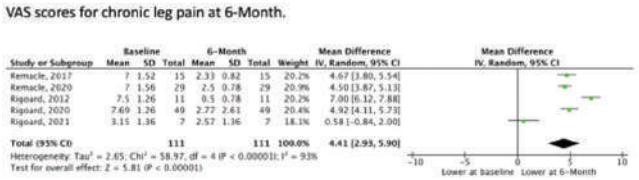
Background and Aims: Failed Back Surgery Syndrome (FBSS) is a challenging condition characterized by persistent chronic low back pain and leg pain despite surgical interventions. Multicolumn spinal cord stimulation (m-SCS) has emerged as a promising therapeutic approach for managing FBSS-associated pain.

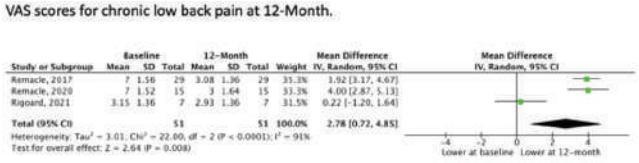
Methods: We aim to analysis the efficacy of m-SCS in alleviating chronic back and leg pain in patients with FBSS. A comprehensive search of electronic databases (PubMed, Web of Science, Scopus, Cochrane Library) was conducted up to October 25th, 2023.

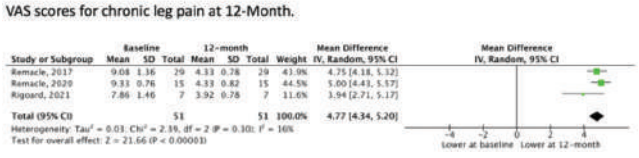
Results: We included 8 articles with 271 patients from 21-center. At 6 months, there were a statistically and clinically significant reduction in the VAS scores for the low back pain (MD, 4.76; 95% CI, 3.78–5.74) and leg pain (MD, 4.41; 95% CI, 2.93–5.90) versus the baseline. Also, at 12 months, there were a statistically and clinically significant reduction in the VAS scores for the low back pain (MD, 4.77; 95% CI, 4.34–5.20) and leg pain (MD, 2.78; 95% CI, 0.72–4.85) versus the baseline.Our meta-analysis demonstrated a significant reduction in both back and leg pain scores among FBSS patients treated with m-SCS compared to the baseline pain scores ($p < 0.05$). Subgroup analyses revealed consistent efficacy across different stimulation parameters and patient demographics. Additionally, improvements in quality-of-life measures and functional outcomes were observed in the m-SCS intervention group.





VAS scores for chronic low back pain and leg pain at 6-month.





VAS scores for chronic low back pain and leg pain at 12-month.

Conclusion: The findings underscore the potential of m-SCS as a valuable therapeutic option in the multidisciplinary approach to FBSS, offering sustained pain relief and improved functional outcomes.

Disclosure: Nothing to disclose.

EPR-322 | Novel electrophysiological and ultrasound biomarkers for trigger point assessment

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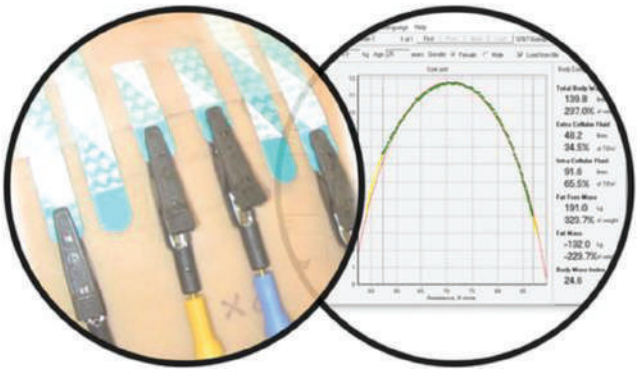
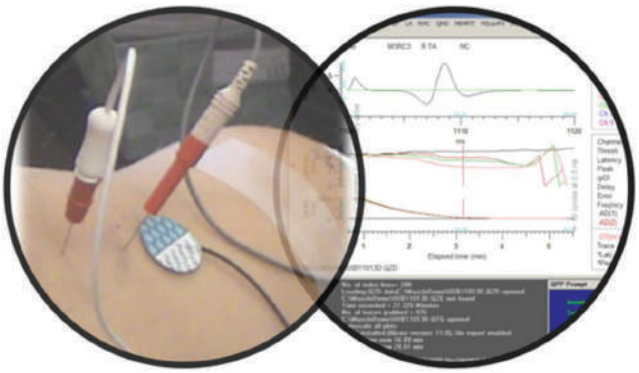
Background and Aims: Although TrPs affect millions of individuals, we do not understand the mechanisms underlying the course of this

condition. Furthermore, most pain studies rely on subjective patient scores as the primary outcome. To address these gaps, we aim to employ three entirely objective and quantitative assessment methodologies to assess these entities. Here we present results from our first group of healthy subjects whose data have been analyzed for repeatability.

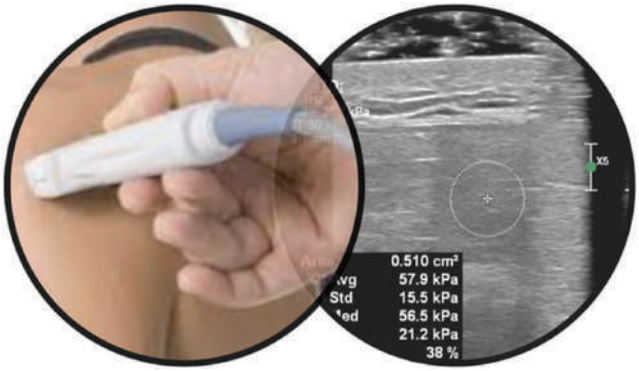
Methods: We performed testing of the three modalities on the right trapezius muscle in healthy participants during two separate visits. Electrical impedance myography (EIM) noninvasively evaluates muscle properties using a painless electrical current. Quantitative muscle ultrasound images translates the brightness of muscle scans into a numerical value, the grayscale level. Myofiber excitability testing (MET) quantifies changes in muscle fiber conduction properties in response to various electrical conditioning stimuli. Intra-class coefficients (ICCs), Bland-Altman analysis and mean percent difference were calculated as a reflection of reliability for each of these modalities.



Electrical impedance myography.



Myofiber excitability test.



Quantitative muscle ultrasound.

Results: Sixteen healthy participants (10 men, 6 women) with mean age ± SD 52.6 ±16.7 years were enrolled. There was a strong intra-class correlation for the EIM phase angle values between first and second ICC = 0.96, and a mean percent difference of 9.35 ±8.89%. Reproducibility of grayscale also demonstrated positive correlation between the visits, ICC = 0.92, with mean percent difference 4.47 ±3.78%, as did MET with mean percent difference 3.47 ±0.37%.

Conclusion: The initial findings indicate the promising use of EIM, grayscale, and MET as potential diagnostic biomarkers for TrPs.

Disclosure: Nothing to disclose.

Movement disorders 5

EPR-323 | Adaptive versus conventional deep brain stimulation in chronically stimulated Parkinson's disease patients

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Background and Aims: Adaptive deep brain stimulation (aDBS) breaks important new ground for patient-personalized neuromodulation treatment, but still needs long-term clinical validation.

Methods: We report an individual comparison between aDBS and conventional DBS (cDBS) of the subthalamic nucleus in 14 patients with Parkinson's disease (PD). Clinical assessment was performed with the UPDRS-III and UDysRS scales and a 3-day diary. Patients were monitored for two weeks in each aDBS or cDBS mode in random order with stimulation delivered with the AlphaDBS device (Newronika SpA, Milan, Italy).

Results: All patients showed significant clinical benefit that was comparable between the two stimulation modes (UPDRS-III % improvement med-off/stim-off to med-on/stim-on cDBS vs. aDBS: 0.66 ±0.15 vs. 0.61 ±0.17; Good-On-Time cDBS vs. aDBS: 11.7 ±4.3 vs. 13.1 ±4.9). Notably, dyskinesias negatively correlated with aDBS-induced UPDRS-III improvement, implying that patients with mild dyskinesias have a greater UPDRS-III improvement (Spearman's ρ: −0.771, $p=0.006$). On the contrary, cDBS-induced UPDRS-III improvement did not correlate with dyskinesias (Spearman's ρ: −0.385, $p=0.282$). In 50% of the patients, the "on time" without dyskinesias in aDBS was >1SD of the average "on-time" without dyskinesia with cDBS. In the end, 90% of patients chose (blinded) preferred aDBS.

Conclusion: We showed that aDBS and cDBS result in similar improvement of PD-related symptoms, with a greater benefit for aDBS in patients with mild dyskinesias. In half of the patients, aDBS provided a greater "on-time" than cDBS, and most patients preferred the adaptive mode.

Disclosure: AP, SM, CC, MA, LK, LR and IUI are funders, employees, or consultant of Newronika SpA. RE, LB, EP, ML, and ARB acted as PI of clinical studies of Newronika SpA. Clinical trial NCT04681534.

EPR-324 | Plasma neurofilament light chain level in isolated REM sleep behavior disorders

A. Calculli[2]; D. Di Martino[2]; G. Ongari[1]; S. Gagliardi[1]; P. Grillo[2]; E. Capriglia[2]; C. Fazio[2]; D. Comolli[2]; M. Terzaghi[1]; A. Pisani[1]

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Background and Aims: Rapid-Eye-Movement (REM) sleep behavior disorder (RBD) is recognized as a precursor to α-synucleinopathies, encompassing Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). The isolated RBD (iRBD) population offers an ideal cohort for detecting neurodegenerative biomarkers. This study explores the role of neurofilament light chain proteins (NfLs) in iRBD, PD and MSA.

Methods: Plasma-NfL levels in iRBD, PD, MSA patients, and healthy controls (HC) were assessed using Ella. Statistical analysis employed PRISM9, with data comparisons via the Mann–Whitney and Spearman test.

Results: Plasma-NfL levels were measured in 69 subjects (PD:19, M:14 F:5; iRBD:19, M:18 F:1; MSA:12, M:5 F:7; HC:19, M:14 F:5). Results revealed elevated NfL levels in PD and MSA compared to HC (PD vs. HC $p=0.0005$; MSA vs. HC $p<0.0001$). Notably, iRBD exhibited increased NfL levels compared to HC (iRBD vs. HC $p=0.0392$) and lower than MSA (MSA vs. iRBD $p=0.0472$). No significant difference existed between PD and iRBD ($p=0.8007$). Correlation analyses with continuous variables (UPDRS-III and MMSE) showed no significance. In iRBD, comparative analysis based on hyposmia, constipation, or orthostatic hypotension were not significant.

Conclusion: The findings suggest axonal damage in iRBD, indicating an ongoing neurodegenerative process. Similar NfL levels between PD and iRBD suggest stability during phenoconversion to PD. Elevated NfL levels in iRBD with orthostatic hypotension hint at a potential link to MSA ($p=0.0620$), warranting confirmation with a larger sample size. Plasma-NfLs emerge as promising biomarkers for irreversible CNS damage when combined with clinical and instrumental data.

Disclosure: Nothing to disclose.

EPR-325 | Occipital atrophy as marker for phenoconversion in patients with isolated REM-sleep behaviour disorder

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Background and Aims: The cuneus and precuneus are considered important for cognition. In patients with isolated rapid-eye-movement behaviour disorder (iRBD), voxel-based morphometry (VBM) studies report structural changes in these structures, however, not consistently. Here we examined atrophy in the cuneus and precuneus of cognitively normal iRBD patients and tested if this can serve as marker of future phenoconversion to Parkinsonism.

Methods: Using VBM, we analysed magnetic resonance images of 20 iRBD patients and compared them to 36 healthy controls (HC). The iRBD patients had a mean Montreal Cognitive Assessment score of 25.5 (SD 2.46) and a mean Mini Mental State Examination score of 28.2 (SD 1.53). The patients were followed for 8 years ($N=17$). Time-to-event analysis was performed using cox regression.

Results: Eight iRBD patients converted during follow-up; four to dementia with Lewy bodies and four to Parkinson's. VBM showed reduced grey matter volume (GMV) in the cuneus and precuneus of the patients compared to HC. Region of interest analysis confirmed significant reduction in GMV in both the left and right cuneus and precuneus in the patients. Patients with GMV at, or below, the group median in the right cuneus had higher hazards of 13.0 (CI: 1.53–110)

for phenoconversion. Lower right cuneus GMV correlated with shorter time to conversion ($p=0.01$). Lower GMV in left and right precuneus trended to increased hazards at 4.20 (CI: 0.80–22.2) and 4.44 (CI: 0.85–23.2) respectively.

Conclusion: Our findings suggest that cuneus GMV can be used as markers of future phenoconversion in iRBD patients even before onset of cognitive symptoms.

Disclosure: Nothing to disclose.

EPR-326 | Cognitive fluctuations in Parkinson's disease patients without dementia

C. Gasca-Salas[1]; S. Obika[1]; R. Rodríguez-Rojas[1]; B. Fernández-Rodríguez[1]; C. Trompeta[1]; P. Guida[1]; G. Goggani[1]; L. Vela[2]
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Background and Aims: Cognitive fluctuations (CF) are spontaneous alterations in cognition, attention, and arousal leading to episodes of perturbed flow of ideas or daytime drowsiness, considered core clinical features of dementia with Lewy bodies and associated with Parkinson's disease (PD) dementia. However, their characteristics remain unexplored in non-demented PD patients. We aimed to identify the frequency of CF, their relationship with neuropsychological tests, and their occurrence in non-demented PD patients who later progress to a worse cognitive state.

Methods: Fifty-one patients underwent clinical and neuropsychological assessments. Administering the CF Scale, a positive answer in three or more of the four items indicated good sensitivity. The Kendall correlation test assessed the relationship between cognitive fluctuations, cognitive tests, and amyloid brain burden (PET). Thirty-eight patients were followed for three years to detect conversion to a more severe cognitive state.

Results: Thirty-two patients scored 0 (62.7%, no positive answers), 11 (21.6%) scored one, and 4 (7.8%) scored two and three points, respectively, on the cognitive fluctuations questionnaire. An association was found between CF and tests of executive function, visual memory, and total amyloid after controlling for the motor-MDS-UPDRS score (confounder). The conversion rate to PD-MCI or dementia at follow-up was higher in patients scoring ≥3 compared to those who did not (100% vs. 23.5%).

Conclusion: Although uncommon in PD patients with dementia, CF, when present, signal an association with progression to a worse cognitive state. This association is reinforced by correlations with lower scores in executive and memory function tests, along with a potential connection with amyloid pathology.

Disclosure: Nothing to disclose.

EPR-327 | TRISTAN – retrospective real world data acquisition of Wilson disease patients with neurological symptoms in Germany

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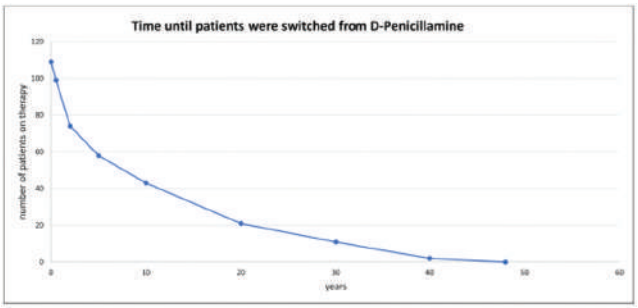
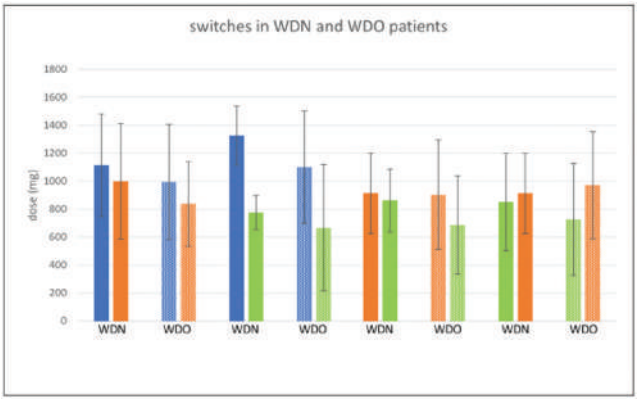
Background and Aims: While D-penicillamine (D-Pen) is recommended as first-line chelating agent for Wilson Disease (WD), administration of trientine (TETA) is a valuable alternative for patients who are intolerant to D-Pen. Since just limited data are available on treatment transitions when switching from D-Pen to TETA and between Trientine formulations, we conducted a retrospective analysis retrieved from 6 specialized WD centres in Germany.

Methods: The study incorporated anonymized data from WD patients receiving TETA with at least one documented follow-up between 2012 and 2021. Information on clinical manifestation and treatment regimen were captured via standardized questionnaires. Patients with an initial neurological affection (WDN) were compared with other types of primary manifestation (WDO).

Results: Our study encompassed data from 143 patients (75 females) with a mean age of 40 (5–85) years. WDN patients ($n=39$) were older at diagnosis than WDO patients (25.0 vs. 14.5). Most patients (88%) underwent 2–4 therapy lines. 32% of patients switched from D-Pen to TETA within the first 2 years, 50% after 7 years of therapy. The conversion factors in WDN and WDO patients were 0.90 and 0.84 for D-Pen to TETA dihydrochloride (TETA-2HCl), 0.59 and 0.60 for D-Pen to TETA-tetrahydrochloride (TETA-4HCl), 0.95 and 0.76 for TETA-2HCl to TETA-4HCl and 1.07 and 1.33 for TETA-4HCl to TETA-2HCl, respectively.



Time until switch from D-Pen.



Conversion factors when switching between treatments in WDN and WDO patients.

Conclusion: Our results emphasize the significance of addressing late-onset complications during D-Pen therapy. Furthermore, this data gives an interesting insight into real-life dosing of chelators and thus might support physicians in future therapy.

Disclosure: This work has been funded by Univar Solutions B.V.

EPR-328 | Comparative study of focused ultrasound unilateral thalamotomy and subthalamotomy for tremor-dominant Parkinson disease

E. Natera-Villalba[1]; E. Natera-Villalba[4]; S. Paschen[2]; S. Paschen[4]; J. Pineda-Pardo[1]; M. del Álamo[1]; R. Rodríguez-Rojas[1]; G. Deuschl[1]; J. Obeso[1]; A. Helmers[3]; A. Helmers[5]; R. Martínez-Fernández[1]; R. Martínez-Fernández[5]

[1]Centro Integral de Neurociencias AC (CINAC), HM Universitario Puerta del Sur, Madrid, Spain; [2]Department of Neurology, University Hospital Schleswig-Holstein, Christian-Albrechts-University, Kiel, Germany; [3]Department of Neurosurgery, University Hospital Schleswig-Holstein, Christian-Albrechts-University, Kiel, Germany; [4]Share first co-author; [5]Share last co-author

Background and Aims: Focused ultrasound thalamotomy (FUS-Vim) is effective in treating Parkinson's disease (PD) tremor. FUS subthalamotomy (FUS-STN) improves PDcardinal features, including tremor.We aimed to compare efficacy in tremor control between FUS-Vim/FUS-STN in tremor-dominant PD (TDPD).

Methods: Retrospective, two-centre study. Medical-refractory TDPD-patients who underwent unilateral FUS-Vim/FUS-STN (2015–2022) were included. TDPD was defined by score = />2 for postural and/or resting tremor on treated-side (t.s.). Data regarding motor status (MDS-UPDRS-III), dopaminergic treatment (LEDD), adverse events were collected at baseline, 4- and12-month post-FUS.

Results: 63TDPD-patients included (23FUS-Vim,40FUS-STN).At baseline, FUS-Vim-patients were older (70.8 ±9.8y [vs.] 58.6 ±8.9y, $p < 0.001$), with equivalent disease progression (6.7 ±3.8y [vs.] 6.1 ±3.4y, $p = 0.525$), t.s.tremor severity (5.6 ±2.3 [vs.] 5.8 ±1.5, $p = 0.267$), total MDS-UPDRS-III (40.3 ±10.6 [vs.] 37.9 ±9.7, $p = 0.37$), and LEDD. (643.5 + 455.7 mg [vs.] 674.2 + 266.3 mg). FUS-STN-patients were more bradykinetic ($p < 0.001$), with more severe t.s. motor status (16.9 ±2.9 [vs.] 18.9 ±3.4, $p = 0.018$). Both groups presented significant improvement in t.s. tremor at 4 and12 month ($p < 0.001$ both, compared to baseline). Whereas benefit was equivalent at 4 months between groups ($p = 0.258$), FUS-Vim improved t.s. tremor less thanFUS-STN at12 months (mean-change 28.2 ±56.7% [vs.] 74.6 ±33.1%, $p < 0.001$), with tremor score in FUS-Vim higher than FUS-STN (3.3 ±2.7 [vs.] 1.5 ±1.8, $p = 0.008$). T.s. rigidity improved at 4 and12 months compared to baseline in both ($p < 0.001$all analyses) with no between-group differences at any timepoint. Improvement in t.s. bradykinesia was observed for both groups at12 months ($p = 0.006$, $p < 0.001$), with higher benefit for FUS-STN (mean-change 14.3 ±71.4% [vs.] 43.1 ±26.9%, $p = 0.025$). At 4 months, FUS-STN group LEDD was reduced compared to FUS-Vim-group ($p = 0.026$), not sustained at12 months ($p = 1.0$). Weight-gain, dyskinesias were more frequent post-FUS-STN ($p = 0.037$, $p = 0.004$); sensory disturbances occurred post-FUS-Vim ($p = 0.004$).Most were mild and resolved by12 months.

Conclusion: InTDPD patients, FUS-STN provides more sustained tremor control and better effect over bradykinesia than FUS-Vim. Adverse events between targets differ in nature but are mostly mild and transient.

Disclosure: Nothing to disclose.

EPR-329 | Advanced DBS programming strategies for unresponsive freezing of gait in real clinical practice

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Background and Aims: Freezing of gait (FOG) unresponsive to both dopaminergic medication and conventional deep brain stimulation of the subthalamic nucleus (STN-DBS) represents one of the most disabling and unresolved problems of patients with advanced Parkinson's disease (PD). However, existing research indicates that the use of alternative stimulation strategies, such as the use of low-frequency STN-DBS and the stimulation of the substantia nigra pars reticulata (SNr) might provide either a transitory or sustained benefit.

Methods: A retrospective analysis of the real clinical practice in our center regarding the use, safety, and efficacy of two distinct advanced programming strategies for treating refractory FOG. Our treatment algorithm for refractory FOG consisted of two sequential steps: use of high-amplitude low-frequency STN-DBS and use of combined high-frequency STN-DBS with low-frequency SNr-DBS.

Results: 32 PD patients who had undergone bilateral STN-DBS between 2007 and 31 January 2020 (the start of the COVID-19 pandemic) and had developed FOG during this follow-up period were identified. 13 (40.6%) of them developed FOG refractory to conventional DBS. 12 of them were then treated with low-frequency DBS with 5 exhibiting clinical worsening, 3 a transitory (163 ±114 days ~5.4 months) and 4 a sustained improvement in FOG (2196 ±312 days ~6 years). Combined high-frequency STN-DBS with low-frequency SNr-DBS was used in 8 patients with uncontrolled FOG, 2 showed a transitory improvement (55.5 ±35.5 days) and 6 sustained improvements for the time being (690 ±424 days).
Conclusion: Low-frequency STN-DBS and combined high-frequency STN-DBS with low-frequency SNr-DBS seem to be helpful in some patients with refractory FOG.
Disclosure: Nothing to disclose.

EPR-330 | **Abstract withdrawn**

Neuroimaging

EPR-331 | Dopaminergic deficits along the spectrum of Alzheimer's disease

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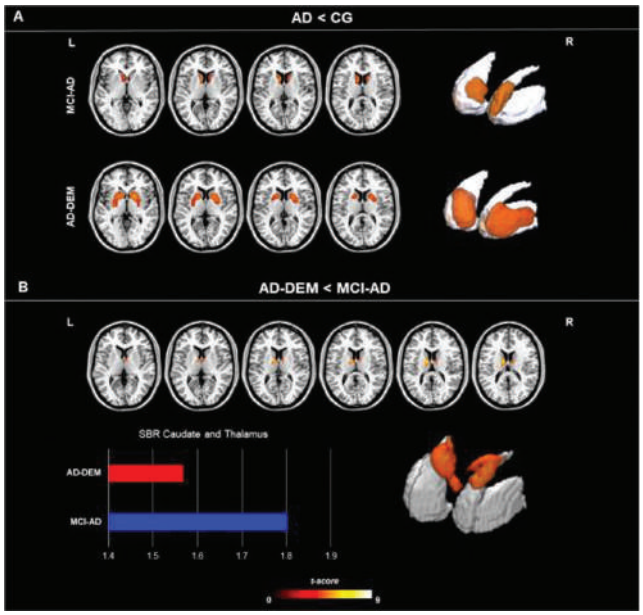
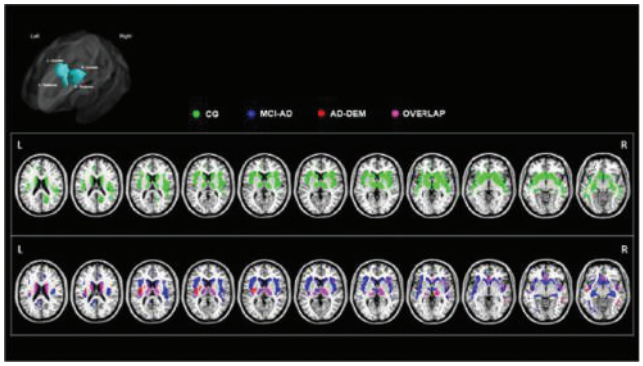
Background and Aims: Both post-mortem and in vivo data argue for dopamine dysfunction in patients with Alzheimer's disease (AD). However, the timing and regional progression of dopaminergic systems alterations in AD are still debated. Aim of the study was to investigate in vivo the pattern of dopaminergic changes and connectivity using DAT-SPECT imaging in patients across the AD spectrum.
Methods: Fifty-nine A+T+N+ AD patients ($n=21$ MCI-AD; $n=38$ AD-DEM) and $n=45$ age and sex-matched controls (CG) entered the study and underwent 123I-FP-CIT dopaminergic imaging. The occipital binding was used as reference region to obtain single-subject binding in different brain regions. Between-groups differences in 123I-FP-CIT binding in both mesolimbic and nigrostriatal dopaminergic pathways were assessed using an ANCOVA test-adjusting for the effect of center of imaging acquisition, age, and sex. Regions resulting from the voxel-wise direct comparison between MCI-AD and AD-DEM were considered as a seed of interest for a voxel-wise interregional correlation analysis.
Results: Both MCI-AD and AD-DEM patients showed dopaminergic depletion within the basal ganglia, whereas cortico-limbic regions (namely hippocampus, amygdala, anterior and middle cingulate, frontal cortex and thalamus) resulted impaired only in the dementia phase. The brain voxel-wise interregional correlation analysis showed a progressive pattern of disruption of caudate/thalamus dopaminergic connectivity to hippocampus and amygdala from MCI-AD to AD-DEM stages.



Voxel-wise 123I-FP-CIT binding differences between groups.



Seed-based connectivity results.
Conclusion: This study indicates basal ganglia dopaminergic alterations and connectivity disruption in the nigrostriatal and mesolimbic

systems already in early stage AD, extending to several cortico-limbic regions in dementia phases.

Disclosure: Nothing to disclose.

EPR-332 | **Abstract withdrawn**

EPR-333 | **The association of imaging biomarkers for tau and neurodegeneration in progressive supranuclear palsy**

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Background and Aims: In progressive supranuclear palsy (PSP), subcortical tau can be assessed with the tracer [18F]PI-2620 and cortical neurodegeneration can be measured using cerebral perfusion. Our aim was to examine the relationship of tau and neurodegeneration across PSP categories.

Methods: In progressive supranuclear palsy (PSP), subcortical tau can be assessed with the tracer [18F]PI-2620 and cortical neurodegeneration can be measured using cerebral perfusion. Our aim was to examine the relationship of tau and neurodegeneration across PSP categories.

Results: We found no significant correlation between individual expression of the respective patterns (tau vs. hypoperfusion) across the group (Figure 1B). However, hypoperfusion in prefrontal clusters was associated with tau deposition in all patients ($r = -0.34$, $p = 0.02$) (Figure 1C) and stronger in PSP-RS ($r = -0.63$, $p = 0.005$) (Figure 1D). The multiple regression analysis revealed that tau in GPI was associated with hypoperfusion in the left frontal pole in the complete group and in the left superior frontal gyrus in the PSP-RS group ($p < 0.001$ uncorrected).

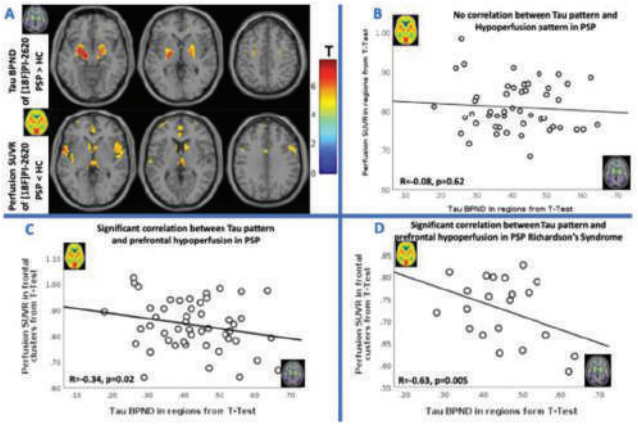

FIGURE 1: The association between pathological tau binding and cerebral hypoperfusion in PSP: A: Two-sample *t*-tests for tau binding potential (upper row) and perfusion SUVR (lower row) between patients and controls for the complete group. Contrasts: Tau.

Conclusion: Subcortical tau is associated with prefrontal hypoperfusion, indicating a restricted remote connection between tau and neurodegeneration. Longitudinal studies are needed to examine whether neurodegeneration follows protein depositions like in Alzheimer's disease or whether neuronal dysfunction occurs in parallel or before tau depositions.

Disclosure: H.T., M.B., H.B, M.T.B., J.C., N.F., J.G., G.H., S.K., J.L., K.M., B.N., C.P., M.R., J.-J.R., J.S., M.Z., O.S., G.N.B., report no conflicts of interests. A.D. reports the following competing interests: Research support: Siemens Healthineers, Life Molecular Imaging, GE Healthcare, AVID Radiopharmaceuticals, Sofie, Eisai, Novartis/AAA, Ariceum Therapeutics. Speaker Honorary/Advisory Boards: Siemens Healthineers, Sanofi, GE Healthcare, Biogen, Novo Nordisk, Invicro, Novartis/AAA, Bayer Vital. Stock: Siemens Healthineers, Lantheus Holding, Structured therapeutics, ImmunoGen Patents: Patent for 18F-JK-PSMA-7 (2-Alkoxy-6-[18F]Fluoronicotinoyl substituted Lys- C(O)-Glu derivatives as efficient probes for imaging of PSMA expressing tissues (Patent No.: EP3765097A1; Date of patent: Jan. 20, 2021)). T.v.E. received or receives honoraria for consulting or in advisory roles from Lundbeck Foundation, Lundbeck Pharma, Orion Pharma, GT Gain Therapeutics SA. Stocks: IBM, Microsoft, NVIDIA. A.S.: Life Molecular Imaging.

EPR-334 | High-dimensional cellular profiling of actively remyelinating lesions in multiple sclerosis

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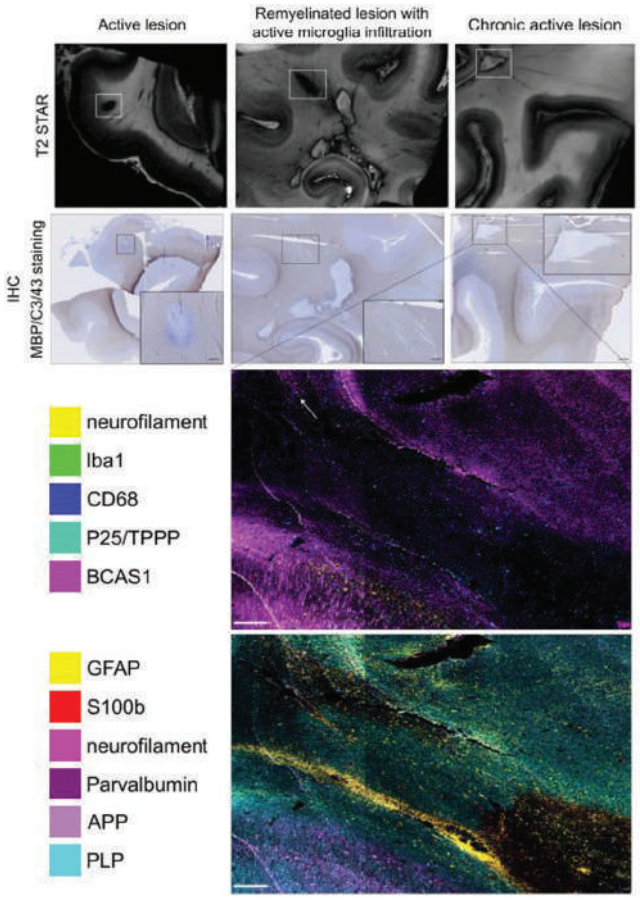
Background and Aims: We have previously shown that lesions hyperintense in quantitative susceptibility mapping (QSM) are pathologically either chronic inactive or actively remyelinating. The molecular characteristics of QSM hyperintense lesions are unknown to date.

Methods: In this project we aim at disentangling the structural and cellular composition of QSM hyperintense lesions, by 9.4T qMRI in postmortem brains, and by multiplex imaging mass cytometry (IMC). Based on QSM maps obtained at 3T, blocks containing lesions of interest were acquired with a Bruker ex vivo MRI scanner at 9.4 Tesla, and the resulting MRI measures integrated in the Multi-Omics Factor Analysis v2 statistical framework. Immunohistochemistry for MBP and CR3/43 was used for lesion classification, and the same blocks were next interrogated by IMC to understand the local cellular composition at a high-dimensional level.

Results: We studied 4 individual lesions from 3 blocks of 2 brains. We observed an increased percentage of GFAP+, S100b+ astrocytes in the demyelinated lesion core when compared to the perilesional area. Axonal content was diminished in actively remyelinating lesions. HLA-DR and CD68+ cells correlated with FLASH with TE = 3.8 ms, TI = 270 ms, TR = 1500 ms sequence intensity, suggesting that these sequences are sensitive to the myeloid inflammatory process, while T2* map MGE sequences with TI = 150 ms captured CD68neg high cellularity, suggesting that other cell types might explain this contrast.



Immunohistochemical and IMC correlate of 9.4T MRI T2 star.

Conclusion: These are preliminary results from a newly developed post-mortem high-dimensional imaging approach. We are currently expanding the single-cell profiling towards immune, astrocyte and remyelination markers.

Disclosure: Nothing.

EPR-335 | Functional MRI neurofeedback on functional connectivity and metabolic profiles in patients with visual snow syndrome

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Background and Aims: Visual snow syndrome (VSS) is a burdensome condition with persistent spurious visual phenomena. Neuronally, VSS patients show altered neuronal excitability, increased grey matter volume and functional hyperconnectivity (FC). In this double-blind, placebo-controlled randomized study, we tested if real-time

functional MRI neurofeedback (NFB) will allow patients to downregulate their lingual gyrus activity (outcome), whether this correlates with changes in FC and glutamate level, and a decrease of VSS symptoms.

Methods: In 20 patients with VSS ($\mu = 31.2$ years, 13 male, migraine $n = 9$) and 20 healthy controls. MRI was performed before and acutely after two days of NFB (lingual gyrus [$n = 10$] or gyrus rectus ([$n = 10$] sham region]).

Results: Pre-NFB hyperconnectivity was seen in patients. Five of ten patients downregulated the lingual gyrus. Hyperconnectivity was seen in the sham versus real group after NFB. Higher Puledda scores were related to higher FC. Glutamate levels were lower after NFB in the real group. Regulation success was stronger in patients with a longer persistence of visual snow and higher VSS scores. No improvement in the VSS scores across both groups and within the real NFB group—comparing pre versus post-NFB time points—was found.

Conclusion: Our results indicate that lingual gyrus based NFB minimizes hyperconnectivity and excitability. Although some severely affected patients regulated the lingual gyrus, no improvement in clinical scores was seen. Larger trials (possibly with a more extensive NFB training) are required to judge the value of lingual gyrus based NFB on VSS.

Disclosure: Nothing to disclose.

EPR-336 | Rare neurovascular compression syndromes of the brainstem: Beyond trigeminal neuralgia

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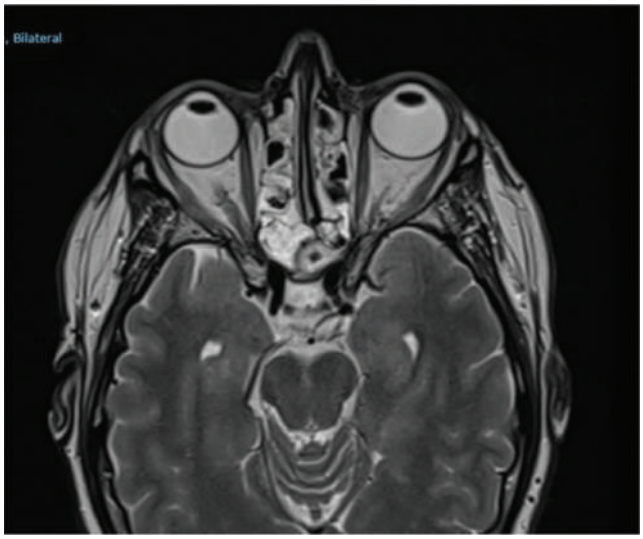
Servicio de Neurología, Complejo Hospitalario de Jaén, España

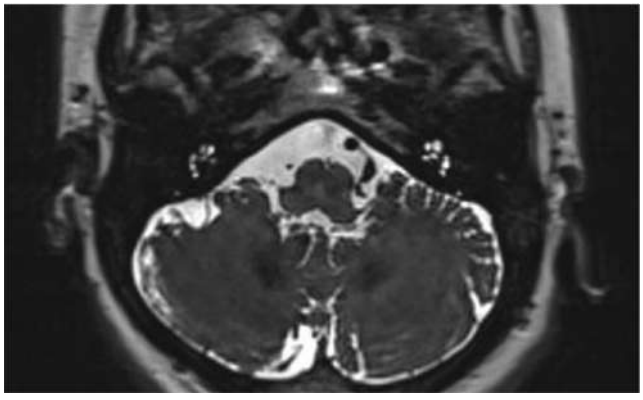
Background and Aims: Neurovascular compression syndromes (NCS) are characterized by the compression of a cranial nerve by an artery. The most common are trigeminal neuralgia and hemifacial spasm, but there are reported cases of rare NCS: glossopharyngeal neuralgia, diplopia due to oculomotor nerve (OMN) compression or vestibular paroxysmia. Magnetic Resonance Imaging (MRI) is a fundamental diagnostic tool. We present a series of 5 cases of rare NCS.

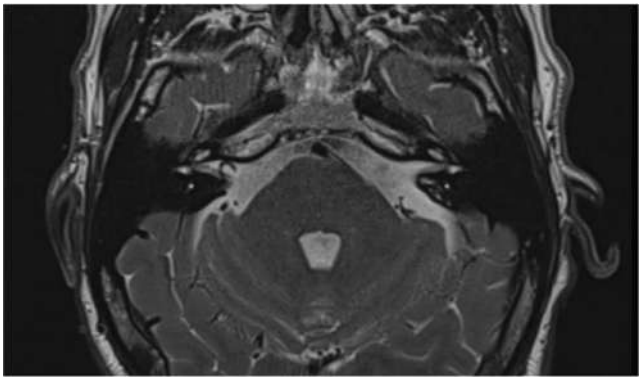
Methods: Case series of 4 males and 1 female, aged between 53 and 70 years old. Two cases of diplopia caused by the compression of the OMN by an aberrant posterior cerebral artery (PCA) and the paraophthalmic internal carotid artery (ICA), two cases of vestibular paroxysmia caused by the compression of the right vestibulocochlear nerve by the inferior cerebellar artery (ICbA) and the anterior inferior cerebellar artery (ICA), and one case of glossopharyngeal neuralgia caused by the compression of the left glossopharyngeal nerve by the posterior inferior cerebellar artery (PICA). See images.

Magnetic resonance imaging (MRI), axial view. Left posterior cerebral artery is aberrant and contacts with the left oculomotor nerve.



Magnetic resonance imaging (MRI), axial view, FIESTA sequence. Right posterior inferior cerebellar artery is in contact and displaces the root zone of the glosopharyngeal nerve.





Magnetic resonance imaging (MRI), axial view. Compression of the right vestibulocochlear nerve by the inferior cerebellar artery (ICbA) that forms a loop and penetrates in the internal auditory canal.

Results: The series presented shows a varied clinical picture of rare NCS. The physiopathology is unclear but could be shared with more frequent NCS like trigeminal neuralgia: vascular compression, demyelination, nucleus excitability and nerve modeling. Clinical characterization of rare NCS allows for early suspicion and optimal use of MRI technique to achieve early diagnosis.

Conclusion: NCS are infrequent disorders with heterogeneous clinical presentations. The mechanisms explaining why certain neurovascular conflicts cause NCS and others are clinically silent are unclear, therefore precise individualized management is lacking. Further clinical descriptions and management oriented research is needed.

Disclosure: Nothing to disclose.

EPR-337 | Brain functional connectivity and cortical neurotransmitter receptor distribution associated to psychotic symptoms in AD

M. Zavarella[1]; S. Basaia[2]; E. Canu[2]; G. Rugarli[1]; G. Cecchetti[3]; E. Spinelli[1]; F. Caso[4]; G. Magnani[4]; M. Filippi[5]; F. Agosta[1]

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Background and Aims: This study aims to explore resting state functional connectivity (RS-FC) of the CN subregions in AD with (ADps) and without (ADnops) psychotic symptoms, with a focus on the relationship between RS-FC changes and cortical neurotransmitter receptor distribution.

Methods: 68 AD patients underwent clinical and neuropsychological assessment, and MRI. Group was divided in 15 patients with untreated psychotic symptoms (ADps) and 53 ADnops. 53 age-matched controls were also selected. Seed-based RS-FC analysis was performed using CN subregions: dorsal caudate nucleus (dCN), ventral-superior CN (vsCN), and ventral-inferior CN (viCN). In patients, connectivity changes were correlated with neuropsychological performances. Spatial correlations between RS-FC changes and atlas-based nuclear imaging-derived neurotransmitter maps were investigated using JuSpace-toolbox.

Results: Both AD groups showed increased connectivity between each CN-subregions and sensorimotor areas. In both, increased dCN connectivity with sensorimotor regions negatively correlated with memory, visuospatial, and praxis performances. ADps had peculiar reduced RS-FC between dCN and right superior frontal gyrus, vsCN with dorsal and anterior cingulate gyrus bilaterally, and viCN with bilateral inferior temporal gyrus. ADnops had reduced connectivity between dCN and vsCN separately, and right operculum, and between viCN and right supracalcarine area. Regarding CN-subregions connectivity, ADps showed relationship with mu-opioid receptor, glutamate-Receptor-5, and 5HT1a distribution.

Conclusion: This study sheds light on the relevance of understanding CN connectivity and its relationship with psychotic symptoms in AD. The specific relationship between RS-FC of CN subregions and cortical neurotransmitter receptor distribution is relevant therapeutic management implications. Funding. Foundation Research on Alzheimer Disease.

Disclosure: M Zavarella, G Rugarli, EG Spinelli, F Caso, G Magnani have nothing to disclose. S Basaia receives research supports from the Italian Ministry of Health. E Canu receives research supports from the Italian Ministry of Health. G Cecchetti received speaker honoraria from Neopharmed Gentili. M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. F. Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, ARiSLA, the ERC, the EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease (France).

EPR-338 | Brain and spinal cord MRI correlates of motor impairment and vibratory sensation in patients with multiple sclerosis

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Background and Aims: Cervical spinal cord (cSC) focal lesions and volume loss significantly contribute to multiple sclerosis (MS) clinical disability, but their association with specific motor-sensory dysfunction requires further exploration. This study aimed to identify MRI

features of cSC damage associated with increased clinical disability and motor-sensory impairment in MS patients.

Methods: One hundred fifty-one MS patients and 69 age- and sex-matched healthy controls (HC) underwent brain and cSC 3T MRI acquisition and a comprehensive clinical assessment including Expanded Disability Status Scale (EDSS) score, 9-hole peg test (9-HPT), finger tapping test (FTT), timed 25-foot walk test (T25FWT), and vibration detection threshold (VDT). Random forest analyses assessed the predictive value of cSC MRI measures (T2-hyperintense lesion volume [T2-LV], total, grey matter [GM], and white matter [WM] cross-sectional areas [CSA] at C2–C3 level) for EDSS milestones (EDSS ≥ 3.0, 4.0 and 6.0), impaired pyramidal and sensory functional systems (P-FS and S-FS ≥ 2), as well as specific motor and sensory tests.

Results: Various combinations of brain and cSC MRI measures were informative predictors of EDSS milestones (out-of-bag [OOB]-area under the curve [AUC] = 0.879–0.900), VDT (OOB-R^2 = 0.194), and impairment at P-FS (OOB-AUC = 0.820), S-FS (OOB-AUC = 0.795), 9-HPT (OOB-AUC = 0.793), FTT (OOB-AUC = 0.740), and T25FWT (OOB-AUC = 0.825). Notably, cSC GM CSA emerged as the most relevant predictor for most outcomes, except for 9-HPT, where cSC T2-LV demonstrated superior predictive value.

Conclusion: A multiparametric approach including both brain and cSC MRI measures may explain clinical disability in MS with high accuracy. Specifically, cSC GM atrophy represents an impactful pathological substrate contributing to motor-sensory impairment.

Disclosure: T. Morozumi, A. Meani, G. Pessina and M. Azzimonti have nothing to disclose. P. Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He has received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPR-339 | Pattern of cortical BOLD responses in visually induced motion aftereffects (MAE)

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Background and Aims: The motion aftereffect (MAE) is a phenomenon of illusory self-motion perception following the end of unidirectional coherent visual motion stimulation. It is attributed to adaptation of neurons and/or mechanisms especially in the temporo-occipital movement-sensitive visual area V5/MT+ causing an inability to promptly react to changed visual input. Aim of our study was to decipher further brain areas involved in MAE processing and their interplay with the vestibular cortical network.

Methods: Twenty-two healthy volunteers underwent 3T fMRI while watching visual motion stimuli (translational, rotational or random direction) as well as static dots, and indicated the end of perceived MAE via button press. Standardized fMRI data preprocessing was performed (SPM12) including group independent component analysis for visual, vestibular and salience network areas with respect to the visual motion and the "pure" MAE period.

Results: All subjects perceived significant MAE after coherent but not after random motion stimulation. BOLD responses in V1 showed none, whereas those in MT+ and salience network areas marked relation to MAE for rotational more than translational stimuli. BOLD responses in the vestibular posterior insula were downregulated bilaterally (rotational > translational) during visual motion stimulation relative to those during random dot and during MAE.

Conclusion: MAE is processed in motion sensitive (MT+) and attention-related areas (salience network), but not in primary visual area V1. Coherent visual motion stimulation, however, induces bilateral downregulation of the vestibular core area in the posterior insula, probably in order to early minimize the intersensory visual-vestibular conflict even so during MAE.

Disclosure: This work was supported by the Deutsche Stiftung Neurologie (DSN) (project 80721017), and the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy (Munich Cluster for Systems Neurology: EXC 2145 SyNergy to MD.

MS and related disorders 5

EPR-340 | Trends in incidence and prevalence of multiple sclerosis through five decades in Finland

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Background and Aims: Impact of the evolution of the diagnostic criteria for multiple sclerosis (MS) on the incidence and prevalence rates of MS in the Nordic countries has, to our knowledge, not been investigated. Our objective is to assess the nationwide MS incidence and prevalence rates in Finland from 1974 to 2021.

Methods: MS patients were identified through the National MS registry and a national social- and healthcare reporting system with ICD-10/ICD-9 codes G35/340. Patients were divided into four subgroups based on the year of MS diagnosis: (1) Time before Poser criteria (1974–1982) (2) Poser criteria (1983–2000) (3) Earlier McDonald criteria (2001–2016) (4) 2017 McDonald criteria (2017–2021) Age-adjusted Incidence and prevalence were calculated per 105 person years with 95% confidence intervals (95% CI).

Results: We observed a significant increase in MS incidence and prevalence during the study period. Over the two periods of McDonald criteria incidence remained stable (9.1 and 8.2; Figure 1) but prevalence increased significantly from 218 (95% CI 214,222) to 241 (95% CI 237,245; Figure 2). Mean age at diagnosis showed no difference, but it was higher among men (Table 1).

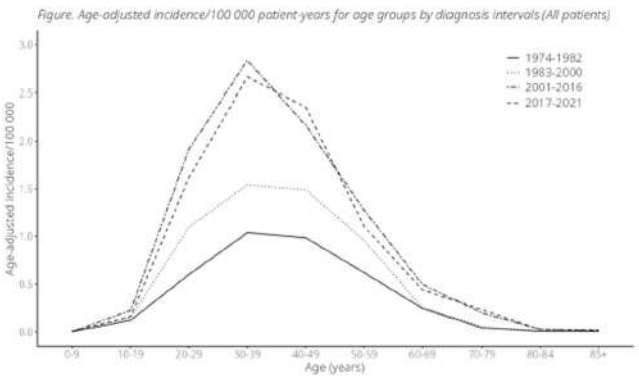

FIGURE 1: Age-adjusted incidence per 105 personyears in different age groups by diagnosis intervals. Age-adjusted incidence increased significantly during the study period, but over the two periods of McDonald criteria incidence remained stable.

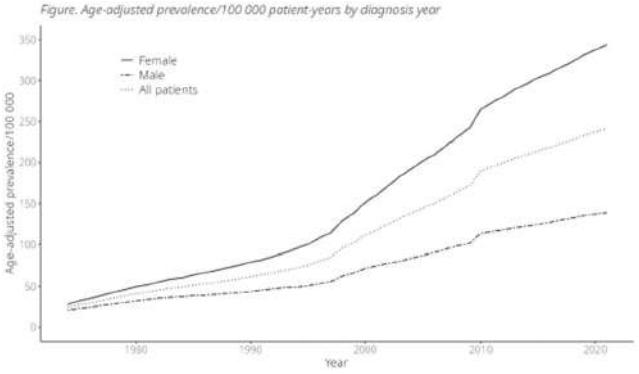

FIGURE 2: Age-adjusted prevalence per 105 person-years by diagnosis year. Age-adjusted incidence increased during the whole study period. Data on prevalence were collected in the years 1974, 2000, 2016 and 2021.

TABLE 1

Table 1. Demographic information and incidence rates per 10 personyears with 95% confidence intervals

	Time before Poser criteria (1974-1982) (n=1558)	Poser criteria (1983-2000) (n=5183)	Earlier McDonald revisions (2001-2016) (n=7758)	Newest McDonald criteria (2017-2021) (n=2276)
Sex (Females); n (%)	955 (61.3 %)	3500 (67.5 %)	5487 (70.7 %)	1581 (69.5 %)
Age at MS diagnosis (years); Mean (SD)	39.5 (12.9)	39.8 (12.1)	39.7 (13.1)	40.6 (13.4)
Females	39.4 (13.0)	39.7 (12.0)	39.4 (13.0)	39.7 (13.0)
Males	39.7 (12.9)	40.0 (12.2)	40.7 (13.2)	42.6 (13.9)
Age-adjusted incidence rate per 10^5 person years (CI)	3.7 (3.5, 3.8)	5.6 (5.4, 5.7)	9.2 (8.9, 9.4)	8.6 (8.3, 9.0)
Females (CI)	4.4 (4.1, 4.7)	7.5 (7.3, 7.8)	13.1 (12.7, 13.4)	12.2 (11.6, 12.8)
Males (CI)	2.9 (2.7, 3.1)	3.6 (3.4, 3.8)	5.3 (5.1, 5.6)	5.2 (4.8, 5.6)
Age-adjusted prevalence rate per 10^5 person years (CI)*	24.3 (22.8, 25.8)	111.4 (108.6, 114.2)	218.0 (214.1, 222.0)	241.3 (237.2, 245.4)
Females (CI)*	27.9 (25.7, 30.1)	151.2 (146.6, 155.8)	308.9 (302.3, 315.5)	343.8 (336.9, 350.7)
Males (CI)*	20.7 (18.7, 22.7)	71.8 (68.6, 74.9)	126.9 (122.6, 131.2)	138.8 (134.4, 143.2)

Footnote to Table 1. *Data on prevalence was collected in the years 1974, 2000, 2016 and 2021

Conclusion: The increasing incidence during the 20th century is most likely due to changes in diagnostic criteria and in the development of magnetic resonance imaging (MRI) technique in the diagnostic set up. The most sensitive diagnostic criteria in 2017 did not further increase the incidence, suggesting also good specificity. Increased prevalence is thought to be the result of increased survival combined with increasing incidence.

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EPR-341 | Hypogammaglobulinemia and severe infections in multiple sclerosis patients on anti-CD20 agents: A multicentre study

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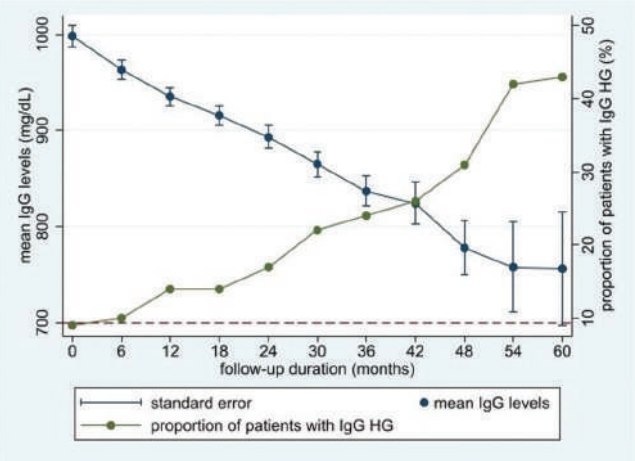
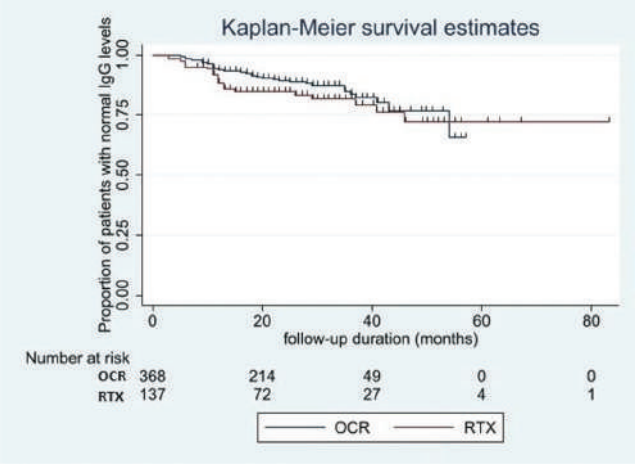
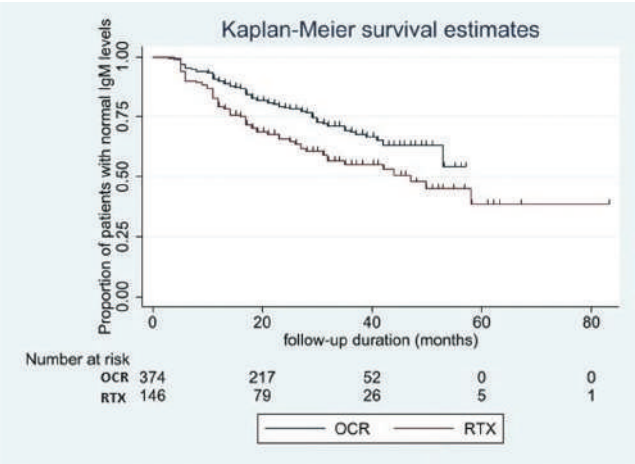
Background and Aims: Hypogammaglobulinemia (HG) is a known side effect of treatment with anti-CD20 monoclonal antibodies, and it is associated with the risk of infections. Aim of this retrospective multicentre study was to assess the frequency of HG in Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disease patients treated with ocrelizumab (OCR) or rituximab (RTX) and its association with the occurrence of infections requiring hospitalization (SI).
Methods: We included 556 patients (190M, 366F) treated for at least one year with either OCR or RTX.
Results: The mean age was 47 years and mean follow-up of 28 months. IgG HG occurred in 20% and IgM HG in 34% of patients. The risk of IgG HG was influenced by an older age (≥50 years) (OR 1.67, 95% CI: 1.08–2.61, $p=0.022$), previous immunosuppressive therapy (OR 1.60, 95% CI: 1.04–2.48, $p=0.033$) and by the number of treatment cycles (OR: 1.19, 95% CI: 1.08–1.31, $p=0.004$). A total of 25 SI occurred (100 person-years rate: 1.8), with a disease phenotype other than relapsing-remitting (OR 1.50, 95% CI: 1.02–2.20; $p=0.039$) and IgG HG (OR 2.65, 95% CI: 1.15–6.12; $p=0.022$) increasing its risk.



Mean IgG levels over time and proportion of patients with IgG HG.



Time to IgG HG, Log-rank: $p=0.170$.



Time to IgM HG, Log rank: $p=0.002$.

Conclusion: IgG and IgM HG occurred in a considerable proportion of patients. IgG HG increased the risk of SI, which were, nevertheless,

relatively infrequent. Our results highlight the importance of monitoring immunoglobulin levels to personalize treatment strategies.

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EPR-342 | Relationship between CSF-GFAP and disease burden measures in newly diagnosed MS patients: Impact of age on association

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Background and Aims: Association between astrocytic pathology and disease activity in multiple sclerosis (MS) patients remains to be elucidated.

Methods: We included 70 treatment naive patients with newly diagnosed MS. Glial fibrillary acidic protein in cerebro-spinal fluid (CSF-GFAP) levels were measured using ELISA. All patients were scanned on a single 3T scanner. Spearman correlation and adjusted linear regression were used to analyse associations between CSF-GFAP and disease activity.

Results: Median of age was 32.8 years, median of Expanded Disability Status Scale (EDSS) score was 2.0 and median of CSF-GFAP was 0.62 ng/mL; 72.9% of patients were females. Higher levels of CSF-GFAP were associated with higher: age ($\rho = 0.40$; $p = 0.001$), T2 lesion volume ($\rho = 0.34$; $p = 0.004$), T2 lesion number ($\rho = 0.24$; $p = 0.043$), but lower normalized whole-brain volume ($\rho = -0.29$; $p = 0.015$). Linear regression analyses adjusted for age did not confirm these results. Similarly, higher levels of CSF-GFAP were associated with lower scores in: Symbol Digit Modalities Test (SDMT) ($\rho = -0.32$; $p = 0.013$; $n = 58$), Paced Auditory Serial Addition Test-3s (PASAT-3s) ($\rho = -0.37$; $p = 0.014$; $n = 53$), and Brief Visuospatial Memory Test (BVMTR) ($\rho = -0.36$; $p = 0.007$; $n = 57$), but not California Verbal Learning Test-II (CVLT2). Except from BVMTR ($B = -0.08$; $p = 0.041$), the significance of these associations was no longer observed in linear regression adjusted for age, depression, and time between psychological and biochemical measures. We did not find association between CSF-GFAP and EDSS.

Conclusion: Age plays a crucial role in the relationship between CSF-GFAP, imaging, and cognitive measures, therefore needs to be considered as an important confounder of CSF-GFAP levels.

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EPR-343 | Multicenter prospective observational study on real-life experience with alemtuzumab in naïve pts with aggressive MS

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Background and Aims: Alemtuzumab (ALEM) is an anti-CD52 monoclonal antibody approved for the treatment of Multiple Sclerosis (MS) which showed high efficacy also in the subgroup of highly active patients (pts). We aimed to evaluate efficacy/safety profile of ALEM-treatment in a population of aggressive MS naïve-pts.

Methods: We conducted a multicenter prospective observational study in a cohort of aggressive naïve-pts treated with ALEM in 29 Italian MS Centers, enrolled from October 2015 to February 2019 and followed up until December 2023.

Results: 138 naïve-pts with a mean FU of 78.1 months (SD 12.2) were included. Baseline characteristics are shown in Figure 1. Efficacy data were analyzed starting from the end of a complete therapeutic cycle (year 1 and year2) since the presence of disease activity between the two administrations is not indicative of a therapeutic failure. At 5 years, 50% of pts were NEDA-3 (Figure 2). A multivariate analysis showed that disability progression had a significative correlation with the higher age at disease onset and higher number of T2 spinal cord lesions. 10.9% of pts needed a third cycle of therapy and 31.9% of pts switched to another DMTs. Adverse events were reported in Figure 3.

Figure 1. Baseline disease characteristics

Baseline disease characteristics (138 pts)	
Sex	61,6% F
Mean age at disease onset	30,5 years (SD 8,7)
Mean age at ALEM start	32,1 years (SD 9,1)
Mean disease duration at ALEM start	19,4 months (SD 25,6)
Mean baseline EDSS	2,7 (SD 1,2)
ARR in the last year before ALEM treatment	1,81 (SD 0,94)
Mean n° of T2 lesions at MRI at disease onset	23,5 (SD 22,3)
Mean n° of gd+ lesions at MRI disease onset	4,5 (SD 5,9)
Mean n° of New T2 lesions on baseline MRI	2,81 (SD 4,86)
Mean n° of Gd+ enhancing lesions on baseline MRI	3,41 (SD 5,07)
Mean n° T2 spinal cord lesions	4,82 (SD 3)

FIGURE 1

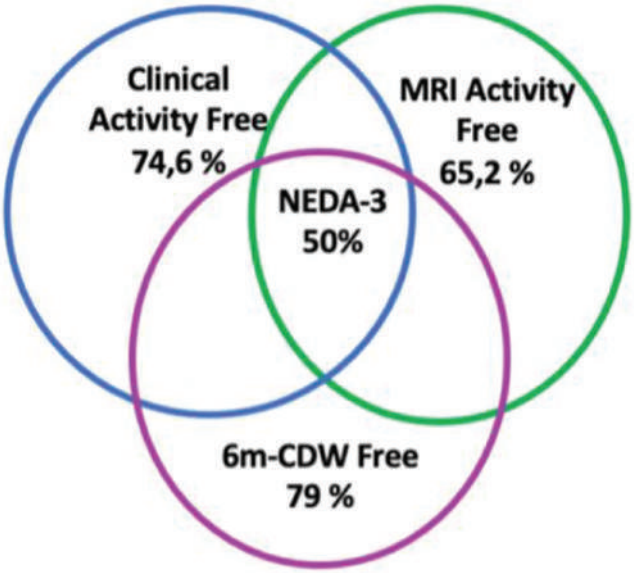

FIGURE 2

Figure 3. Adverse events

Adverse Events of special interest (138 pts)		
Thyroiditis	38 pts, 27,5 %	vs 40 % in CT
Nephropathies	0 pts	
Thrombotic thrombocytopenic purpura	1 pts 0,72%	vs 3% in CT
Infections of special interest	13 pts 9,4 %	
Neoplasia	1 pt 0,72% (death for breast cancer)	
Cardiovascular and pulmonary events	0 pts	
HPV	1 pt 0,72%	
Others autoimmune	2 pts 1,4 %	

FIGURE 3

Conclusion: These results showed that ALEM is highly effective in this population and highlighted that aggressive naïve-pts are ideal candidates for immune system resetting, likely due to young age, short disease duration and low disability. Furthermore, absence of previous immunomodulating/immunosuppressant drugs altering the immune system play a key role in determining effectiveness of this powerful drug. Larger studies are needed to confirm our data.

Disclosure: M.DiCristinzi received honoraria for speaking from Sanofi, Merck, Novartis. C.Zanetta received honoraria for speaking from Alexion, Astrazeneca, Biogen, BMS, Janssen, Merck, Novartis, Roche, Sanofi L. Brambilla received honoraria for speaking from Novartis, Sanofi. F.Rinaldi received honoraria for speaking from Sanofi, Teva P.Annovazzi received honoraria for speaking and travel from Merck, Biogen, Teva, Sanofi, Mylan, Almirall, Roche, Novartis J.Frau received honoraria for speaking from Merck, Sanofi, Biogen, Teva G. Lus received honoraria for speaking from Bayer, Biogen Idec, Merck, Novartis, Sanofi, Teva, Almirall, Allergan, Merz, Ipsen, Roche S.Malucchi, G.Puorro and A.Bianco have no disclosures. G.Marfia received honoraria for speaking from Almirall, Bayer Schering, Biogen Idec, Merck, Novartis, Sanofi, Teva. P. Cavalla received honoraria from Biogen, Merck, Teva, Roche, Novartis, Sanofi. R.Cerqua received honoraria for speaking from Sanofi, Merck, Teva. A.Gallo received honoraria for speaking from Biogen, Sanofi, Merck, Teva. C. Lapucci received travel funds from Roche. M. Filippi received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA L. Moiola received honoraria for speaking from Merck, Celgene, Biogen-Idec, Sanofi, Novartis, Roche, Alexion.

EPR-344 | Switch from fingolimod to ozanimod for safety or intolerance reasons

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Background and Aims: ozanimod is a new generation of sphingosine 1-phosphate (S1P) treatment approved for Multiple Sclerosis (MS) with higher selectivity on S1PR1 and S1PR5, minimizing potential safety concerns around S1P3 receptor activation compared with fingolimod. The objective of the study is to compare the adherence and persistence on treatment in MS patients switched to ozanimod from fingolimod for lymphopenia or liver enzymes increase.

Methods: we retrospectively recruited patients treated with fingolimod that switched to ozanimod for safety reason with at least 12 months of follow-up. We collected demographic, clinical, biochemistry and safety data during fingolimod and after the switch to ozanimod to evaluate the lymphopenia and hypertransaminasemia on fingolimod and ozanimod in order to evaluate the persistence over six months after switch on ozanimod treatment and percentage of NADE (no adverse events) patients during ozanimod.

Results: we recruited 50 RR-MS patients with mean age 42.8 ± 10.21 treated with fingolimod for a mean of 5.6 ys who switched to ozanimod for lymphopenia (85.7%) or hypertransaminasemia (14.2%); 48/50 (96%) of patients persisted on treatment with ozanimod after switch for a mean of 1.2 ys (SD 0.37); we observed a reduction of mean lymphopenia from 0.48 to 0.61 ($p = 0.013$) in all population and reduction of lymphopenic patients from 85.7% on fingolimod to 5% on ozanimod; patients with hypertransaminasemia were 14.2% with fingolimod and 8% on ozanimod disease. Percentage of NADE patients on ozanimod were 82.8%.

Conclusion: Switching from fingolimod to ozanimod might be a good strategy in patients who experienced lymphopenia or hypertransaminasemia during fingolimod therapy.

Disclosure: Nothing to disclose.

EPR-345 | Long term effectiveness and safety of ocrelizumab in multiple sclerosis: A single centre real-world study

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Background and Aims: Literature is poor of long-term studies about efficacy and tolerability of ocrelizumab and most data come from open-label extensions of randomized controlled trials and early results from real-world studies. This observational single-centre study aimed to evaluate long-term effectiveness and safety of ocrelizumab treatment in a real-life clinical setting.

Methods: We retrospectively collected data from 244 patients with relapsing multiple sclerosis (RMS) and 71 with primary progressive MS (PPMS) treated with ocrelizumab for at least one year at the MS Centre of San Raffaele Hospital (Milan) up to 31 August 2023.

Results: Patients were followed-up for a mean of 3.95 years (range 1.08–6.82). Ocrelizumab led to a significant reduction in clinical and radiological activity in both RMS and PMS patients; significant Expanded Disability Status Scale (EDSS) worsening despite treatment occurred in PPMS patients. Older age, longer disease duration and higher EDSS at baseline were associated with progression in RMS patients; in PPMS baseline EDSS was instead the only significantly predictor of disability progression. Adverse event profile was consistent with that reported in clinical trials, with hypogammaglobulinemia and recurrent infections being the most frequent. A total of 20 pregnancies occurred in our cohort with outcomes reflecting epidemiology in the general population.

TABLE 1: Clinical and radiological activity before and after ocrelizumab (OCR) treatment.

Table 1. Clinical and radiological activity before and after ocrelizumab (OCR) treatment

		Previous year	During OCR treatment	p-value
Annualized relapse rate (ARR) (mean, 95% CI)	RMS (n=244)	0.41 (0.362 – 0.458)	0.02 (0.008 – 0.025)	<0,001
	PPMS (n=71)	0.07 (0 – 0.160)	0 (0 – 0.016)	0,001
MRI activity (n. patients, 95% CI)	RMS (n=244)	133 (54.5%) (48.2 – 60.8)	50 (20.5%) (15.4 – 25.6)	<0,001
	PPMS (n=69)*	38 (55.1%) (43.0 – 67.1)	16 (23.2%) (13.0 – 33.4)	<0,001

*2 pts without data

TABLE 2: Comparison of OCR effectiveness outcomes between RMS and PPMS groups.

Table 2. Comparison of OCR effectiveness outcomes between RMS and PPMS groups

	RMS (n=244)	PPMS (n=71)	p-value
ARR during the whole follow-up (mean, 95% CI)	0.02 (0.008 – 0.025)	0 (0 – 0.016)	0,074
MRI activity during OCR treatment (% patients, 95% CI)	20.5% (15.4 – 25.6)	22.5% (13.0 – 32.1)	0,710
6 month Confirmed Disability Progression (CDP) Since OCR start to last infusion (% patients, 95% CI)	13.9% (9.1 – 18.8)	46.5% (37.4 – 55.5)	**<0,001**
6 month-Confirmed Disability Improvement (CDI) Since OCR start to last infusion (% patients, 95% CI)	18.2% (13.0 – 23.4)	4.2% (0 – 12.4)	**0,005**
NEDA-3 during the whole follow-up (% patients, 95% CI)	65.2% (59.2 – 71.2)	33.8% (22.7 – 44.9)	**<0,001**

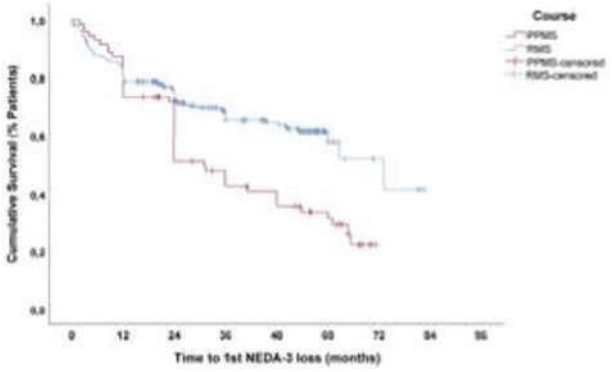

FIGURE 1: Time to loss of NEDA-3 (RMS and PPMS patients).

Conclusion: Ocrelizumab showed a high and long-lasting efficacy on inflammatory disease activity, with greater impact on RMS patients and a favourable safety profile. Treatment start in the early phases of the disease may enhance neuroprotection preventing irreversible disability accumulation.

Disclosure: LM received compensations for speaking activities and/or for participating to advisory board from Merck, Celgene, Biogen, Sanofi, Novartis, Roche, Alexion CZ received compensation for speaking activities and/or consulting activities from Biogen, Bristol Myers Squibb, Janssen, Roche, Astrazeneca, Sanofi, Merck, Alexion, Novartis GA received consulting fees from Novartis EF received compensation from Merck and Biogen. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva. FM received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA. SG, TZ, VV, IG, AN nothing to disclose.

EPR-346 | The MTHFR A1298C polymorphism is associated with multiple sclerosis severity

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Background and Aims: The 5–10-methylenetetrahydrofolate reductase (MTHFR) enzyme is critical for cellular homeostasis, orchestrating pivotal processes within the one-carbon metabolic pathway, including the catabolism of methionine and folate, as well as the biosynthesis of nucleic acids and proteins. We aimed to evaluate the association between MTHFR gene variants and Multiple Sclerosis (MS) severity.

Methods: We enrolled two independent populations to investigate the association of MTHFR polymorphisms with MS. An Italian population of 230 MS subjects genotyped for the MTHFR C677T and A1298C polymorphisms at Vanvitelli University (Naples, Italy); clinical data was retrospectively collected for a 5-year follow-up period. A UK cohort of 298 MS brain donors; MTHFR genotypes, clinical, and neuropathological features from this population were retrieved from the UK MS Society Tissue Bank, Imperial College London (London, UK). Logistic, ordered, and Cox regression analyses were employed to explore the associations.

Results: Italian population: The MTHFR A1298C polymorphism was associated, in the recessive model (CC vs. A/C and AA), with more relapses ($p=0.022$), higher EDSS ($p=0.003$), and a higher likelihood of confirmed disability progression ($p=0.010$). UK Population: The MTHFR 1298CC genotype was associated with a lower age at death in recessive and additive models ($p=0.026$, $p=0.037$, respectively); neuropathological evaluation found a higher frequency of active lesions lesions in the recessive and additive models ($p=0.005$, $p=0.002$, respectively), and a higher numbers of infiltrating mononuclear cells in the perivascular and in the meninges ($p=0.048$ recessive, $p=0.037$ additive models) indicating higher levels of inflammation.

Conclusion: These findings strongly support the association between MTHFR A1298C polymorphisms and MS severity.

Disclosure: Nothing to disclose.

EPR-347 | Comparative effectiveness of natalizumab and ocrelizumab on disability progression in RRMS in the Italian MS register

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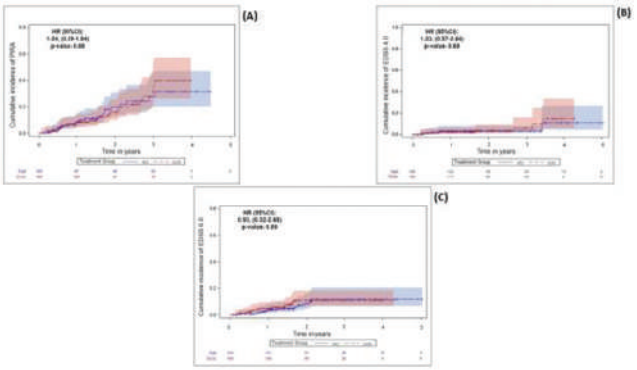
Background and Aims: To compare the risk of 6-months confirmed progression independent of relapse activity (PIRA), relapse associated worsening (RAW), and irreversible Expanded Disability Status Scale (EDSS) 4.0 and 6.0 in a real life-cohort of naïve relapsing-remitting multiple sclerosis (RRMS) patients treated with natalizumab (NTZ) or ocrelizumab (OCR).

Methods: RRMS patients with a first visit within one year from disease onset, treated with NTZ or OCR and ≥3 EDSS score evaluations were extracted from the Italian MS and Related Disorders Register. To mitigate the impact of potential biases, pairwise propensity score (PS)-matched analyses were performed. Risk of reaching the outcomes were estimated using multivariable Cox proportional hazards models.

Results: A total of 770 subjects were included (NTZ = 568; OCr = 212). The median (IQR) follow-up after treatment start was 1.63 (0.87–2.72) and 1.60 (0.80–2.68) years, respectively. The PS-matching retrieved 195 pairs. No RAW events were recorded. No differences between the two groups (NTZ – treated group as reference) were found in the risk (HR, 95% CI) of reaching a first PIRA (1.04, 0.59–1.84; $p = 0.88$) event, an irreversible EDSS 4.0 (1.23, 0.57–2.66; $p = 0.60$) and EDSS 6.0 (0.93, 0.32–2.68; $p = 0.89$).



Cumulative incidence of PIRA (A), irreversible EDSS 4.0 (B) and irreversible EDSS 6.0 (C) in NTZ and OCR treated patients.

Conclusion: Both OCR and NTZ strongly suppress RAW events in RRMS patients. In the short-term, the number and the risk of achieving PIRA events, EDSS 4.0 and 6.0 milestones are not significantly different between the two groups. A longer follow-up is essential to confirm the results on disability outcomes.

Disclosure: The authors report no conflicts of interest with respect to the contents of the current study, but note they have received advisory board, speaker honoraria, travel support, research grants or clinical trial support from the manufacturers of DMTs.

EPR-348 | Vagus nerve stimulation improves remyelination in a rat toxic demyelination model

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Background and Aims: Multiple sclerosis (MS) is a neuroinflammatory and neurodegenerative disease of the central nerve system, characterized by immune-mediated demyelination. Current MS treatments poorly address the chronic inflammation nor offer effective remyelination for axonal protection. Vagus Nerve Stimulation (VNS) shows potential in tackling both neuroinflammation and remyelination in MS. In this preclinical study the effect on remyelination was investigated in a toxic demyelination model.

Methods: In 35 Lewis rats, lysolecithin (LPC) was injected in the corpus callosum to induce a demyelinated lesion. Three days post-injection (dpi), 22/35 rats were perfused to analyse the lesions during demyelination and peak inflammation. 13/35 rats were perfused at 11 dpi to analyse the lesion during remyelination. VNS (0.5sON/29sOFF, 1.0 mA intensity, 30 Hz frequency, 250 μs pulse width) or sham stimulation was performed from two days before injection, until the day of perfusion (either three or 11 dpi). The extent of demyelination was evaluated by a luxol fast blue staining and cresyl violet counterstaining.
Results: At 11 dpi (timepoint of partial remyelination), demyelination was significantly reduced by 57.4% in VNS compared to sham, indicating improved remyelination by VNS. At three dpi (timepoint of demyelination) no significant difference was found between VNS and sham, indicating that VNS does not prevent against the direct demyelinating effects of LPC with the applied stimulation parameters.
Conclusion: Histological evaluation of LPC-induced demyelination showed that VNS significantly improves remyelination, suggesting a possible role for VNS as remyelinating strategy in MS. Further investigation is required.
Disclosure: Helen Bachmann, Evelien Carrette, Robrecht Raedt, Guy Laureys have nothing to disclose. Kristl Vonck received consultancy fees from LivaNova Europe and Synergia Medical. Paul Boon received consultancy fees from Livanova Europe. Helen Bachmann is a fellow of the Research Foundation Flanders (FWO) (1S25620N), research funding was provided by the Charcot Research Fund (https://www.fondation-charcot.org/).

Neurorehabilitation

EPR-349 | Power of pepper kids robot to train social skills in children with neurological disorders

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Background and Aims: The aim was to investigate child-robot interaction (CRI) in children with neurological disorders (ND) for designing social neurorehabilitation.
Methods: Study took place in Tartu University Children's Clinic. 89 children (4–16 years) participated: 50 with ND, 39 typically developed n control group (CG). 49/89 interacted directly, 40 via video. Interaction was examined in three ways: survey based on four socio-cultural concepts, therapists' observations and children's evaluation of emotional state.

FIGURE 1: Interaction session between child and robot pepper.

Results: Children quickly engaged with Pepper, median contact time was 2.0 [IQR 1.0–3.0] seconds. 93.8% sustained eye contact during whole session (8–10 min). 40% of children with ND believed the robot was very safe compared to 17.9% of CG ($p = 0.025$). Children who communicated with robot through video showed significantly less gesticulations and were more static compared to direct interaction group (55.9% vs. 80%; $p = 0.040$). Direct communication was more effective, but interaction via video also attracted children. 55% of children attributed three or four out of four anthropomorphistic characteristics to Pepper. On Smilyometer, 65 children evaluated their own and Pepper's mood as happy (Mdn 4 out of 5).

FIGURE 2: Child with ND using non-verbal communication with robot Pepper.

Conclusion: Anthropomorphic design of Pepper enhances acceptance, interaction and communication quality in children of all ages. Children found robot friendly, cheerful, smart and safe allowing long-term engagement. In the future, robot Pepper can be used as a therapist to advance children's social skills in neurorehabilitation sessions.

Disclosure: Authors declare no relevant or material financial interests that relate to research. Study was funded by Estonian Science Foundation PRG789.

EPR-350 | Validation of the Brief Evaluation of Receptive Aphasia (BERA) tool in post-comatose patients

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Background and Aims: The Brief Evaluation of Receptive Aphasia (BERA) is a new tool to assess receptive phonological, semantic and morphosyntactic abilities in patients with severe brain damage, based on visual fixation of a target image next to a specific distractor. We here aim to provide validation data regarding the administration of the BERA in post-comatose patients, including patients with disorders of consciousness.

Methods: The BERA and Simplified evaluation of CONsciousness disorders scale (SECONDs) were administered to 35 post-comatose patients on two consecutive days, by two blinded raters, to determine the validity and reliability of the BERA. For internal and concurrent validity, versions 1 and 2 of our tool were considered, and BERA results were compared to a language index score extracted from the SECONDs assessment.

Results: The BERA tool showed satisfactory intra- and inter-rater reliability, as well as internal and concurrent validity in patients with and without disorders of consciousness.

Conclusion: This ongoing validation study suggests that the BERA may complement the SECONDs for assessing and diagnosing post-comatose patients. The BERA scores may also indicate selective receptive difficulties for phonological, semantic and morphosyntactic abilities, which would help to orient speech-language therapies.

Disclosure: Nothing to disclose.

EPR-351 | Immersive virtual reality as a complement to physical therapy for Parkinson's disease – A randomized controlled trial

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Background and Aims: Virtual reality (VR) can provide intensive motor-cognitive training through multisensory environments, holding potential to complement PD rehabilitation programs.

Methods: In an open-label rater-blinded, randomized-controlled trial, we aimed to assess the efficacy, safety, and usability of combining immersive VR (IVR) with physiotherapy. Thirty PD patients were randomly assigned into two groups: 12-week physiotherapy plus IVR (VRG), or sequential 6-week physiotherapy followed by 6-week physiotherapy plus IVR (SG). Training occurred three times/week. Assessments were conducted on medication at baseline, 6-week, 12-week, and 4-week after intervention ended. Primary outcome was change from baseline to 6-week in TUG with cognitive dual-tasking (TUGcog).

Results: Twenty-nine participants were analyzed. VRG ($n=15$) was younger (median [IQR] age (years) in VRG=61 [58, 66] vs. SG=67.5 [60.5, 71.5]; $p=0.044$) and had higher MDS-UPDRS-3 score (VRG=31 [23, 35.5] vs. SG=22.5 [12, 23.8]; $p=0.008$). No other baseline differences were found. Our primary outcome did not significantly differ between groups [median TUGcog change in VRG = −0.557 [−1.448, 0.422] vs. SG=0.063 [−1.476, 1.157], estimated difference=0.567 (95% CI −1.063; 2.087); $p=0.505$]. Both groups improved in motor, cognitive and QoL measures. Significantly greater changes from baseline to 12-week in SG compared to VRG in TUGcog ($p=0.041$) and TUGmotor ($p=0.020$) suggest added benefits from VR training after 6 weeks of physiotherapy. Adverse events ($n=144$) were mostly mild (68.8%), and more frequently reported during IVR training. IVR was considered easy-to-use.

Conclusion: IVR was safe and usable for PD. Integrating IVR into a PD-specialized program could enhance physiotherapy positive effects, and possibly contribute to more sustained effects. Further research should validate VR's added value in PD rehabilitation.

Disclosure: This work was granted with Prémio João Lobo Antunes – Santa Casa da Misericórdia de Lisboa (grant to DPS).

EPR-352 | Examining EEG asymmetry changes in post-stroke UL rehab with rTMS in late subacute and chronic patients

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Background and Aims: Interhemispheric rivalry theory suggests inhibition from the unaffected hemisphere hampers recovery after a stroke. This study aims to assess interhemispheric symmetry using EEG properties (entropy, total power, waiting time), and the Brain Symmetry Index (BSI) in response to a neuromodulation protocol stimulating injured hemisphere and inhibiting contralateral.

Methods: Crossover AB/BA clinical trial with 20 participants, Therapy A (bilateral rTMS ×5 weekly sessions ×2 weeks), Therapy B (Therapy A + Motor imagery-EEG-neurofeedback). Patients received concurrent physical and occupational therapy. Fugl Meyer Assessment-Upper Limb (FMA-UL) and 64 electrodes EEG (resting state and finger tapping tasks) were recorded at six time points.

Results: Although functional improvement was observed in both therapies with differences favouring therapy B ($p<0.001$), symmetry differences were not clearly evidenced nor using the selected EEG properties nor BSI in any case ($p>0.05$). No statistically significant correlation was detected between changes in functionality and EEG asymmetry ($p>0.05$).

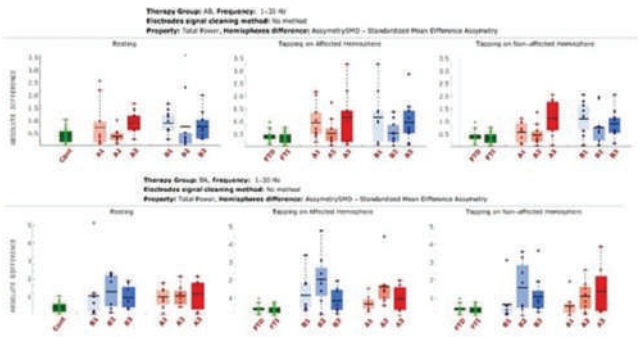

FIGURE 1: AssymetrySMD. Total power.

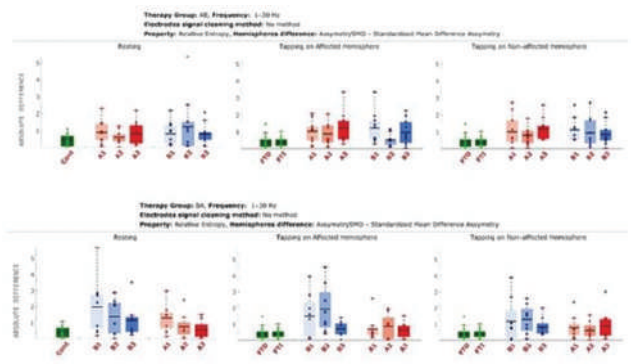

FIGURE 2: AssymetrySMD. Relative entropy.

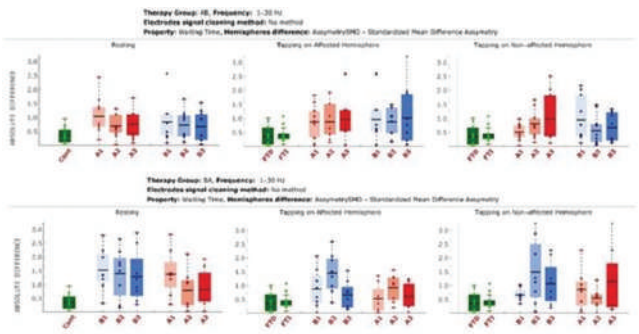

FIGURE 3: AssymetrySMD. Waiting time.

Conclusion: Although the neuromodulation in combination with conventional rehabilitation was effective regarding functional outcomes, it did not reflect in asymmetry changes measured with EEG which indicates that although our protocol was oriented to mitigate the interhemispheric inhibition it might have acted through different yet unveiled mechanisms that deserve further investigation.
Disclosure: There are no conflicts of interest to disclose.

EPR-353 | Nfl quantification in blood as rehabilitation outcome in a cohort of Parkinson's disease (PD) patients

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Background and Aims: Neurofilament-light (Nfl) is a cytoskeletal intermediate filament protein that is expressed in neurons to provide structural support for the axon. Neurofilaments are released into the extracellular space and into the cerebrospinal fluid and blood following neuro-axonal damage or neurodegeneration. Exercises and rehabilitation-therapies were proposed as no-pharmacological treatments to maximize functional capacity, improve quality of life and minimize secondary complications in PD-treatment. The aim of the study is the quantification of plasma-Nfl as a possible rehabilitation outcome to monitor the effectiveness of exercise performed by PD-patients.
Methods: Nfl plasma-concentration was measured by Simoa-assay in 40 PD-patients; they were randomized into two groups of 20-patients: (a) the first formed by PD-patients undergoing an extensive rehabilitation section for 3 months (MAC); compared to (b) the second formed by PD-patients who did not undergo any rehabilitation cycle (CTRL). Patients' plasma was collected from whole-blood and collected for both groups at: (1) baseline (T0) before starting; (2) after 3-months (T1) and (3) after 6-months (T2) of the end of the rehabilitation cycle.
Results: Results have shown (1) significant ($p < 0.05$) decrease in plasma Nfl concentration post-rehabilitation (MAC T1 vs. T0); (2) significant ($p < 0.01$) increase in Nfl release in CTRL (T1 vs. T0). In the MAC patients no significant difference was shown between T1 and T2, instead after 6 months of the end of the rehabilitation activity the Nfl values were equal to the T0 level losing the significant effect that was shown at T1.
Conclusion: Nfl levels could be a rehabilitation outcome for personalize physical activity and rehabilitative-program.
Disclosure: "Nothing to disclose."

EPR-354 | Motor decision-making as a common denominator in motor pathology and a possible rehabilitation target

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Background and Aims: Learned non-use (LNU) is a frequent complication in neurological conditions such as stroke or traumatic brain injury. We suggest that applying neuroeconomic principles to understand patient decision-making in both cognitive and motor domains could be a new fruitful area of LNU research and in motor neurorehabilitation in general.
Methods: We introduced a 'risk-and-reach' task using a touch screen application to study how goal parameters affect motor choices. Tasks involved reaching for iteratively appearing goals, whose position represents different probabilities and rewards. The experiment starts by individualizing each participant's motor abilities and continues with the varying risk-reward scenarios in the motor domain (Figure 1), which is then compared with participant risk preferences in the cognitive domain and questionnaires-based mental traits such as impulsivity and sensation-seeking.

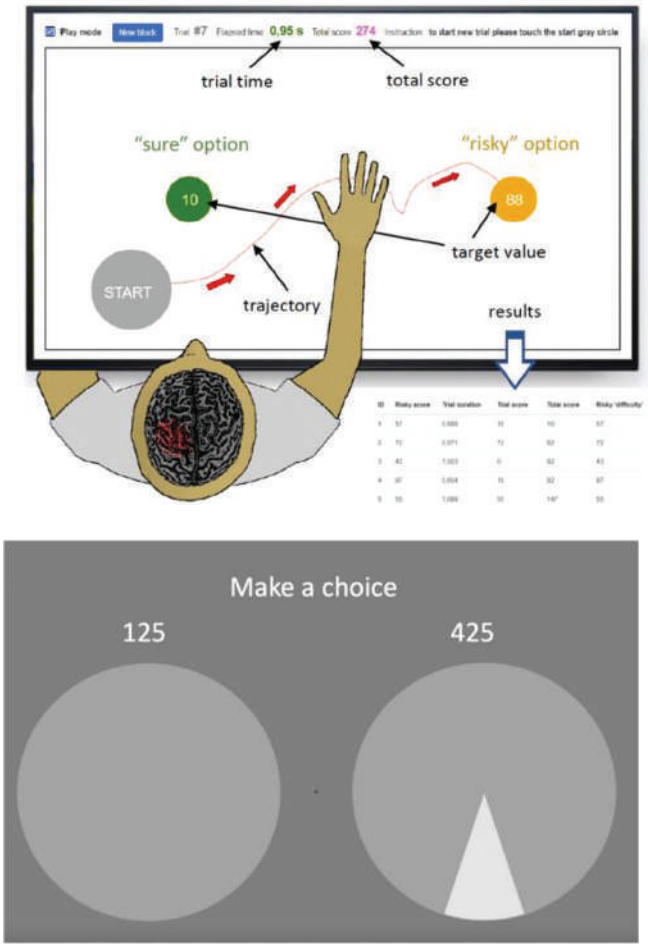

FIGURE 2: Example of a cognitive lottery trial.

Results: Analysis of 20 healthy participants showed that the presence of choice in the motor domain increased movement time ($t = -2.58$, $p = 0.032$). When comparing choices from motor and cognitive lotteries, participants preferred risky options in motor tasks compared to the cognitive ones ($p = 0.001$). Impulsivity and sensation-seeking traits were predictive for higher risky motor choice, while the Bomb Risk Elicitation Task scores predicted aversion to risk in the motor domain.

Conclusion: We showed that the presence of choice in the motor domain invigorates reaching movements. Furthermore, we observed that the motor choices were riskier compared to the cognitive ones. We recommend integrating neuroeconomic parameters in neurorehabilitation tasks. It could provide valuable insight into motor impairment, e.g., LNU, leading to more engaging and ecological interventions.

Disclosure: Nothing to disclose.

EPR-355 | Coordination index to detect cycling characteristics in early Parkinson's disease patients

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Background and Aims: Interestingly, many PD patients, despite experiencing severe freezing of gait, can still ride a bicycle. However, detailed analyses to explore unique cycling characteristics in PD have been limited. This study aims to identify key variables associated with the cycling patterns of PD patients, utilizing the Ultiracer®, an innovative indoor cycling system.

Methods: A prospective study involved 32 PD patients (modified H&Y ≤2) and 42 control participants were evaluated using the Ultiracer® for 15 min at a comfortable speed . The Ultiracer® was equipped with rollers beneath each wheel and a frame-attached rod, enabling medio-lateral sliding and tilting motions, and is outfitted with force-torque sensors. Parameters analyzed included the coordination index, clinical PD data, lower extremity strength, and gait analysis.

Results: The momentum X-axis of the coordination index (CI-Mx), representing roll direction moment, negatively correlated with bicycle velocity in PD patients but not in controls and was significantly higher in PD patients. In a multivariable logistic regression, CI-Mx was a key predictor differentiating PD patients from controls and effectively distinguished between the two groups with high accuracy in receiver operating curve analysis. A significant positive correlation between the coordination index and UPDRS scores in the PD subgroup with less dynamic cycling abilities.

Conclusion: The results suggest that while PD patients retain the ability to cycle, their cycling behaviors differ notably from those of normal controls, particularly with increased CI-Mx. This suggests that the Ultiracer® system provide additional information possibly assisting the diagnostic process for individuals with early-stage PD.

Disclosure: This work was supported by the Ministry of Culture, Sports and Tourism and Korea Sports Promotion Foundation of the government of the Korea.

EPR-356 | Association of plasma cholinergic markers with post-stroke walking performance

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Background and Aims: Stroke is the second highest cause of mortality and disability worldwide. Physical disability is often reported in post-stroke patients, wherein sedentary behavior might modify the risk of future stroke incidents. We had previously reported that SMS-guided training instructions delivered to stroke patients showed positive clinical outcome in walking performance at 3 month follow-up (The STROKEWALK Study) (1). In this study, we evaluated markers of cholinergic pathway to investigate whether they can serve as indicators of post-stroke recovery in walking ability.

Methods: Post-stroke patients were randomly selected to receive SMS instructions (Intervention group) or not (Control group). Plasma samples were collected at baseline ($n = 28$) and after 3-months follow-up ($n = 28$), respectively. All patients performed the six-minute walking test (6MWT) at baseline and follow-up. Enzyme activity was measured for the cholinergic pathway markers – choline acetyltransferase (ChAT) and butyrylcholinesterase (BChE) and were normalized to total protein content for respective sample. The cholinergic index was determined by calculating the ratio of ChAT/BChE (2).

Results: All patients ($n = 56$) were stratified into those showing clinically relevant improvement in walking ability in 6MWT (≥34-m, Improved group) versus who displayed lesser walking ability (<34-m, Unchanged group). Spearman rank correlation analyses showed association between the changes in cholinergic index and 6MWT performance, respectively from baseline to follow-up, among improved group but not in unchanged group.

Conclusion: Cholinergic index could be a useful biomarker to evaluate post-stroke walking performance. Validation studies are warranted in larger cohorts.

Disclosure: Nothing to disclose.

EPR-357 | Contralateral silent period and its association with upper extremity motor function in people with chronic tetraplegia

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Background and Aims: Contralateral silent period (CSP) is a transcranial magnetic stimulation (TMS)-based measure of corticospinal inhibition that is relevant to motor function but remains poorly understood after spinal cord injury (SCI). To advance the understanding of corticomotor inhibition after SCI, we studied CSP characteristics across muscles with varying degrees of weakness and investigated their relationship with the upper extremity function.

Methods: The data were collected as a part of a multi-site clinical trial (NCT03892746). We investigated CSP onset, offset, duration and depth in the stronger (biceps, muscle power = 3–5) and the weaker (triceps, muscle power = 1–3) muscles and examined their relationship with upper extremity function as assessed using the Capabilities of the Upper Extremity Test (CUE-T).

Results: The participants were 27 adults with chronic C1-C8 SCI (age 48.8 ±16.1 years) and 16 able-bodied (age 33.2 ±11.8 years) controls. Participants with SCI had prolonged CSPs for biceps (83.8 ±45.5 ms vs. 37.0 ±24.5 ms, $p < 0.001$), and delayed (52.4 ±15.0 ms vs. 33.4 ±5.0 ms, $p < 0.001$) and diminished CSPs (38.5 ±24.8% vs. 58.6 ±10.3%, $p = 0.032$) for triceps. Early CSP onset for biceps ($\rho = -0.53$, $p = 0.005$), and prolonged duration ($\rho = 0.74$, $p < 0.001$) and depth ($\rho = 0.73$, $p < 0.001$) for triceps CSP associated with better upper extremity function.

Conclusion: The CSPs in muscles with different extent of weakness following chronic tetraplegia reflect changes in corticospinal inhibition in relation to the neural level of injury. Individuals with better corticospinal inhibitory profiles as indicated by earlier onset, longer, and deeper CSPs for weaker muscles demonstrate better upper extremity function.

Disclosure: This work was supported by The Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense through the Spinal Cord Injury Research Program under Award No. W81XWH1810530.

Neuro-ophthalmology/neuro-otology

EPR-358 | Prevalence and functional impact of vestibular symptoms in patients with migraine: A cross-sectional study

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Background and Aims: Dizziness is a common symptom in migraine patients, impacting daily life. This study aimed to assess the prevalence and impact of this symptom in migraine patients.

Methods: This cross-sectional study surveyed patients and family members from both the headache unit and neurology clinic.

Results: A total of 388 participants were included, with 274 (70.6%) having migraine and 114 (29.4%) serving as controls. Mean age was 41.9 years (±13.3), with females comprising 76.8%. Baseline characteristics are summarized in Table 1. Moderate and severe anxiety prevalence was higher in migraine patients (20.1% and 17.5%, respectively) than controls (9.6% and 2.6%). Additionally, 27.7% of migraine patients reported persistent photophobia, 24.5% persistent phonophobia, and 25.2% persistent osmophobia. Vestibular symptoms were more prevalent in migraine patients (54%) than controls (15%; OR 6.7, 95% CI 3.8–11.8; $p < 0.001$). Analysis of the Dizziness Handicap Inventory (DHI) showed severe functional and emotional handicaps in 23%, and severe physical handicaps in 54.7%. Logistic regression analysis revealed a significant association between dizziness and persistent photophobia, higher HIT-6 scores, unilateral pain, headache exacerbated by movement, nausea, and elevated anxiety levels.

TABLE 1

Total cohort		Controls	Migraine	Total
n (%)		114 (29.4)	274 (70.6)	388
Age [years], median +/- SD		42.3 +/-15.4	41.7 +/-12.4	41.9 +/-13.3
Sex female, n (%)		59 (51.8)	239 (87.2)	298 (76.8)
GAD-7 (Generalized Anxiety Disorder)				
Minimal, n (%)		54 (47.4)	62 (22.6)	116 (29.9)
Mild, n (%)		46 (40.4)	109 (39.8)	155 (39.9)
Moderate, n (%)		11 (9.6)	55 (20.1)	66 (17)
Severe, n (%)		3 (2.6)	48 (17.5)	55 (13.1)
Migraine features				
Unilateral pain, n (%)			165 (60.2)	
Throbbing, n (%)			234 (85.4)	
Intensity, median +/- SD			7.96 +/-1.5	
Worsens with head movements, n (%)			239 (87.2)	
Nausea, n(%)			193 (70.4)	
Photophobia, n (%)			250 (91.5)	
Phonophobia, n (%)			249 (90.9)	
Osmophobia, n (%)			166 (60.6)	
HIT-6, median +/- SD			63.7 +/-7	
Sensitivity symptoms				
Persistent photophobia, n (%)			76 (27.7)	
Persistent phonophobia n (%)			67 (24.5)	
Persistent osmophobia n (%)			69 (25.2)	
Vestibular symptoms	Chronological relationship^			
Dizziness, n (%)		17 (15)	148 (54)	165 (42.5)
	Before, n (%)		48 (32.4)	
	During, n (%)		124 (83.8)	
	After, n (%)		65 (43.9)	
	Independent, n (%)		47 (31.8)	
Dizziness Handicap Inventory*				
Emotional impact				
	Mild		69 (46.6)	
	Moderate		45 (30.4)	
	Severe		34 (23)	
Functional impact				
	Mild		66 (44.6)	
	Moderate		45 (30.4)	
	Severe		34 (23)	
Physical impact				
	Mild		27 (18.2)	
	Moderate		40 (27)	
	Severe		81 (54.7)	

^Chronological association with migraine attacks, *Calculated on the 148 migraine patients with dizziness

Conclusion: Migraine patients are six times more likely to experience dizziness than healthy controls. Since dizziness mainly occurs during migraine attacks and factors like higher headache burden and symptoms of central sensitization, such as persistent photophobia and nausea, increase the likelihood of dizziness, it's plausible that dizziness is linked to central sensitization. These symptoms notably impact overall quality of life, as shown by the DHI scale.

Disclosure: The authors have no conflicts of interest regarding this study.

EPR-359 | Differentiating vestibular from somatosensory disequilibrium: Postural sway signatures while standing on foam

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Background and Aims: Standing on foam with eyes closed, the vestibular Romberg test (vRt), is employed in the clinical assessment of peripheral vestibulopathy. Nevertheless there is lack of evidence regarding whether and to what extent vRt can effectively differentiate between (somato)sensory and vestibular causes of balance impairment.

Methods: Static balance was assessed in 39 patients with peripheral vestibulopathy (PV), 30 patients with pure sensory neuropathy (SN) and 30 healthy controls (C) while standing on firm surface or foam with eyes open or closed. Postural sway was analyzed by means of linear (sway area and standard deviation) and nonlinear (Shannon entropy) time and frequency domain metrics. The latter was based on comparisons of the percentage of energy in each of three frequency bands: low (0–0.5 Hz), middle (0.5–2 Hz) and high frequency (2–20 Hz).

Results: The majority of linear sway metrics were found to be greater in both PV and sensory neuropathy SN compared to controls C. Romberg quotients (eyes closed/eyes open on firm support) of linear sway metrics showed significant differences between SN and C, as well as between SN and PV. In contrast, vestibular Romberg quotients (eyes closed/eyes open on foam) were found to be similar in PV, SN, and C. A modified Romberg quotient (eyes closed on foam/eyes closed on firm support) did, however, reveal some notable differences between PV and SN.

Conclusion: The classical vRt proves fruitless in discriminating between PV and SN. However, comparing standing on firm support or foam, while keeping the eyes closed, appears to be a suitable test for distinguishing PV from SN.

Disclosure: Nothing to disclose.

EPR-360 | Auditory dysfunction and its relationship with cognitive impairment and MRI morphometry data in Parkinson's disease

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Background and Aims: Among sensory dysfunctions, auditory processing has received increasing interest as it may contribute to

dementia in PD. Additionally to well-known a neuroprotective role of dopamine in the peripheral auditory system, efferent auditory pathways from different cortical regions also protect and provide modulation for auditory nerves and cochlea. Since there is PD-related neurodegeneration, we investigated the relationship between auditory dysfunction, cognitive deficits and MRI changes in PD patients.
Methods: Participants included 34 non-demented PD patients and 30 age-matched controls. To assess hearing we used Speech, Spatial and Qualities of Hearing (SSQ) questionnaire. Audiometric evaluation consisted of pure tone audiometry (PTA), auditory brainstem response (ABR) and Otoacoustic Emissions (DPOAE). We also applied MRI voxel-based morphometry and neuropsychological tests.
Results: PTA revealed slight decrease in hearing at high frequencies in 5 PDpatients and 4 controls. Despite this, PDpatients performed worse on the SSQ, indicating significant problems to hear speech in a variety of competing contexts. ABR reviled the I–V interval increase reflecting a slowdown in signal transmission throughout the auditory pathway in PD. DPOAE responses were reduced in PDpatients indicating involvement the efferent olivocochlear system (Table 1). DPOAE date correlated with the TMT and MoCA as well as volume in the auditory association cortex, cingulate cortex, insula and amygdala (Table 2).

TABLE 1: Comparative assessment of the PD patients group and the control group.

Parameters	PD patients group n = 34	Control group n = 30
	Median (IQR)	
Age, years	63 (57 68)	60 (55 70)
H & Y stage	2,5 (2–3)	-
Disease duration (years)	7 (6 – 13)	-
UPDRS		-
SSQ total	250 (228 – 284)	284 (271 – 315)*
Part 1: Speech hearing	53 (46 – 63)	70 (61 – 77)*
Part 2: Spatial hearing	92 (88 – 109)	100 (96 – 113)
Part 3: Qualities of hearing	105 (94 – 112)	114 (109 – 125)
Neuropsychological tests		
MMSE	28 (27 – 29)	29 (28 – 30)
MoCA	24 (22 – 28)	27 (26 – 29)
Trails Making Test Part A (s)	60 (46 – 69)	43 (36 – 58) *
Trails Making Test Part B (s)	119 (103 – 158)	87 (76 – 120) *
Otoacoustic Emissions by Distortion Product (DPOAE) dB		
819 Hz	2,62 (2,35 -- 3,05)	4,71*(4,45 – 5,02
1639 Hz	3,87 (3,49 -- 4,2)	6,13*(5,85 – 6,48
3278 Hz	-3,69 (-4,01 -- -3,45)	-1,58*(-1,92 -- -1,22)
4918 Hz	-10,84 (-11,13 -- -10,48)	-9,66*(-9,99 -- -9,35)
Auditory Brainstem Response (ABR)		
I latency	1,69 (1,59 – 1,8)	1,63 (1,55 – 1,76)
III latency	3,86 (3,78 – 4,1)	3,61 (3,58 – 3,79)*
V latency	5,79 (5,42 – 5,98)	5,6 (5,29 – 5,96)
I–III interval	2,22 (2,09 – 2,33)	2,1 (2,01 – 2,15)
III–V interval	1,9 (1,83 – 1,98)	1,82 (1,7 – 1,9)
I–V interval	4,09 (3,92 – 4,26)	3,81 (3,72 – 4,31)*

MMSE - Mini-mental State Examination
MoCA - Montreal Cognitive Assessment
* - p ≤ 0,05 - Significant differences between PD patients and control group (Mann-Whitney test)

TABLE 2: Spearman correlation analysis between neuropsychological tests, MRI voxel-based morphometry data and variables DPOAE frequencies (f1).

Parameters	DPOAE f1			
	819 Hz	1639 Hz	3278 Hz	4918 Hz
MoCA	P = 0,085	P = 0,078	p<0,05*	p<0,05*
Trails Making Test Part A	p<0,05*	p<0,05*	p<0,01*	p<0,001*
Trails Making Test Part B	p<0,001*	p<0,005*	p<0,0001*	p<0,001*
SSQ Part 1: Speech hearing	P=0,05	p<0,01*	p<0,005*	p<0,01*
I–V interval BAEPs	P=0,174	P=0,085	p<0,01*	p<0,01*
Middle temporal gyrus	P=0,06	P=0,005	p<0,001*	p<0,001*
Cingulate cortex	P = 0,075	p<0,05*	p<0,05*	p<0,001*
Insula	P = 0,08	p<0,01*	p<0,01*	p<0,005*
Amygdala	P=0,05	p<0,05*	p<0,01*	p<0,01*

Conclusion: Auditory dysfunctions in PD, even without significant hearing losses, manifest as an inability to extract and respond to appropriate auditory information. Interdependence between auditory dysfunctions and neurodegeneration in the auditory association cortex and non-auditory regions responsible for cognition, opens new therapeutic prospects in PD.
Disclosure: Nothing to disclose.

EPR-361 | Diagnostic role of biceps muscle biopsy in progressive external ophthalmoplegia

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Background and Aims: Mitochondrial diseases are a heterogeneous group of disorders characterized by alterations in oxidative phosphorylation and caused by mutations in nuclear or mitochondrial genes. Tissues that require more oxygen, such as the extraocular eye muscles, are more likely to be affected. Progressive External Ophthalmoplegia (PEO) is one of the mitochondrial disorders which should be considered in patients with pupil sparing symmetric ophthalmoplegia and ptosis. We aimed to determine the diagnostic rate of muscle biopsy and its correlation with genetic tests in our PEO patient group.
Methods: We retrospectively reviewed the clinical and laboratory findings of patients who undergone biceps muscle biopsy with the suspicion of PEO between 2019 and 2023.
Results: A total of 96 patients had biceps muscle biopsies with the suspicion of mitochondrial myopathy due to negative mitochondrial mutation in serum samples. Of these 96 patients, 33 had ptosis/ophthalmoplegia or both. Although the clinical features of the patients

were typical for PEO, mitochondrial cytopathy was present only in 10 out of 33 (33%). Genetic testing for mitochondrial DNA mutations was done in all biopsy samples and common deletion was detected in 4 of 10 patients with mitochondrial cytopathy (40%). In addition, 7 out of 23 patients with normal muscle biopsy were also positive for common deletion in muscle samples (30.4%).

Conclusion: In patients with PEO, negative genetic testing of the serum and negative extremity muscle biopsy do not rule out the diagnosis. Genetic testing of affected muscles may be considered.

Disclosure: Nothing to disclose.

EPR-362 | Visually induced motion aftereffects (MAE) in patients with functional vertigo

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Background and Aims: Variants of the motion aftereffect (MAE), an illusory self-motion percept after prolonged exposure to coherent moving visual pattern, was extensively studied in healthy subjects and suspected to involve not only visual motion-sensitive, but also vestibular areas in terms of a central visual-vestibular interplay. Aim of our study was to psychophysically evaluate the MAE in patients with functional vertigo (persistent perceptual-postural vertigo, PPPD [1]) that typically present with increased symptom [1] Staab, Jeffrey P. et al. 2017.

Methods: Twenty PPPD patients and 10 healthy controls (HC) watched visual motion stimulation of different directions (translational, rotational or random dots) and speeds (angular velocity 7–210°/s) repeatedly presented. Subjects indicated the end of perceived MAE via button press.

Results: All participants perceived significant MAE in opposite direction following rotational and translational stimulation. With random dot motion HC reported no MAE, but a quarter of the PPPD patients unspecific aftereffects without systematic direction. With translational stimulation, the MAE duration increased with increasing angular velocity over both groups typically up to a maximum at ≥120°/s. With rotational stimulation MAE was the longest in HC at 90–120°/s, whereas PPPD patients with high symptom severity showed maximum duration at lower angular velocities (<90°/s) that came near to the HC curve with decreasing symptom severity.

Conclusion: Compared to HC, the peak inducing angular velocity of rotational MAE is lowered in functional vertigo syndromes (PPPD) as a function of their symptom severity, probably reflecting their increased sensitivity to typically slowly moving visual stimuli in everyday life.

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EPR-363 | Retinal oxygen saturation in patients with RVCL-S, a monogenic small vessel disease

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Background and Aims: Investigating mutation carriers with retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations (RVCL-S) provides an opportunity to discover biomarkers during both the pre-symptomatic and symptomatic phases of cerebral small vessel disease. RVCL-S is an autosomal dominant small vessel disease caused by mutations in TREX1. As oxygen saturation measurements have shown potential to detect retinal and vascular changes in several neurodegenerative diseases, we aimed to determine if retinal oxygen saturation differs between RVCL-S patients and controls.

Methods: Retinal oxygen saturation was assessed in 17 eyes from RVCL-S patients and 19 eyes from controls by using a non-invasive measuring tool (Oxymap T1 retinal oximeter). Mean arterial and venular oxygen saturation and arteriovenous difference per eye were measured, as well as vessel calibre.

Results: No differences in arterial oxygen saturation were found between RVCL-S patients and controls (median [IQR]: 94.5% [92.7–98.9] vs. 93.4% [87.2–98.3], p-value = 0.12). However, the venular oxygen saturation of RVCL-S patients was considerably higher than in control patients, median of 71.5% [IQR: 55.0–77.2] and 55.5% [IQR: 51.2–59.9] respectively (p-value < 0.001). In line with these findings, the arteriovenous difference was decreased in RVCL-S patients (median [IQR]: 22.6% [18.5–38.3] vs. 38.5% [34.1–39.9], p-value < 0.001). Finally, RVCL-S patients exhibited a reduced calibre in both arterial and venular vessels.

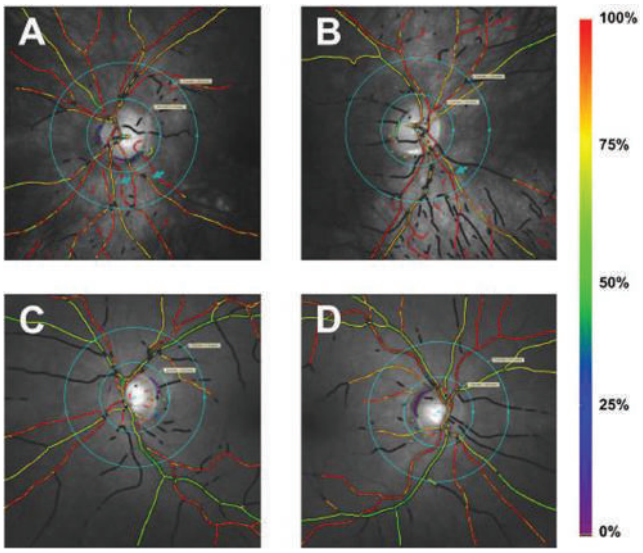

FIGURE 1: Pseudo colour fundus map of RVCL-S patient and control. Retinal oximetry images of the left (A) and right (B) eye of a RVCL-S patient and the left (C) and right (D) eye of a control individual are shown.

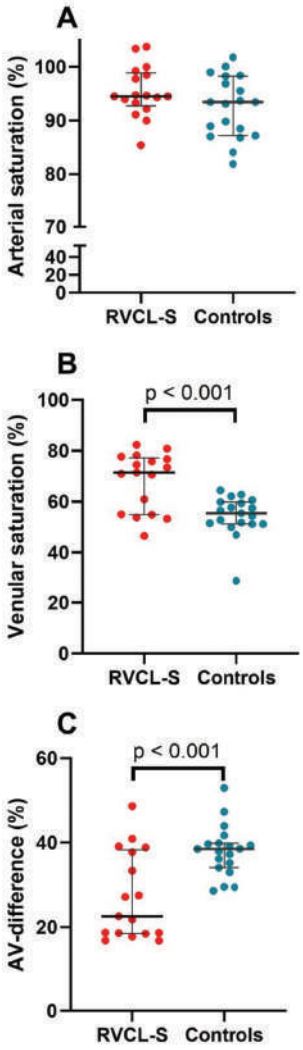

FIGURE 2: Retinal oxygen saturation in RVCL-S. Arterial (A) and venular oxygen saturation (B) and arteriovenous difference (AV-difference) (C) in RVCL-S patients and controls. Thickened line displays the median and the bars the interquartile range.

Conclusion: Retinal oximetry measurements have great potential to serve as (early) biomarkers for RVCL-S. Such precise objective instruments may also provide important non-invasive tools in determining disease activity for follow-up of common small vessel diseases.

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EPR-364 | Breaking new ground in vestibular migraine treatment with CGRP-based therapies

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Background and Aims: Vestibular migraine (VM) is a complex neurological condition characterized by a combination of headache and vestibular symptoms. Despite its prevalence, treatments for VM are limited and the recommendations are borrowed from migraine sphere. Recent advancements have highlighted the role of Calcitonin Gene-Related Peptide (CGRP) in migraine and VM, suggesting a potential breakthrough in treatment with anti-CGRP drugs.

Methods: This retrospective study, conducted at Aster Gardens Specialty Clinic, Dubai, evaluated the efficacy of CGRP-based therapies in VM. Total 12 patients (Mean 37.83 years, 7 females, 5 male) with VM were selected, excluding those with therapy duration less than 3 months or confounding medical conditions. Interventions included Erenumab, Rimegepant, and Eptinezumab, with treatment tailored as per FDA-approved dosing guidelines. Assessment tools like MIDAS and Dizziness Handicap Inventory (DHI) scores, alongside numerical (1–10) scale and subjective improvement were used for baseline and post-treatment evaluations at 3 months. Data analysis was performed using IBM SPSS software, ensuring ethical compliance and security.

Results: Statistically significant improvements were noted in headache and vestibular symptoms over 3 months, as shown by decreased MIDAS and DHI scores. Headache symptoms improved in 50% of patients, while 75% reported significant improvement in vestibular symptoms. Results demonstrate the potential of CGRP therapies in managing VM, aligning with recent literature on their effectiveness in migraine treatment.

Conclusion: Present study reinforces the efficacy of CGRP-based therapies in treating VM, advocating for the inclusion of CGRP therapies in standard treatment protocols and highlighting need for further research in this area.

Disclosure: None.

EPR-365 | Activation of the CD40/CD154 pathway in Muller cells induces ocular hypertension-induced death of retinal ganglion cells

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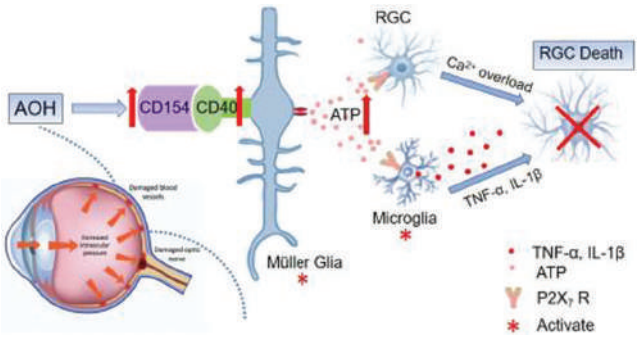
Background and Aims: In glaucoma, high ocular hypertension causes death in retinal ganglion cells (RGCs) that eventually leads to blindness. In this study, we explored whether activation of CD40 receptor with its ligand CD154, can participate in ocular hypertension-triggered ATP release from Muller glial cells, which subsequently trigger RGC death.

Methods: Acute ocular hypertension (AOH) was established in C57BL/6J mice. Then the survival of RGCs and reactivity of glial cells were examined by immunostaining and western blotting. The expression of CD40, CD154, P2X7R (ATP receptor) and several inflammation-related cytokines were measured by qPCR. The in vitro experiments on the Muller cell line using CoCl2 to induce hypoxia were also performed, with the changes in CD40 expression and ATP levels quantified.

Results: After AOH insult, the RGC survival decreased sharply within 1–4 days. The retinal expression of CD40, P2X7R, TNF-a and IL-1b were transiently increased at 1 day post-surgery and then returned to the level of sham control, whereas the microglia and Muller cells remained activated for 7 days. Meanwhile, the serum concentration of CD154 slightly increased after AOH. The hypoxia caused an up-regulation of CD40 in Muller cells in vitro, and exogenous addition of CD154 proteins to the CoCl2-treated Muller cells triggered ATP release.

Conclusion: AOH-induced RGC death may be mediated by the activation of CD40, P2X7R and inflammation. Co-activation of CD40 and CD154 triggers the release of ATP from Muller cells in vitro. Whether the CD40/CD154 pathway also participates in glaucomatous pathogenesis in vivo is under investigation using CD40-null mice.



Graphic Abstract: In glaucoma, increased intraocular pressure induces the co-activation of CD40 and CD154 in Muller cells, which

triggers the release of ATP that further activates P2X7R on both RGCs and microglia that lead to RGC death.

Disclosure: Nothing to disclose.

EPR-366 | Evaluation of retinal changes in patients with chronic migraine

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Background and Aims: Few studies have assessed the retinal changes in patients with migraine using optical coherence tomography (OCT). We investigate changes in macular thickness (MT) through OCT in migraine patients with and without aura compared to healthy controls.

Methods: This is a cross-sectional case-control study conducted at the Ophthalmology and Neurology Departments of the Habib Bourguiba University Hospital in Sfax. This study included migraine patients and control subjects. All patients and controls underwent a complete ophthalmological examination. OCT was used to measure average MT and pericentral quadrants conforming to the segmentation of the Early Treatment Diabetic Retinopathy Study.

Results: One hundred and twenty eyes from 60 patients (60 eyes in the migraine without aura (MWoA) and 60 eyes in the migraine with aura (MWA) were included. Control group included 30 age and gender matched healthy participants (60 eyes). The mean age of patients was 37.2 years, with a sex ratio (M/F) of 0.22. OCT revealed that MT thickness were significantly reduced in MWoA and MWA groups compared with the control group ($p < 0.001$), with the exception of the foveal thickness in the MWoA and MWA groups compared with the control group. We found a significant decrease in parafoveal thickness in the MWA group compared to the MWoA group in the superior and temporal quadrant.

Conclusion: MT are significantly thinner in patients with migraine. Our findings could be explained by hypoperfusion and retrograde trans-neuronal degeneration related to this disease.

Disclosure: "Nothing to disclose."

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ABSTRACT

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Ageing and dementia 1

EPO-001 | Development of small molecules promoting tau clearance in Alzheimer disease

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Background and Aims: A major pathological hallmark of Alzheimer disease (AD) is the intracellular accumulations of neurofibrillary tangles composed of paired helical filaments (PHFs) of tau protein. Lowered efficiency of degradation pathways, such as ubiquitin proteasome system, further exacerbates the aggregated tau accumulation. Proteolysis-Targeting Chimeras (PROTACs) are heterobifunctional molecules that can bring E3 ligase into the vicinity of protein of interest, leading to protein ubiquitination, followed by proteasomal degradation. Since 2016, PROTACs have been applied to resolve tau pathologies. Most of these PROTACs have only been evaluated in cell models and the exploration is still at the early stage. In this study, we aim to perform intensive research to develop novel small-molecule PROTACs to initiate tau degradation for AD treatment.
Methods: We screened a library of tau binders from a public database (bindingdb.org) by performing global molecular docking into the 3D structure of PHFs. The top ranked compounds were selected to design new PROTACs, with different linkers connected to the ligands binding to E3 ligase, for instance cereblon and carboxyl terminus of Hsp70 interacting protein (CHIP). We are performing modeling of the ternary complex (tau-PROTACs-E3 ligase) and the highly scored PROTACs will be synthesised. Their protein binding affinities and tau-reducing effects will be evaluated in cell models.
Results: We perform the development of small-molecule PROTACs according to the methods listed above. We selected the top ranked tau binders and designed new PROTACs.
Conclusion: The hit PROTACs will move on to in vivo study and provide pre-clinical evidence for novel treatment of AD tauopathies.
Disclosure: The authors declare no conflict of interest.

EPO-002 | Functional connectivity as biomarker of neurodegenerative disease

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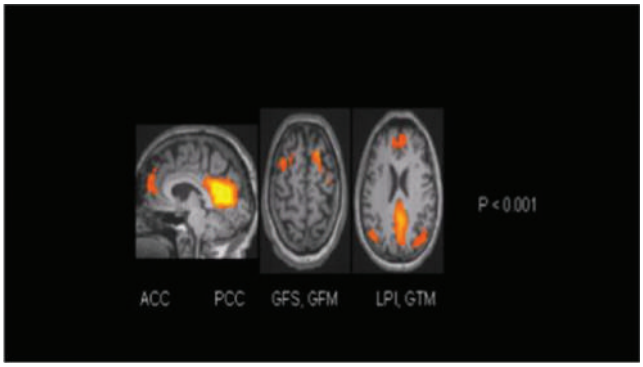
First Moscow State Medical University, Russia

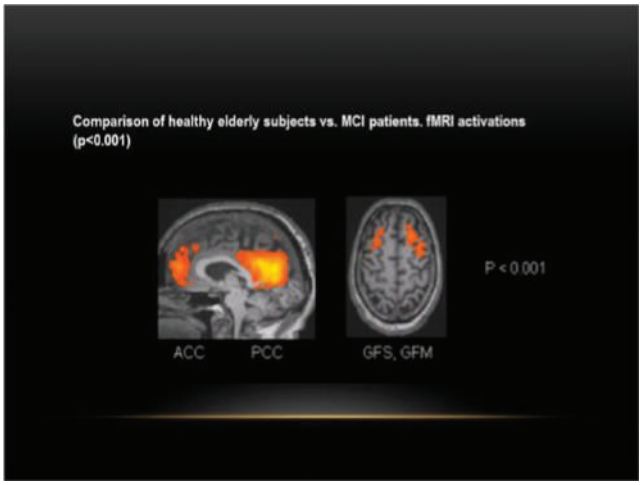
Background and Aims: Alzheimer's disease (AD) selectively involves cerebral neuronal networks. The aim was to correlate fMRI patterns and EEG-coherence in Alzheimer's disease (AD), amnestic Mild cognitive impairment (aMCI), non amnestic Mild cognitive impairment (nMCI), Frontotemporal Dementia (FTG) and controls.
Methods: 90 patients with AD, 90 aMCI, 85 nMCI, 60 FTD patients and 90 age-matched controls underwent fMRI (3 Tesla, TRIO, Siemens) and resting EEG-recordings (NeuroScan Synamps System). EEGs were recorded using a standard protocol and montage. Coherences between regions of interest, based on fMRI activation patterns were calculated.



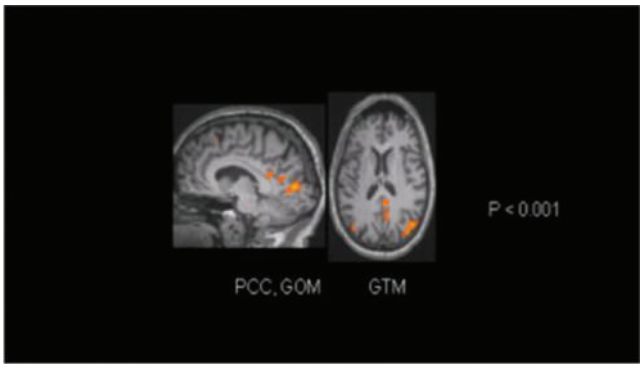
Comparison of controls vs. AD patients. fMRI activations ($p < 0.001$)

Results: There were significant differences between AD and aMCI for theta coherences between anterior cingulate gyrus (ACC) and left temporal gyrus (LTG) (AD < aMCI, $p < 0.05$) Fig.2; between AD and controls for theta between ACC and right temporal gyrus, between ACC and left hippocampus, and between ACC and right parietal gyrus (AD < controls, $p < 0.01$) Fig. 1. aMCI-subjects showed reduced coherence compared with controls between ACC and left frontal superior gyrus within delta, theta and alpha1-band. Theta coherence was significantly between anterior and posterior cingulate gyrus, between right and LTG (aMCI < controls, $p < 0.05$) Fig. 3. There were significant differences between FTG and controls, between

ACC and left temporal gyrus in delta and theta (FTG < controls, $p < 0.05$). There were not found significant differences between AD, FTD and nMCI.



Comparison of controls vs. aMCI patients. fMRI activations ($p < 0.001$)



Comparison of aMCI vs. AD patients. fMRI activations ($p < 0.001$)

Conclusion: EEG coherence seems to be a useful approach, which helps to detect the early stage of cognitive decline.

Disclosure: Nothing to disclose.

EPO-003 | Improving FTD diagnosis with NODDI metrics and machine learning integration

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Background and Aims: To investigate microstructural gray matter (GM) and white matter (WM) alterations in FTLD patients and to develop machine learning (ML) algorithm that classifies patients according to NODDI metrics and neuropsychological data.

Methods: Thirty-five behavioral-variant frontotemporal dementia (bvFTD), 20 semantic-variant primary progressive aphasia (svPPA), 14 nonfluent-variant primary progressive aphasia (nfvPPA), 9 semantic-bvFTD (sbvFTD) and 48 controls performed multi-shell diffusion-brain MRI. Fractional anisotropy (FA), Intra-cellular Volume Fraction (ICVF) and Orientation Dispersion Index (ODI) maps were estimated. GM and WM comparisons between FTLD groups were performed. ML algorithm was trained on (i) mean GM/WM values of FA, ICVF and ODI maps subdivided in brain lobes and (ii) neuropsychological data.

Results: FA maps showed widespread WM damage in FTLD patients relative to controls. ICVF maps showed damage in FTLD patients relative to controls in frontotemporal for bvFTD, left temporal-frontal for svPPA and nfvPPA, right temporal for sbvFTD. ODI maps showed a GM reduction with a similar ICVF-GM pattern. WM alterations in patients relative to controls was observed: (i) WM reduction in corpus callosum and corona radiata (bvFTD, svPPA, nfvPPA) and right corona radiata (sbvFTD); (ii) WM increase in temporo-occipital WM bundles (bvFTD) and stria-terminalis (svPPA). ML model

(ICVF + ODI + neuropsychological data) showed a 95.9% accuracy in the classification of each patient syndrome.

Conclusion: NODDI and ML algorithm hold potential for advancing our understanding of FTLD pathology and facilitating diagnosis, personalized treatment strategies at individual-level. Funding: European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease; Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

Disclosure: S Basaia research support from Italian Ministry of Health (IMH). S Pisano, C Cividini, F Facente, EG Spinelli, V Castelnovo, A Ghirelli, F Caso, G Magnani, P Caroppo, S Prioni, C Villa, L Tremolizzo, I Appollonio, F Verde nothing to disclose. E Canu research support from Italian Ministry of Health. G Cecchetti speaker honoraria from Neopharmed Gentili. N Ticozzi consulting services for Amylyx Pharmaceuticals, Zambon Biotech SA and lectures for Italfarmaco; funding from IMH and AriSLA. V Silani consulting services and/or speaking activities for AveXis, Cytokinetics, Italfarmaco; and research support from IMH, AriSLA, and E-Rare Joint Transnational Call. M Filippi consulting or speaking activities or advisory boards for Alexion, Almirall, Biogen, Bayer, Bristol-Myers Squibb,Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM. F Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from IMH, Italian Ministry of University and Research, ARiSLA, ERC, EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease.

EPO-004 | Aging features through connectome analysis and advanced diffusion-weighted metrics with a machine learning approach

S. Basaia[1]; S. Pisano[2]; E. Sibilla[1]; E. Spinelli[3]; E. Canu[1]; M. Filippi[4]; F. Agosta[3]

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Background and Aims: To develop machine learning algorithm combining connectome analysis and advanced diffusion-weighted metrics to classify different features underlying aging process.

Methods: Forty-eight young-controls (YC), 20–31 years, 21 middle-aged [MC] and 44 elderly-controls [EC], 41–85 years, underwent brain multi-shell diffusion-MRI and cognitive evaluation. Fractional anisotropy (FA), Intra-cellular Volume Fraction (ICVF) and Orientation Dispersion Index (ODI) maps were estimated. TBSS and connectomics were performed. Support-vector-machine (SVM) model trained on FA, ICVF and ODI values of all connections resulted different in TBSS and connectomics, was used for the identification of features (TBSS- or connectome-related) of aging process. Features that better distinguished three groups were used as variables in a multivariate polynomial regression to predict subject's age. Correlation coefficient between the predicted age by the model and the age of the subjects.

Results: SVM models showed 99.7% and 100% accuracy in the classification of YC relative to MC/EC, ODI values of TBSS-related connections as best selected feature. SVM models demonstrated 83.4% accuracy between MC-EC groups, identifying FA connections values as the most informative feature for classification. Mean ODI of TBSS- and FA of connectome-related connections were inserted in the multivariate polynomial regression to predict subject's age. Correlation analysis indicated relationship between age-predicted and actual age of subjects ($r = 0.93$; $p < 0.001$).

Conclusion: Combination of SVM and neuroimaging achieved high accuracy in group classification and age prediction, highlighting the potential for understanding brain connectivity patterns and age-related changes. Funding. European-Research-Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer's disease; Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

Disclosure: S Basaia research support from Italian Ministry of Health (IMH). S Pisano, E Sibilla and EG Spinelli have nothing to disclose. E Canu research support from Italian Ministry of Health. M Filippi consulting or speaking activities or advisory boards for Alexion, Almirall, Biogen, Bayer, Bristol-Myers Squibb,Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM. F Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from IMH, Italian Ministry of University and Research, ARiSLA, ERC, EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease.

EPO-005 | Clinical characteristics and biomarker profile in early and late-onset Alzheimer's disease: The Shanghai Memory Study

J. Wu; Z. Xiao; X. Ma; X. Zhou; D. Ding; Q. Zhao
Institute of Neurology, Huashan Hospital, Fudan University, Shanghai, China

Background and Aims: Early-onset Alzheimer's disease (EOAD) constitutes approximately 5%–10% of Alzheimer's disease (AD). Its difference with Late-onset Alzheimer's disease (LOAD) was not well documented. The current study explored their characteristics covering clinical, neuropsychological and biomarker profiles.

Methods: Ninety-ninety patients with LOAD and 104 with EOAD were enrolled from a Chinese hospital-based cohort, the Shanghai Memory Study. Clinical features, cognitive performance, and full-panel of plasma biomarker were compared cross-sectionally. Disease progression and longitudinal cognition change were analyzed as well.

Results: Results: Patients with EOAD presented more severe impairment in global cognition, attention, and language function (all $p<0.05$). Levels of plasma Aβ40, Aβ42, Aβ42/Aβ40, and neurofilament light (NfL) were higher in the LOAD group, while plasma p-tau181 concentration was higher in the EOAD group (all $p<0.05$). After adjusting for age, gender, disease severity, and comorbid disease, younger age at onset (AAO) was associated with lower levels of plasma Aβ40 (B = 1.827, 95% CI 1.205 to 2.450, $p<0.001$), Aβ42 (B = 0.106, 95% CI 0.064 to 0.147, $p<0.001$), and NfL (B = 0.280, 95% CI 0.145 to 0.415, $p<0.001$), while with higher concentrations of p-tau181 (B = −0.040, 95% CI −0.069 to −0.012, $p=0.006$). The level of plasma p-tau181 was significantly correlated with global cognition, memory, attention, and visuospatial function in patients with EOAD, but not in LOAD.

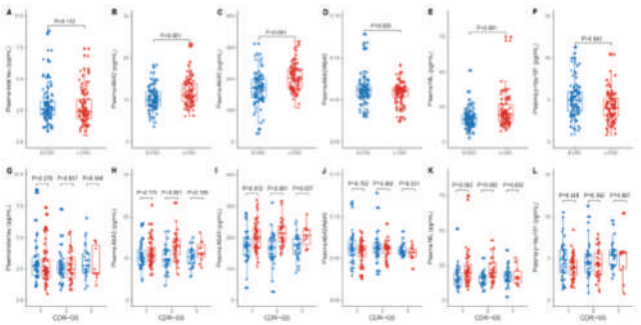

FIGURE 1 Concentrations of plasma biomarkers among patients with different age-at onset and disease severity.

TABLE 2 multiple linear regression of plasma biomarkers and age at onset Note: a mode 1, data were adjusted for CDR-global score, gender, education duration, and APOE genotype; b in model 2, data were adjusted for gender, education duration, CDR-glo.

Plasma biomarkers	Model 1[a]		Model 2[b]	
	B (95%CI)	P value	B (95%CI)	P value
total-tau	-0.011 (-0.033, 0.010)	0.285	-0.017 (-0.038, 0.004)	0.107
Aβ42	0.117 (0.075, 0.160)	<0.001*	0.106 (0.064, 0.147)	<0.001*
Aβ40	2.095 (1.429, 2.760)	<0.001*	1.827 (1.205, 2.450)	<0.001*
Aβ42/Aβ40	0 (0,0)	0.076	0 (0, 0)	0.140
NfL	0.303 (0.166, 0.441)	<0.001*	0.280 (0.145, 0.415)	<0.001*
P-tau181	-0.040 (-0.068, -0.012)	0.006*	-0.040 (-0.069, -0.012)	0.006*

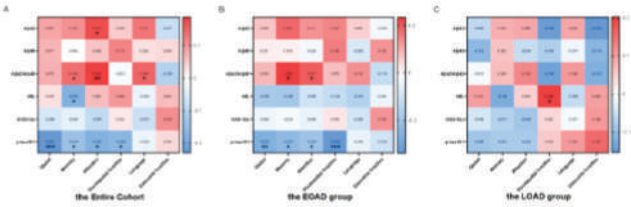

FIGURE 2 correlations between plasma biomarker concentrations and cognitive domains. Note: The plasma biomarkers concentrations were log transformed. A, correlations between plasma biomarker concentrations and cognitive domains in all participants; B, co.

Conclusion: Conclusion: Patients with EOAD differed from LOAD in cognitive performance and biomarker profile. Plasma p-tau181 level showed more tremendous change in EOAD.

Disclosure: Nothing to disclose.

EPO-006 | Sleep disturbances and the impact in neuropsychiatric symptoms in Alzheimer's disease

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Background and Aims: Sleep disturbances are common in Alzheimer's disease (AD), contributing to accelerate cognitive deterioration and

progression of neuropsychiatric symptoms (NPS). Understanding the sleep disturbances in AD can expand our knowledge and improve treatment of NPS. Evaluate the association between sleep disturbances and NPS in patients with AD.

Methods: We performed a cross-sectional study, including patients with the diagnosis of AD supported by biomarkers. NPS were assessed with Frontal Behavioral Inventory (FBI) and Neuropsychiatric Inventory (NPI). Sleep disturbances were evaluated with Pittsburgh Sleep Quality Index (PSQI), STOP-BANG score, Epworth scale (ES) and REM Behavior Disorder screening questionnaire (RBDSQ). Statistical analysis comprised univariate analysis and statistical significance was set at $p<0.05$.

Results: We included 61 patients (68.9% female) with average age of onset of 64.2(±6.8) years. The median education was 4.0 (IQR=5.0) and MMSE of 20 (IQR=8). According to the STOP-BANG score, 11 patients (21.2%) were at intermediate or higher risk of obstructive sleep apnea (OSA) and 18 patients (29.5%) reported sleep disturbances in PSQI (score >5). Total PSQI scores were correlated with FBI indifference ($r=0.031$; $p=0.012$), inattention ($r=0.380$; $p=0.006$), aphasia ($r=0.429$; $p=0.002$) and perseveration ($r=0.294$; $p=0.038$). STOP-BANG score was correlated with FBI indifference ($r=0.290$; $p=0.043$), logopenia ($r=0.358$; $p=0.012$), aphasia ($r=0.513$; $p<0.001$), perseveration ($r=0.440$; $p=0.002$), comprehension deficit ($r=0.316$; $p=0.027$), hyperorality ($r=0.498$; $p<0.001$) and utilization behaviors ($r=0.295$; $p=0.038$). No correlation was found between NPS symptoms and ES and RBDSQ.

Conclusion: Sleep disturbances were associated with NPS frontal dysfunction showing that sleep quality influences the diurnal function of AD patients. Interestingly, patients at higher risk of OSA presented with more prominent frontal features suggesting a possible pattern of AD phenotype related to hypoxia, meriting further studies.

Disclosure: Nothing to disclose.

EPO-007 | Effect of Aβ on Alzheimer's disease tau spreading

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Background and Aims: Alzheimer's disease (AD) is characterized by the accumulation of Amyloid-beta (Aβ) plaques initiated approximately two decades before the symptom onset followed by buildup and spreading of neurofibrillary tau aggregates. Although it has been suggested that the Aβ amplifies tau spreading the observed spatial disparity called it into question. Yet it is unclear how neocortical Aβ remotely affects early pathological tau, triggering it to leave the early formation area, and how Aβ facilitates tau aggregate spreading throughout cortical regions. I aimed to investigate how Aβ can facilitate tau spreading through neuronal connections in the AD pathological process by combining fMRI normative connectomes and longitudinal in vivo molecular imaging data.

Methods: In total, the imaging data of 317 participants including, 173 Aβ-negative non-demented and 144 Aβ-positive non-demented participants have entered the study from ADNI. Furthermore, normative resting-state fMRI connectomes were used to model tau spreading through functional connections.

Results: It was observed that the Aβ in regions with the highest deposition (Aβ epicenter) is remotely associated with connectivity-based spreading of tau pathology. Moreover, Aβ in regions that exhibit the highest tau pathology (tau epicenter) is associated with increased connectivity-based tau spreading to non-epicenter regions.

Conclusion: The findings provide a further explanation for a long-standing question of how Aβ can affect tau aggregate spreading through neuronal connections despite spatial incongruity. The results suggest that Aβ pathology can remotely and locally facilitate connectivity-based spreading of tau aggregates.

Disclosure: Nothing to disclose.

EPO-008 | Solanezumab treatment for Alzheimer disease: Meta analysis for non expedition trials

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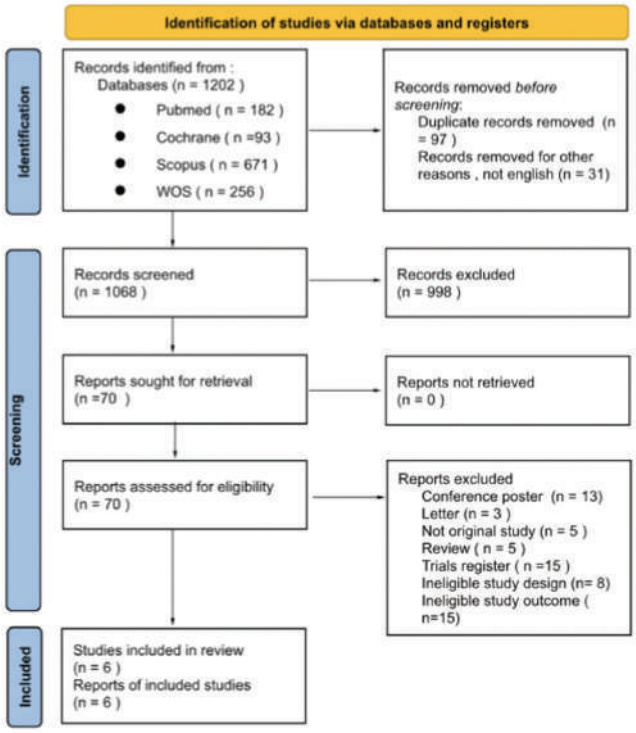
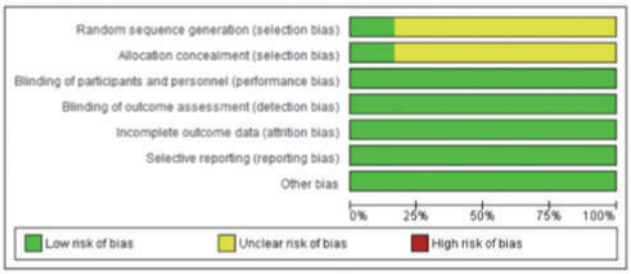
University of Warith Al-Anbiyaa, College of Medicine

Background and Aims: Solanezumab, a monoclonal antibody, has shown promise in treating Alzheimer's disease by targeting beta-amyloid plaques, potentially slowing cognitive decline. Despite mixed initial trials, ongoing research indicates potential benefits.

Methods: It is a systematic review and meta-analysis. We included only RCTs for Non-EXPEDITION Trials. 1202 records were screened based on our search strategy on main database (Pubmed, Scopus, WOS, Cochrane). Continuous Outcomes were pooled using Random Effects, Inverse Variance and Mean Difference.



Flow chart of study selection and included study based on PRISMA



ROB for included study

Results: 6 RCTs, 4956 participant used Solanezumab. 5 RCTs included, outcome of (ADAS-Cog14, ADAS-Cog11, MMSE, CDR-SB Score), intervention number in each Trial (n1 = 578, n2 = 102, n3 = 50, n4 = 1057, n5 = 659). Improvements in cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog14) were observed by 5 studies. The overall pooled results showed that Solanezumab is associated with a significant reduction in ADAS- Cog 14 scores as compared to placebo. (MD −1.18, 95% CI (−1.96, −0.40); $p = 0.003$, $I^2 = 0\%$). Improvements in cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog11) were observed by 2 studies. Pooled analysis showed that Solanezumab is associated with a significant reduction in ADAS- Cog 11 scores as compared to placebo. (MD −1.68, 95% CI (−2.80, −0.55); $p = 0.003$, $I^2 = 0\%$).

Baseline characteristic of included study

Conclusion: Solanezumab treatment for Alzheimer's disease presents a promising avenue in the quest for effective interventions. While its ability to halt or reverse the disease remains uncertain, it offers hope by targeting the underlying amyloid plaques, a key hallmark of Alzheimer's.

Disclosure: Nothing to disclose.

EPO-009 | Gender disparities in down syndrome-associated Alzheimer's disease and related pathologies

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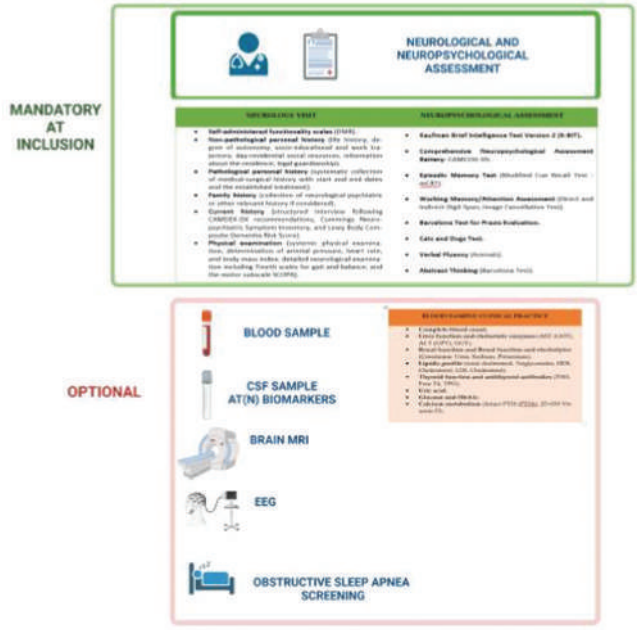
Background and Aims: Down syndrome (DS) constitutes a genetically determined form of Alzheimer's disease (DSAD). While gender differences in risk factors and the clinical course of Alzheimer's have been identified in the general population, this aspect remains unexplored in DS. Our primary aim is to investigate gender influences on DSAD diagnosis and related comorbidities in DS.

Methods: Observational cross-sectional study in a population-based cohort of adults with DS, regardless of intellectual disability (ID) and cognitive status, with dual purposes (clinical and research), from January to December 2023. Conducted adapted neurological-neuropsychological evaluations to determine ID and cognitive status in relation to DSAD. Optional procedures included brain MRI, lumbar puncture for AT(N) biomarker study, and blood analysis, addressing both clinical and research objectives.



Protocol of baseline visit of clinical and research cohort of adults with DS

Results: Recruited 115 participants, 46.9% women, average age 46.32 years (25–65). No gender differences in ID (89.9% mild to moderate) or cognitive status for DSAD (35.6% symptomatic). Similarly, no distinctions in age of cognitive symptom onset (51.1 ± 5.4 years), prodromal (51.4 ± 4.7 years), and DSAD dementia (53.6 ± 5.7 years) diagnosis; and or global cognition, episodic memory, neuropsychiatric inventory, functional autonomy scales, and quantitative neurological assessment (balance, gait scales, and screening for rigid-akinetic syndrome) scores. No differences observed in epilepsy and obstructive sleep apnea prevalence. The only comorbidities with statistically significant differences (more prevalent in women) were hypothyroidism and vitamin D deficiency.

		FEMALE	MALE	
Number of adults with DS		54 (46.9 %)	61 (53.1%)	
ID	Mild	45.7%	37.4%	p = 0.48
	Moderate	47.8%	50%	
	Severe/Profound	6.5%	12.6%	
Diagnosis 1st visit	aDS	60.9%	66.7%	p = 0.29
	pAD	15.2%	5.6%	
	dAD	23.9%	27.8%	
Age 1st visit (mean + SD)		46.9 +/- 9.5 years	45.8 +/- 9.3 years	p = 0.57
Age DSAD symptoms onset		50.9 +/- 5.4 years	51.3 +/- 5.3 years	p= 0.46
Age prodromal DSAD		51.2 +/- 4.7 years	51.5 +/- 4.7 years	p= 0.93
Age dementia DSAD		53.4 +/- 5.7 years	53.4 +/- 5.6 years	p= 0.91
Epilepsy		18.4%	17.5%	p= 0.45
Sleep apnea syndrome		20.4%	24.6%	p= 0.79
Neuropsychiatric symptomatology		28.3%	24.1%	p= 0.63
Hypothyroidism		56.5%	38.9%	p= 0.05
Vitamin D deficiency		45.7%	27.8%	p= 0.05

Down syndrome population data

Conclusion: The influence of gender on the clinical course of symptomatic Alzheimer's and more frequent comorbidities may be lesser, possibly not significant, in genetically determined forms, or at least in DSAD.

Disclosure: Nothing to disclose.

EPO-010 | MHC-II receptor enrichment in locus coeruleus since Alzheimer's disease early stages

N. Rabaneda Lombarte[1]; F. Pereira[2]; A. Ehrenberg[2]; V. Paes[3]; C. Suemoto[4]; R. Leite[4]; R. Rodriguez[4]; R. Ferretti-Rebustini[4]; E. Ferrioli[4]; R. Nitrini[4]; W. Jacob-Filho[4]; C. Pasqualucci[4]; W. Seeley[5]; S. Spina[5]; B. Miller[6]; L. Grinberg[7]

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Background and Aims: The locus coeruleus (LC), a key noradrenergic nucleus for memory and arousal, is an early-damaged region in Alzheimer's disease (AD) with tau vulnerability. The molecular mechanism for this remains unclear. We conducted RNA analysis on LC and substantia nigra (SN), a less vulnerable nucleus, in subjects at progressive AD stages, to explore the molecular basis of LC's selective vulnerability to AD-tau.

Methods: RNA sequencing was conducted on RNA extracted from the LC and SN regions of postmortem brains belonging to healthy controls (HC; $n = 11$) and AD patients ($n = 40$) across distinct Braak stages (BB) (Fig. 1).

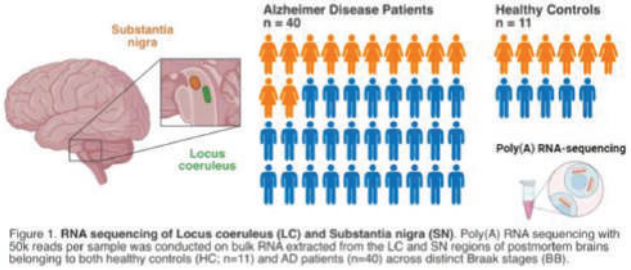

Figure 1. **RNA sequencing of Locus coeruleus (LC) and Substantia nigra (SN)**. Poly(A) RNA sequencing with 50k reads per sample was conducted on bulk RNA extracted from the LC and SN regions of postmortem brains belonging to both healthy controls (HC; n=11) and AD patients (n=40) across distinct Braak stages (BB).

FIGURE 1

Results: Genes linked to the MHC-II receptor ontology term showed upregulation from the initial BB in the LC (Fig. 2). Notably, the expression of HLA-DQB1 gene, a key player in the immune system,

exhibits a 1-fold increase at BB 1 compared to BB 0. In BB 2 and BB 3 cases, an increase in the expression of CD4 and HLA-DRA genes was observed compared to HC. In the advanced stages of the disease (BB 4–6), all MHC-II genes exhibited higher RNA expression compared to HC. Notably, the SN showed none of these changes.

BB1		BB2		BB3		BB4-6	
LC	SN	LC	SN	LC	SN	LC	SN
HLA-DQB1↑	HLA-DQB1	HLA-DQB1	HLA-DQB1	HLA-DQB1↑	HLA-DQB1	HLA-DQB1↑	HLA-DQB1
HLA-DRA ↑	HLA-DRA	HLA-DRA ↑	HLA-DRA	HLA-DRA ↑	HLA-DRA	HLA-DRA ↑	HLA-DRA
HLA-DRB1↑	HLA-DRB1	HLA-DRB1	HLA-DRB1	HLA-DRB1	HLA-DRB1	HLA-DRB1↑	HLA-DRB1
CD4 ↑	CD4	CD4 ↑	CD4	CD4 ↑	CD4	CD4 ↑	CD4
CD74 ↑	CD74	CD74	CD74	CD74	CD74	CD74 ↑	CD74

Figure 2. **Genes linked to the MHC-II receptor gene ontology term fold-change**. Genes in green had no significant fold-change between Braak Stage (BB) indicated in first row and BB 0, while genes in blue had an increased fold-change in BB (indicated in the first row) and BB 0. The comparison was performed in Braak-by-Braak manner, employing a linear regression test for gene differential expression, while accounting for the Braak Stage and correcting for Sex and Age of Death.

FIGURE 2

Conclusion: Multiple lines of evidence back MHC-II involvement in AD. This study uniquely shows early MHC-II activation, especially in the vulnerable human brain region. This suggests therapeutic potential in modulating this axis for AD treatment and offers insights into unknown disease origins. Further research is crucial to validate these findings and explore the earliest AD stages in subcortical nuclei.

Disclosure: NRL was a recipient of the "Rotación Externa de Formación en Neurología" grant from the Spanish Society of Neurology.

EPO-011 | Combined plasma biomarkers for the diagnosis of Alzheimer's Disease in clinical scenario

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Background and Aims: The implementation of plasma biomarkers in clinical settings is pivotal for a rapid screening and diagnosis, as well as for tracking disease progression reducing the costs and burden of CSF assessments. Aim of the study was to evaluate the ability of plasma markers to discriminated Alzheimer's disease (AD) and both healthy controls (HC) and other neurodegenerative diseases (NDD).

Methods: The cross-sectional study included patients with AD (A+T+N+), patients with non-AD NDD, and healthy controls. Each patient underwent standard core-standard CSF analyses, plasma p-tau181, p-tau 217, Aβ42, and Aβ40 were measured using single molecule arrays (SIMOA) analyses. The ability of blood-based biomarkers to detect AD pathology was assessed by using ROC and linear regression analyses.

Results: two-hundred eighty-six individuals, namely 124 AD, 50 NDD, and 112 HC entered the study. P-tau 181, p-tau 217, p-tau 181/Aβ42 ratio, and p-tau 217/ Aβ42 ratio levels were elevated in AD compared to NDD and HC. P-tau 217 biomarker showed the highest area under the receiver operating curve (AUC) for identifying AD from HC (AUC = 0.933), compared to p-Tau 181 (AUC = 0.88) and other considered biomarkers. p-tau 217/ Aβ42 ratio exhibited the highest AUC for identifying AD from NDD (AUC = 0.858).

Conclusion: plasma p-tau 217 was the most accurate biomarker in ruling out AD individuals from HC, whereas its combination with Aβ42 was the best biomarker in identifying AD from other neurodegenerative diseases.

Disclosure: None.

EPO-012 | Primary progressive aphasia in Italian and English: A cross-linguistic cohort study

S. Mazzeo[1]; C. Hardy[2]; J. Jiang[2]; C. Morinelli[3]; V. Moschini[3]; J. Johnson[2]; A. Chokesuwattanaskul[4]; A. Volkmer[5]; J. Rohrer[2]; A. Ingannato[6]; S. Bagnoli[6]; S. Padiglioni[3]; B. Nacmias[6]; S. Sorbi[6]; V. Bessi[6]; J. Warren[2]

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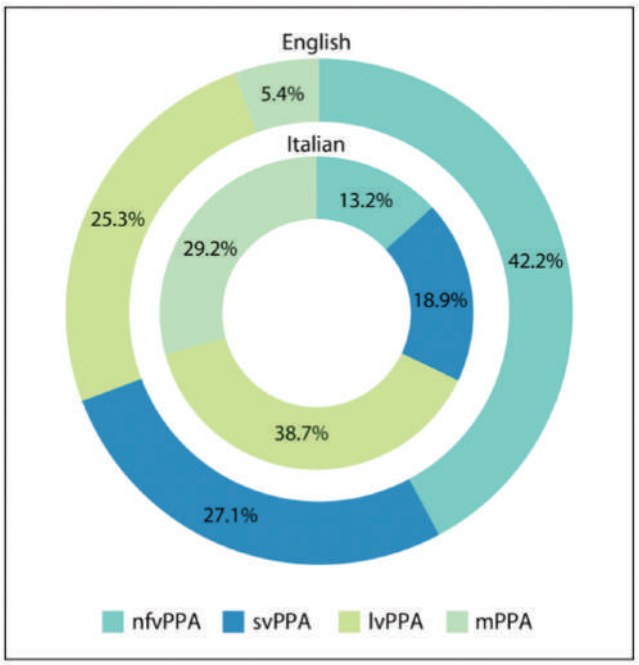
Background and Aims: Primary Progressive Aphasia (PPA) is a neurodegenerative disorder primarily affecting language abilities, with clinical variants (nonfluent/agrammatic variant [nfvPPA], semantic variant [svPPA], logopenic variant [lvPPA], and mixed-PPA [mPPA]) categorized based on linguistic features. This study aims to compare PPA cohorts of native speakers of English and Italian.

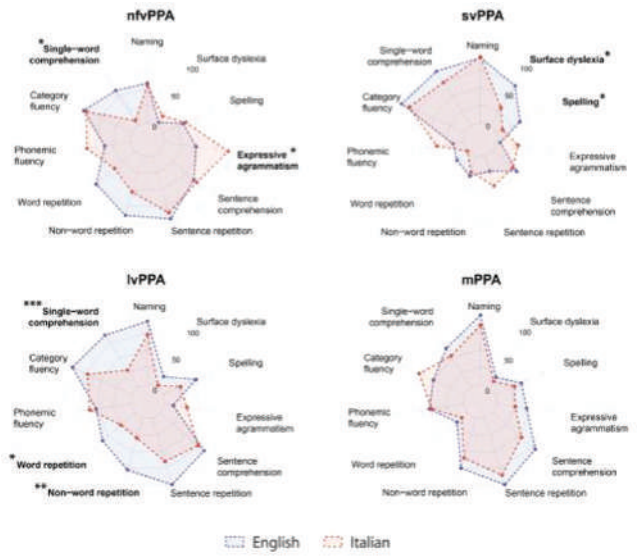
Methods: We considered 166 English participants (70 nfvPPA, 45 svPPA, 42 lvPPA, 9 mPPA) and 106 Italian participants (14 nfvPPA, 20 svPPA, 42 lvPPA, 31 mPPA). Starting from the neuropsychological battery used to assess patients, we extracted one test for each cognitive and linguistic function that can be compared between cohorts. Comparisons were adjusted for symptom duration and Mini-mental State Examination.

Results: The English cohort included a higher proportion of nfvPPA patients (42% vs. 13%, $p < 0.001$), while the Italian cohort showed higher proportions of lvPPA (25% vs. 38%, $p = 0.019$) and mPPA (5% vs. 29%, $p < 0.001$) (Fig. 1). English nfvPPA patients were more frequently impaired in single-word comprehension (60% vs. 8%, $p = 0.013$), while Italian nfvPPA patients exhibited more agrammatism

(46% vs. 93%, $p=0.015$). English svPPA had a higher proportion of surface dyslexia (68% vs. 30%, $p=0.046$) and spelling impairment (38% vs. 10%, $p=0.021$). English lvPPA had broader impairments, including single-word comprehension (89% vs. 29%, $p<0.001$), repetition of words (61% vs. 26%, $p=0.03$), nonverbal working memory (69% vs. 36%, $p=0.005$), and visuospatial perception (89% vs. 25%, $p<0.001$) (Fig. 2).



Donut plots showing proportion of PPA variants in English and Italian cohorts. Significant differences between cohorts are coded as follows: *$p<0.05$ ***$p<0.001$



Profiles of neurolinguistic and general cognitive impairment in the Italian and English cohorts. Significant differences between cohorts are coded as follows: *$p<0.05$; **$p<0.01$; ***$p<0.001$

Conclusion: Language-specific characteristics impact the clinical presentation of PPA. Cultural and linguistic nuances should be considered in PPA diagnosis and management, calling for more tailored assessments and criteria.

Disclosure: Nothing to disclose.

EPO-013 | Distinctive longitudinal cortical atrophy progression patterns in clinical variants of frontotemporal dementia continuum

E. Spinelli[1]; A. Ghirelli[1]; F. Orlandi[2]; E. Canu[3]; S. Basaia[3]; V. Castelnovo[3]; E. Sibilla[3]; G. Cecchetti[4]; F. Caso[5]; G. Magnani[5]; P. Caroppo[6]; S. Prioni[6]; C. Villa[6]; L. Tremolizzo[7]; I. Appollonio[7]; F. Verde[8]; N. Ticozzi[9]; V. Silani[9]; M. Filippi[10]; F. Agosta[1]

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Background and Aims: Recently, diagnostic criteria have been proposed for a variant of frontotemporal dementia (FTD) showing distinctive right temporal damage, named semantic behavioural variant FTD (sbvFTD). Our aim was to describe longitudinal patterns of disease progression for each FTD syndrome, with a particular focus on sbvFTD.

Methods: Our cohort included a total of 59 FTD patients with a diagnosis of behavioral variant of FTD (bvFTD, $n=38$), sbvFTD ($n=8$), or semantic variant of primary progressive aphasia (svPPA, $n=13$), who underwent at least two MRI scans on a 3T scanner. Fifty-two healthy controls underwent the same protocol. Cortical thickness analyses were performed at baseline and longitudinally to describe cortical atrophy progression.

Results: At baseline, patients with sbvFTD had an intermediate atrophy pattern between bvFTD and svPPA, with right-predominant temporal pole involvement associated to significant right frontal atrophy. Longitudinally, bvFTD patients were found to progress

widely bilaterally, while svPPA continued steady progression restricted to the temporal lobes, and sbvFTD showed progression only in the left temporal lobe with limited further volume loss in the right hemisphere.

Conclusion: Our study has characterized structural neuroimaging hallmarks of each FTD variant and recognized variant-specific patterns of disease progression. These findings could aid in the identification of imaging biomarkers able to improve FTD diagnosis and prognostic stratification. Moreover, our results singled out sbvFTD as a relatively distinct entity. Funding. Supported by European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease; Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

Disclosure: EG Spinelli, A Ghirelli, F Orlandi, V Castelnovo, E Sibilla, F Caso, G Magnani, P Caroppo, S Prioni, C Villa, L Tremolizzo, I Appollonio, F Verde have nothing to disclose. E Canu research support from Italian Ministry of Health (IMH). S Basaia research support from Italian Ministry of Health. G Cecchetti speaker honoraria from Neopharmed Gentili. N Ticozzi consulting services for Amylyx Pharmaceuticals, Zambon Biotech SA and lectures for Italfarmaco; funding from IMH and AriSLA. V Silani consulting services and/or speaking activities for AveXis, Cytokinetics, Italfarmaco; and research support from IMH, AriSLA, and E-Rare Joint Transnational Call. M Filippi consulting or speaking activities or advisory boards for Alexion, Almirall, Biogen, Bayer, Bristol-Myers Squibb,Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM. F Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from IMH, Italian Ministry of University and Research, ARiSLA, ERC, EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease.

EPO-014 | Clinical and neuroanatomical characterization of the semantic behavioural variant of frontotemporal dementia

E. Spinelli[1]; A. Ghirelli[1]; E. Canu[2]; S. Basaia[2]; V. Castelnovo[2]; G. Cecchetti[3]; E. Sibilla[2]; G. Magnani[4]; F. Caso[4]; P. Caroppo[5]; S. Prioni[5]; C. Villa[5]; L. Tremolizzo[6]; I. Appollonio[6]; F. Verde[7]; N. Ticozzi[8]; V. Silani[8]; F. Agosta[1]; M. Filippi[9]

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Background and Aims: Semantic behavioral variant of frontotemporal dementia (sbvFTD) is a neurodegenerative condition presenting with specific behavioral and semantic derangements and predominant atrophy of the right anterior temporal lobe (rATL). Our objective was to evaluate clinical, neuropsychological, neuroimaging and genetic features of an Italian sbvFTD cohort, defined according to recently proposed guidelines, compared to semantic variant primary progressive aphasia (svPPA) and behavioral variant FTD (bvFTD) patients.

Methods: Fifteen sbvFTD, 63 bvFTD and 25 svPPA patients and 40 healthy controls were enrolled. Patients underwent clinical, cognitive evaluations and brain MRI. Emerging symptoms of sbvFTD patients were recorded. Grey matter atrophy was investigated using voxel-based morphometry.

Results: sbvFTD patients developed early person-specific semantic knowledge loss (67%), object semantic loss (67%), complex compulsions and rigid thought process (60%). Sequentially, additional behavioral symptoms emerged (apathy/inertia, loss of empathy, anxiety, suspiciousness). sbvFTD patients showed sparing of attentive and executive functions, especially compared to bvFTD, and better performance at language tests, compared to svPPA. sbvFTD had predominant rATL atrophy, almost specular to svPPA. Three sbvFTD patients showed pathogenic genetic variants.

Conclusion: We applied sbvFTD diagnostic guidelines to an Italian cohort, demonstrating that the presence of two out of three core diagnostic criteria (person-specific semantic knowledge loss, mental

rigidity and loss of empathy), along with the evidence of preserved executive functions and frontal lobes at MRI should prompt a diagnosis of sbvFTD. Funding. This study was supported by European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease; Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

Disclosure: EG Spinelli, A Ghirelli, V Castelnovo, E Sibilla, G Magnani, F Caso, P Caroppo, S Prioni, C Villa, L Tremolizzo, I Appollonio, F Verde have nothing to disclose. E Canu research support from Italian Ministry of Health (IMH). S Basaia research support from Italian Ministry of Health. G Cecchetti speaker honoraria from Neopharmed Gentili. N Ticozzi consulting services for Amylyx Pharmaceuticals, Zambon Biotech SA and lectures for Italfarmaco; funding from IMH and AriSLA. V Silani consulting services and/or speaking activities for AveXis, Cytokinetics, Italfarmaco; and research support from IMH, AriSLA, and E-Rare Joint Transnational Call. F Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from IMH, Italian Ministry of University and Research, ARiSLA, ERC, EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease. M Filippi consulting or speaking activities or advisory boards for Alexion, Almirall, Biogen, Bayer, Bristol-Myers Squibb,Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM.

EPO-015 | Gantenerumab for early Alzheimer's disease: A systematic review and meta-analysis

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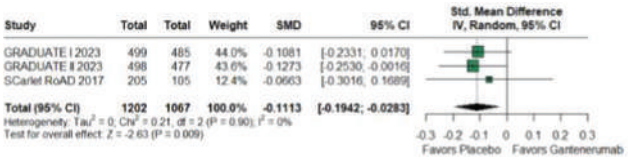
[1]Federal University of Mato Grosso, Sinop, Brazil; [2]Santa Marcelina University, São Paulo, Brazil; [3]Sciences Medical School of Santos, Santos, Brazil; [4]Federal University of Acre, Rio Branco, Brazil; [5]Federal University of Bahia, Anísio Teixeira, Brazil; [6]Faculdade de Saúde Santo Agostinho, Vitória da Conquista, Brazil; [7]Extremo Sul University, Criciúma, Brazil; [8]Feevale University, Novo Hamburgo, Brazil; [9]Department of Medicine, Federal University of Mato Grosso, Sinop, Brazil, [10]Department of Neurology, Massachusetts General Hospital, Brigham and Woman's Hospital, Harvard Medical School, Boston, MA

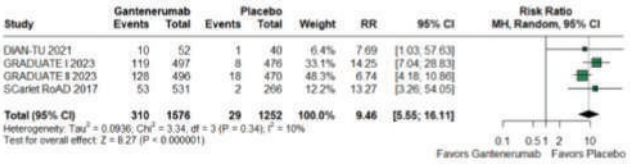
Background and Aims: Gantenerumab is a monoclonal antibody targeting amyloid β protein (Aβ) in early Alzheimer's disease (AD). Hence, we sought to evaluate gantenerumab safety and efficacy in early AD patients.

Methods: MEDLINE, Embase, and Cochrane databases were systematically searched until December 02, 2023. Data were examined using the Mantel-Haenszel method and 95% confidence intervals (CIs). Heterogeneity was assessed using I^2 statistics. Meta-regression analysis was conducted to evaluate a possible link between baseline Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB) and amyloid-related imaging abnormalities (ARIA) at follow-up. R, version 4.2.3, was used for statistical analysis.

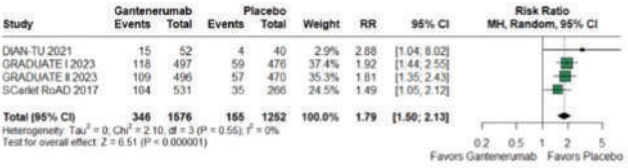
Results: A total of 4 RCTs and 2848 patients were included, of whom 1580 (55%) received subcutaneous gantenerumab. Concerning clinical scores, the placebo group achieved better rates of change in the Disease Assessment Scale (ADAS-Cog13) (SMD −0.1113; 95% CI −0.1942 to −0.0283; $p=0.009$; $I^2=0\%$). Gantenerumab was strongly associated with the occurrence of ARIA-E and ARIA-H: (19.67% vs. 2.31%; RR 9.46; 95% CI 5.55–16.11; $p=<0.000001$; $I^2=10\%$) and (21.95% vs. 12.38%; RR 1.79; 95% CI 1.50–2.13; $p=<0.000001$; $I^2=0\%$), respectively. Only injection site events showed a statistically significant difference between groups, tending towards the placebo group (17.64% vs. 7.53%; RR 2.23; 95% CI 1.81–2.73; $p=<0.000001$; $I^2=61\%$). The meta regression between baseline CDR-SB and ARIA showed no significant link.



ADAS-Cog 13



ARIA-E



ARIA-H

Conclusion: In this meta-analysis, consistent results suggest that gantenerumab is not safe and efficient for early AD, showing no improvement in clinical scores for AD and being associated with the occurrence of ARIA-E, ARIA-H, and injection site events.

Disclosure: The authors declare that they have no disclosure.

Autonomic nervous system diseases 1

EPO-016 | Haemodynamic determinants of supine hypertension in patients with classical orthostatic hypotension

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Background and Aims: The underlying mechanisms of, and relation between supine hypertension (SH), classical orthostatic hypotension (cOH), and the severity of the orthostatic systolic blood pressure (SBP) fall are currently largely unknown. We investigated the relative importance of heart rate (HR), stroke volume (SV) and total peripheral resistance (TPR) to these issues.

Methods: Tilt table tests recorded with beat-to-beat BP recordings (Finapres NOVA and BMEye Nexfin) were assessed and divided in four groups: Controls without SH (SH−; i.e., supine SBP < 140 mmHg) ($n = 19$), controls/SH+ ($n = 61$), cOH/SH− ($n = 30$) and cOH/SH+ ($n = 50$). We used linear regression to relate cOH severity to supine SBP, and used the logratio method to analyse the relative contributions of hemodynamic parameters to upright BP. We used a p value of 0.003 after Bonferroni correction.

Results: In both patients and controls high supine SBP was caused by high TPR (Figure 1). The orthostatic SBP fall increased with supine SBP in patients (Figure 2). The main difference in the upright position between cOH/SH+ and cOH/SH− patients was TPRLR, which was higher in cOH/SH− than in cOH/SH+ ($p < 0.002$). A secondary difference was that SVLR decreased more in cOH/SH− than in cOH/SH+ ($p < 0.003$) (Figure 3). HRLR had similar relative contributions to orthostatic SBP ($p = 0.028$) (Figure 3).

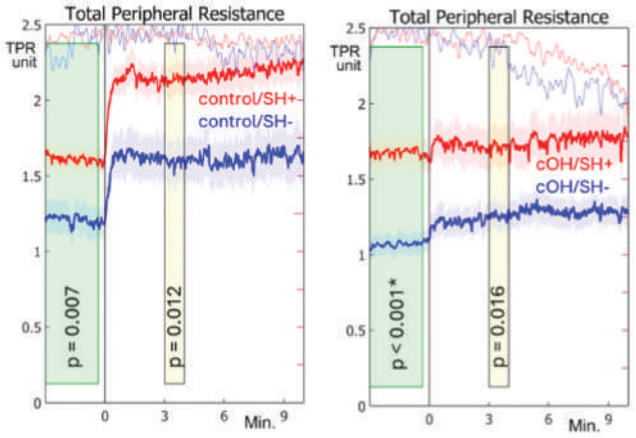

FIGURE 1 Measured total peripheral resistance (TPR) over time. The black line indicates completion of tilt. Both orthostatic hypotension (cOH) patients and controls are divided by the SBP>140 mmHg criterion for supine hypertension (SH). * = Significant.

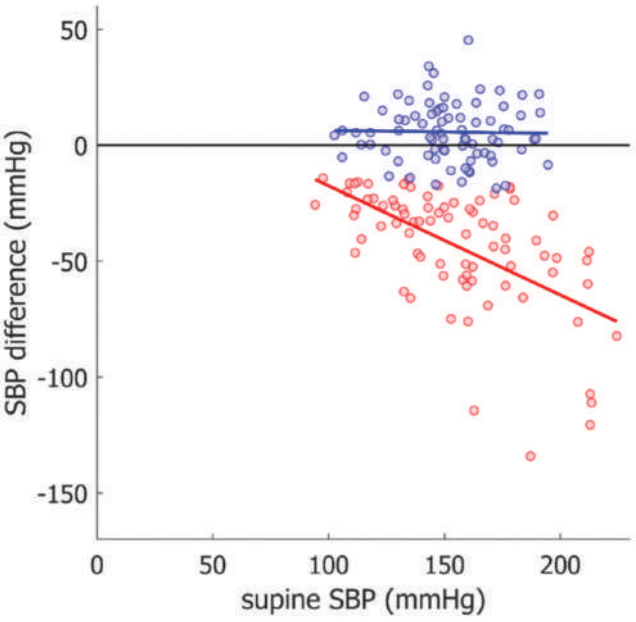

FIGURE 2 Relationship between the blood pressure fall three minutes after tilt and the supine blood pressure for controls (blue) and orthostatic hypotension patients (red).

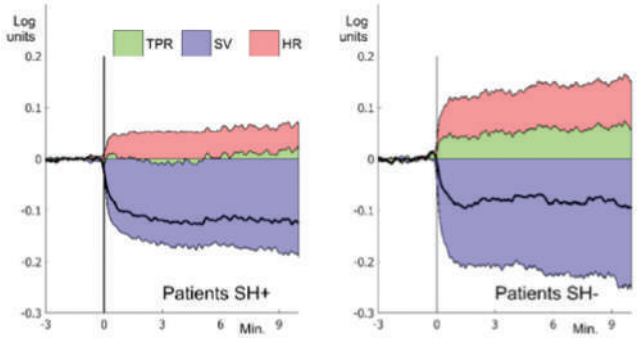

FIGURE 3 Relative contributions of the three hemodynamic parameters to orthostatic blood pressure. Orthostatic hypotension patients are divided by the SBP>140 mmHg criterion for supine hypertension (SH). The black line shows the mean arterial pressure.

Conclusion: High supine TPR explained SH; a failure to increase TPR explained the orthostatic SBP fall. The latter was likely due to autonomic failure, which can however not directly explain high supine TPR. Explaining this requires other mechanisms, such as residual sympathetic tone, denervation supersensitivity or humoral factors.
Disclosure: AvdS was supported by MJFF grant MJFF-020200.

EPO-017 | Morphological and functional assessment of the vagus nerve in multiple sclerosis

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Background and Aims: Autonomic dysfunction (AD) has been linked to vagal nerve atrophy in some neurodegenerative diseases, but atrophy of the vagus nerve in multiple sclerosis (MS) and its association with AD has not been studied. The aim of this study was to determine the relationship between the cross-sectional area (CSA) of the vagus nerve and parasympathetic function in people with MS (pwMS) and healthy controls (HC).
Methods: 40 pwMS (65.0% females, 36.03±9.08 years) and 39 HC (79.5% females, 38.23±7.19 years) were enrolled. The subjects underwent an ultrasound of the vagus nerve and testing of the parasympathetic nervous system was evaluated with the respiratory sinus arrhythmia (RSA), Valsalva ratio (VR) and heart rate variability (HRV).
Results: The mean vagal CSA in pwMS was 1.98±0.44 mm^2 on the right and 1.72±0.39 mm^2 on the left side. The mean vagal CSA in the HC group was 2.08±0.53 mm^2 on the right and 1.73±0.36 mm^2 on the left side. There was no significant difference between the two groups in right ($p=0.33$) or left ($p=0.90$) vagal CSA. In the HC, there was significant correlation between right vagal CSA and RSA (rp=0.330, $p=0.040$), and right-left vagal CSA ratio and RSA (rp=0.345, $p=0.031$). The right-left vagal CSA ratio correlated with the LF/HF (rp=0.322, $p=0.049$). No correlation was observed in pwMS.
Conclusion: The ultrasound characteristics of the vagal nerves correlate with the parasympathetic nervous system measures in HC. This correlation was not observed in pwMS.
Disclosure: Nothing to disclose.

EPO-018 | Peripheral visual exploration in postural tachycardia syndrome is reduced during standing: The cause of tunnel vision?

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Background and Aims: Patients with postural tachycardia syndrome (POTS) report strongly disturbing visual symptoms such as tunnel vision and focusing problems in everyday life, but this phenomenon has not yet received any attention from research. The aim of this study was to characterise visual symptoms in POTS and to investigate possible underlying pathophysiological mechanisms.
Methods: Fifteen patients with POTS and 15 healthy controls were included in this study. Hemodynamics, (visual) symptoms, eye movements and pupil diameter were measured in all participants during free exploration of images in the supine position and during 60° head-up tilt using continuous cardiovascular monitoring, subjective symptom assessment and eye tracking.
Results: During head-up tilt, patients with POTS showed a reduced number and duration of fixations as well as a reduced number, peak velocity and amplitude of saccades compared to their supine eye movements and to those of healthy subjects. This reduction in visual exploration occurred mainly in the peripheral two-thirds of the visual field and paralleled the onset of subjective visual symptoms. There were no differences in the saccade main sequence between the two groups in either body position. The pupil diameter of patients increased excessively during head-up tilt.

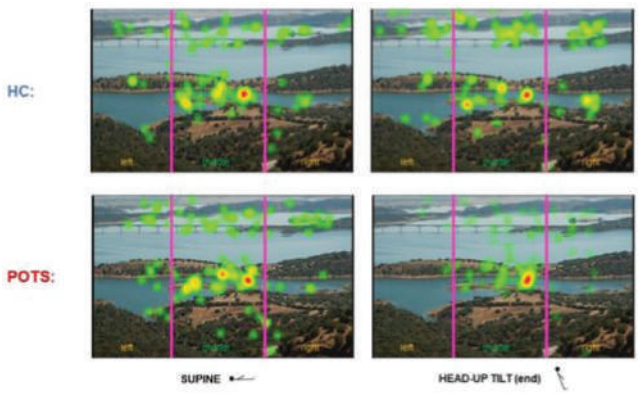
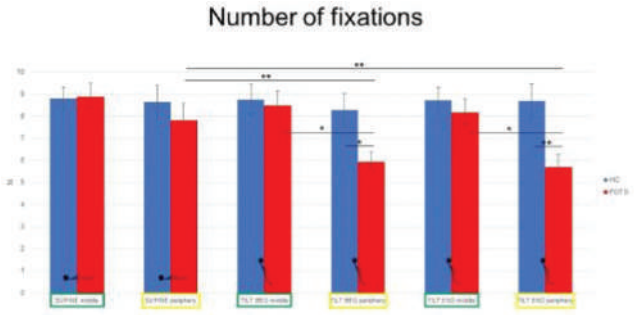
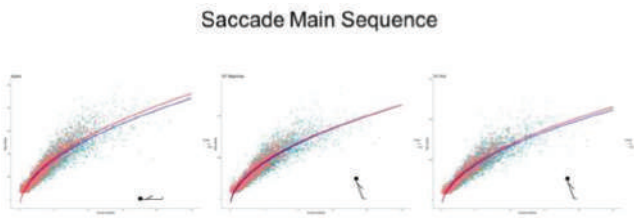


Illustration of fixations. The darker the marking, the more strongly the area was fixated. The image was divided into three areas of interest, whereby the values of the left and right areas were cumulated and used as "periphery" for further analysis.



Bar graphs showing the number of fixations of POTS (red) and healthy controls (blue) in the supine position, during the first and last half of a ten-minute 60° head-up tilt. Values are given as means ± S.E.M. *$p \leq 0.05$, **$p \leq 0.01$.



Saccade main sequence (relationship of saccade peak velocity (degrees/second) and amplitude (degrees)) shown for POTS (red) and healthy controls (blue) in the supine position, during the first and last half of a ten-minute 60° head-up tilt.

Conclusion: Patients with POTS have a reduced exploration of the peripheral visual field exclusively in the upright body position, possibly leading to tunnel vision. Since the saccade main sequence was normal in patients in both body positions, the reduction of peripheral visual exploration is likely due to a position-dependent dysfunction of the frontal eye field.

Disclosure: Nothing to disclose.

EPO-019 | Autonomic dysfunction in people with multiple sclerosis: A 6-year longitudinal study

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Background and Aims: The aim of this study was to investigate the evolution of autonomic dysfunction in pwMS over a six-year follow-up.

Methods: This was a prospective cohort study in which 121 consecutive pwMS (85 females, age at baseline 32.2 ± 8.7 years) were enrolled at the time of diagnosis and evaluated every two years for six years. ANS symptoms were evaluated with the Composite Autonomic Symptom Score (COMPASS-31). Heart rate (HR) and blood pressure (BP) responses to the Valsalva maneuver, HR response to deep breathing (RSA), BP response to passive tilt and quantitative sudomotor axon reflex test (QSART) were performed with CNSystems Task Force® Monitor device. The severity and distribution of ANS function was quantified using adrenergic (AI), cardiovagal (CI) and sudomotor (SI) indices of the Composite Autonomic Severity Scale (CASS).

Results: There was no significant change in the frequency of autonomic symptoms measured with COMPASS-31 over the years ($p = 0.454$). During the follow-up, there was a significant progression of autonomic dysfunction (31% of pwMS experienced conversion of the CASS score from 0 at baseline to >0 at year 6, $p = 0.038$). This difference was mainly driven by progression of parasympathetic (19% of pwMS experienced conversion of the CI from 0 at baseline to >0 at year 6, $p = 0.001$) and sudomotor (32% of pwMS experienced conversion of the SI from 0 at baseline to >0 at year 6, $p = 0.003$) dysfunction. Increase in age was an independent predictor of progression of autonomic dysfunction (Exp(B) 1.107, 95% CI 1.038–1.180).

Conclusion: Substantial proportion of pwMS experience progression of autonomic dysfunction over time.

Disclosure: Nothing to disclose.

EPO-020 | Delayed orthostatic hypotension in Parkinson's disease and in the aging general population

B. Calió[1]; F. Leys[1]; G. Matteucci[2]; N. Campese[1]; G. Rivasi[2]; G. Goebel[1]; G. Testa[2]; R. Granata[1]; S. Duerr[1]; J. Ndayisaba[1]; K. Radl[1]; M. Thurner[1]; K. Seppi[1]; W. Poewe[1]; S. Kiechl[1]; A. Ungar[2]; G. Wenning[1]; M. Rafanelli[2]; A. Fanciulli[1]

[1]*Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria;* [2]*Department of Geriatrics, Careggi University Hospital, Florence, Italy*

Background and Aims: Delayed orthostatic hypotension (dOH) is considered a prodromal form of classic OH (cOH), but its frequency and associated clinical features in Parkinson's disease (PD) and aging individuals are not well known.

Methods: We retrospectively studied individuals with PD and age-matched aging individuals without parkinsonism referred to the Innsbruck and Florence dysautonomia centers for head-up tilt-test under continuous noninvasive blood pressure (BP) monitoring. In both study cohorts, we reviewed the medical records of the 6 months preceding and following the examination for history of syncope and falls.

Results: Two-hundred thirteen individuals with PD [35% women; 73(69; 76) years of age; 6 (3; 10) years of disease duration] and 213 age-matched aging individuals [45% women; 73(69; 77) years of age] were included. DOH occurred in 18% of patients with PD and 9% of the aging individuals, and was significantly associated with a diagnosis of PD [OR = 2.69 (95% C.I.: 1.3–5.7), $p = 0.010$]. Patients with PD had a more severe systolic BP fall during prolonged head-up tilt

with respect to aging individuals ($p < 0.001$). Syncope and syncope-related falls history were more frequent in the aging individuals ($p < 0.001$).

Conclusion: Delayed OH is more common in PD than in aging individuals. In PD, the systolic BP fall drives dOH development and the slow onset of symptoms may reduce the occurrence of syncope-related falls. Nonetheless, due to the frequency of dOH and its potential progression into cOH, a closer monitoring of the affected individuals should be considered.

Disclosure: Nothing to disclose.

EPO-021 | Long-term efficacy of antihypotensive drugs for neurogenic OH: Real-world data in patients with alpha-synucleinopathies

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Background and Aims: Treatment of neurogenic orthostatic-hypotension (nOH) relies on consensus-based approaches; real-world data on long-term efficacy and safety are lacking. We evaluated response to anti-hypotensives in a longitudinal cohort of patients with synuclein-related nOH (PAF, PD, DLB and MSA).

Methods: Severity of cardiovascular autonomic failure was assessed with autonomic function testing. Response to medications was measured with a semi-composite questionnaire assessing the number of falls/month and hospitalizations/trimester, the burden of orthostatic symptoms, quality of life (OHQ, SF-36, PGI scale) and BP monitoring (with structured diary and ambulatory monitoring). Demographic measures are reported as median + IQR, all other measures as mean ± SD.

Results: 101 patients completed the questionnaire (49-PAF, 27-PD, 21-MSA and 4-DLB). 61 patients were on long-term treatment (26 on one, 35 on multiple anti-hypotensives); 40 on non-pharmacological measures, due to early-stage disease, severe supine-hypertension, immobilization, or medication unresponsiveness. Number of falls and hospital admission were 2 ± 12 and 0.3 ± 1 respectively. The OHQ composite score (range 1–10) was 7.24 ± 1.7. SF36 physical and mental composite scores (range: 0–100) were 33.2 ± 37.5 and 38.9 ± 37.8 respectively. PGI score (range: 1–7) was 4.7 ± 1.4. The magnitude of nOH was 56/27 (±34/19) mmHg in treated patients, compared to 29/6 (±22/11) mmHg in those untreated.

Conclusion: Despite multiple anti-hypotensive use, two-thirds of patients were significantly symptomatic with nOH, as corroborated by falls rates and hospital admissions. These findings emphasized the critical nature of nOH, its current gaps in pharmacological management and its profound impact on patients' daily functioning.

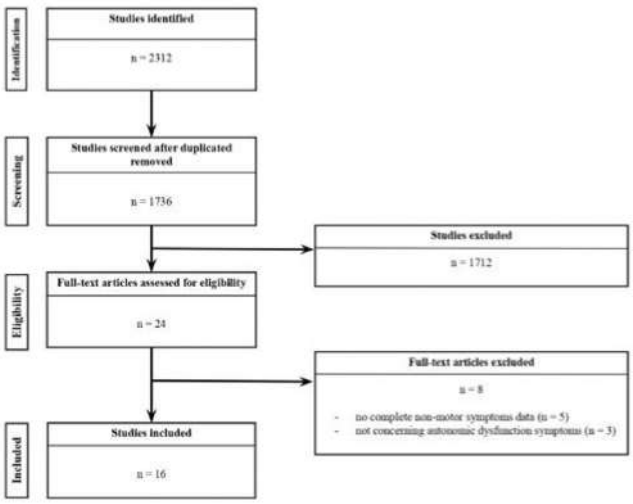
Disclosure: Nothing to disclose.

EPO-022 | A systematic review of the effects of LCIG infusion on autonomic symptoms in advanced Parkinson's disease

S. Galli[1]; L. De Carolis[1]; E. Bianchini[1]; M. Alborghetti[1]; B. Calió[2]; P. Pacilio[1]; A. Fanciulli[2]; F. Pontieri[1]; D. Rinaldi[1]
[1]*Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy;* [2]*Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria*

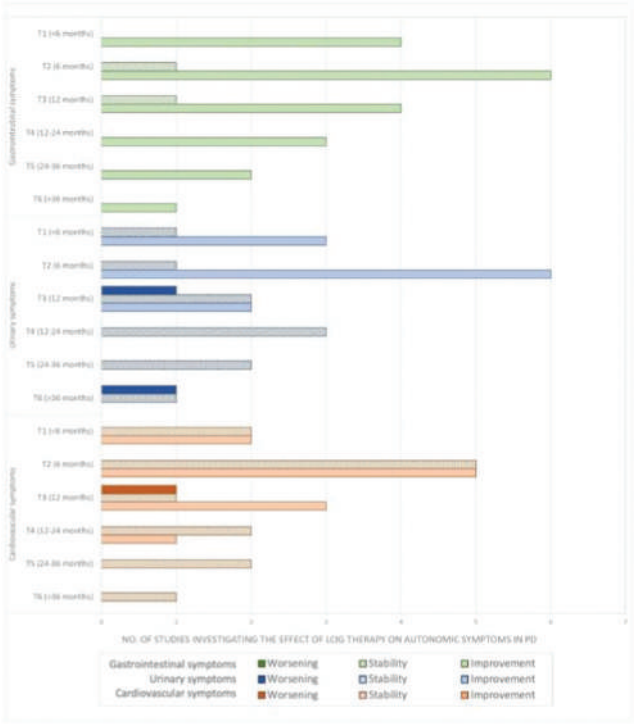
Background and Aims: Autonomic dysfunction significantly affects Parkinson's disease (PD) patients' quality of life, especially in the advanced stages. Levodopa/carbidopa intestinal gel (LCIG) infusion represents an established therapeutic approach for advanced PD characterized by severe motor complications and is considerably helpful in addressing some non-motor symptoms (NMS). However, the impact of LCIG on autonomic symptoms remains less elucidated. We conducted a systematic review to investigate the influence of LCIG therapy on autonomic dysfunction in patients with PD.

Methods: Following the PRISMA guidelines, we systematically searched Pubmed for studies reporting autonomic outcome measures in LCIG-treated PD patients published between January 2005 and June 2023 (Figure 1).

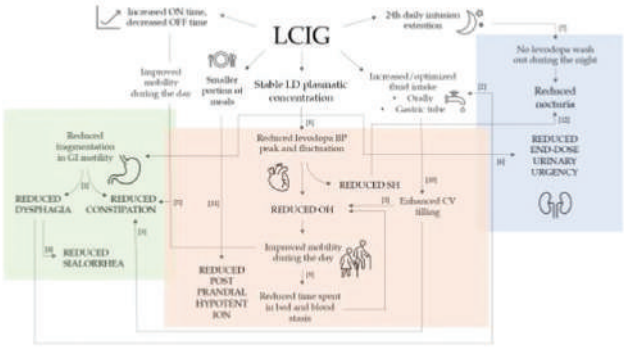


Flowchart of the systematic review process.

Results: Among the 2,312 studies identified, 16 met the inclusion criteria and underwent quality assessment and data extraction, encompassing a cohort of 1,361 patients with Parkinson's disease (PD) (Figure 2). Thirteen studies reported improvement or stability in gastrointestinal, urinary, and cardiovascular symptoms throughout the interventional period. Conversely, one study reported worsening cardiovascular symptoms, while two studies observed worsening urological symptoms. Regarding safety, seven studies reported gastrointestinal (8.4%), urinary (0.5%), cardiovascular (1.1%), and autonomic LCIG-related AEs.



Number of studies reporting improvement, stability, or worsening of gastrointestinal, urinary, and cardiovascular symptoms at each timepoints.



Proposed mechanisms for LCIG's beneficial effects on autonomic symptoms in PD.

Conclusion: LCIG infusion is relatively safe and may help reduce autonomic symptoms burden in advanced PD.
Disclosure: Nothing to disclose.

EPO-023 | Characterize autonomic involvement and its correlation with electrophysiological parameters in various subtypes of GBS

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All India Institute of Medical Sciences, New Delhi

Background and Aims: GBS is an inflammatory demyelinating disorder of peripheral nerves. About 2/3 rd of patients of GBS have autonomic dysfunction. No studies have clearly mentioned type and severity of autonomic dysfunction in different types of GBS.
Methods: This was a prospective cohort study in which 68 patients of GBS underwent clinical workup along with autonomic function testing (heart rate variability with deep breathing, orthostatic blood pressure measurement, isometric handgrip test, cold pressor test and valsalva manoeuvre). The study was done in All India Institute of Medical Sciences, New Delhi. Autonomic function tests were done at two times, at admission and at 15th day. Primary outcome was to determine the predominant pattern of autonomic dysfunction in subtypes of GBS.
Results: 71 patients were screened for eligibility and 68 patients completed the study. At baseline, 79% of patient had dysfunction on laboratory autonomic function tests while only 25% had positive scores on Composite Autonomic Symptom Score (COMPASS-31). Sympathetic dysfunction was the predominant abnormality accounting for 85.71% patients in AIDP group and 68.18% patients in axonal group (AMAN and AMSAN) combined. There was no correlation of any pattern of autonomic dysfunction with degree of axonal involvement ($p = 0.681$).
Conclusion: This study showed that sympathetic dysfunction is the predominant pattern of autonomic involvement in GBS patients. No correlation could be found out between types of autonomic dysfunction and variants of GBS/degree of axonal involvement in axonal variants.
Disclosure: Nothing to disclose.

EPO-024 | Nuclear imaging and autonomic biomarkers predict phenoconversion in pure autonomic failure

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[1]*Autonomic Unit, National Hospital for Neurology and Neurosurgery, London, UK;* [2]*Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, University College London, London, UK;* [3]*UCL Queen Square Institute of Neurology, Faculty of Brain Sciences, University College London, London, UK;* [4]*Institute of Nuclear Medicine, UCLH NHS Foundation Trust, London, UK*

Background and Aims: Abnormal DaTSCAN is a potential biomarker of central nervous system involvement in pure autonomic failure (PAF) and can predict phenoconversion to more widespread alpha-synucleinopathies. We aimed to describe whether combining DaTSCAN, MIBG cardiac scintigraphy and autonomic biomarkers can help assess likelihood of phenoconversion.
Methods: As part of our longitudinal program on alpha-synucleinopathies, the Queen Square Autonomic Prodromal Project (QSA-PRODROMAL), a subgroup of consecutive patients with an initial diagnosis of PAF underwent a multimodal assessment with cardiovascular autonomic function performed with Finapres NOVA, DaTSCAN and cardiac MIBG.

Results: 23 PAF patients with available DaTSCAN and cardiac MIBG were included. Within a median disease duration of 8 (IQR 6–12) years, 6 patients phenoconverted: 2 to Lewy body disorders ([LBD], 1 to Parkinson's disease and 1 to dementia with Lewy bodies), 1 to multiple system atrophy (MSA), and 2 met the research criteria for possible prodromal MSA. Nuclear imaging was abnormal up to 4 years prior to phenoconversion. Both LBD had abnormal DaTSCAN and cardiac MIBG with low supine plasma noradrenaline levels (<200 pg/ml). MSA had abnormal DaTSCAN, normal cardiac MIBG and normal supine plasma noradrenaline levels (>200 pg/mL). The 2 possible prodromal MSA had preserved cardiac innervation and either normal (cerebellar) or abnormal (parkinsonian) DaTSCAN, depending on their clinical phenotype.

Conclusion: The combination of DaTSCAN, cardiac MIBG and catecholamine profiles identified PAF patients at risk of developing other alpha-synucleinopathies and helped predate their phenoconversion by up to 4 years.

Disclosure: The authors have nothing to disclose.

EPO-025 | Pain subtypes and sleep dysfunction in Parkinson's disease

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[1]*Department of Neurology, County Clinic Hospital, Brasov, Romania;* [2]*Faculty of Medicine, Transilvania University, Brasov, Romania*

Background and Aims: In Parkinson's disease (PD), sleep is often affected, pain being among the possible causes. This can lead to difficulties in initiating and maintaining sleep, one of the consequences being sleep fragmentation. We aimed to characterize the link between pain and sleep dysfunction in patients with Parkinson's disease.

Methods: 131 PD patients were enrolled in this case-control study. Pain domains (according to the King's Parkinson's Disease Pain Scale-KPPS) were analyzed according to the presence of sleep disturbances. Based on a Pittsburgh Sleep Quality Index (PSQI) score >5, patients with PD were considered "bad sleepers", and those with a score ≤5 were considered "good sleepers".

Results: 33 (25.19%) patients fell into the "good sleepers" category, and 98 (74.8%) into the "bad sleepers" category. "Bad sleepers" patients presented more significant pain than "good sleepers" for all the component domains of the KPPS scale, the results for the following domains being statistically significant: musculoskeletal pain (5.48 ± 3.50 vs. 2.70 ± 2.67, $p < 0.001$), chronic pain – respectively central pain (1.19 ± 2.01 vs. 0.15 ± 0.71, $p = 0.004$), nocturnal pain – respectively pain in relation to akinesia (2.26 ± 2.74 vs. 0.64 ± 1.22, $p = 0.001$) and radicular pain (4.35 ± 4.20 vs. 2.45 ± 3.55, $p = 0.022$).

Conclusion: The majority of the patients assessed have a diminished quality of sleep. In their case, pain is more prominent than in individuals with uninterrupted sleep. Focusing on treatment of pain would potentially improve the sleep of these PD patients.

Disclosure: Nothing to disclose.

EPO-026 | Circadian rhythm in patients with hereditary transthyretin amyloidosis and asymptomatic mutation carriers

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Background and Aims: Hereditary or variant transthyretin amyloidosis (ATTRv) is a life-threatening disease with effective disease modifying treatments (DMT). Cardiovascular autonomic failure is a key feature. Abnormal circadian blood pressure (BP) rhythm might represent a risk factor for cardiovascular events. This study evaluates BP profile in ATTRv patients and carriers.

Methods: 97 patients with ATTRv and 12 TTR mutation carriers underwent ambulatory 24h BP measurements (ABPM; 29% females, mean age 58y, range 28–78 y, 43% T60A mutation). Dipping profile was defined according to the consensus criteria. Autonomic function testing (AFT) included tilt table/standing/pressor tests, heart rate responses to Valsalva Manoeuvre and deep breathing using Finapres NOVA.

Results: 54/97 patients were on treatment affecting BP (22 on pressor agents, 39 on antihypertensives), carriers had no treatments affecting BP. 74/109 subjects showed an abnormal dipping profile: 53 had reduced dipping, 21 were non- or reversed dippers. 4/74 subjects were carriers (all reduced dippers): three had mild AFT impairment, one was normal. 6/8 carriers with normal ABPM showed abnormal AFT. Only two carriers and two patients had unremarkable autonomic assessment throughout. No significant dipping profile difference was found at first assessment in patients with (12/97) or without DMT.

Conclusion: Pathologic BP profiles are common in ATTRv and may be an early feature in certain carriers. Both ABPM and AFT are needed to detect subtle autonomic impairment. ABPM might be a useful screening tool but does not allow for quantitative parasympathetic/

sympathetic assessment requiring formal AFT. Longitudinal studies are needed to investigate changes in circadian rhythm and their response to DMT.

Disclosure: LS holds a grant from the University of Basel, Switzerland. GC, AT, GTI, CA, CJW, MMR, CJM: nothing to disclose. JDG provides consultancy for Alnylam, AstraZeneca, Bridgebio, Ionis, Intellia and ATTRalus. VI is supported by the National Institute for Health Research, University College London Hospitals Biomedical Research Centre.

EPO-027 | Sympathetic dysfunction as an early autonomic indicator in Parkinson's disease without orthostatic hypotension

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Background and Aims: This study aimed to evaluate the characteristics of autonomic dysfunction in drug-naïve patients with early-stage PD without orthostatic hypotension (OH) by analyzing Valsalva maneuver (VM) parameters.

Methods: Drug-naïve patients without orthostatic hypotension ($n=61$) and controls ($n=20$) were retrospectively analyze. The patients were subcategorized into early-PD ($n=35$) and mid-PD ($n=26$) groups based on the Hoehn and Yahr staging. VM parameters driven by Finapres®, including changes in systolic blood pressure at late phase 2 (ΔSBPVM2), ΔHRVM3, Valsalva ratio (VR), pressure recovery time, adrenergic baroreflex sensitivity, and vagal baroreflex sensitivity, were assessed.

Results: In the early-PD group, ΔSBPVM2, a marker of sympathetic function, was significantly lower compared to that in controls (risk ratio = 0.95, $p=0.027$). Receiver operating characteristic (ROC) curve analysis showed an optimal cutoff value of −10 mmHg for ΔSBPVM2 ($p=0.002$, area under the curve [AUC]: 0.737) and 17 mmHg for ΔDBPVM2 ($p=0.002$, AUC: 0.736). VR and age exhibited an inverse relationship with Unified Parkinson's Disease Rating Scale Part 3 scores (VR: $p=0.038$, $\beta=-28.61$; age: $p=0.027$, $\beta=0.35$) in the multivariable regression analysis.

Conclusion: The ΔBPVM2 parameter of the VM may help detect autonomic nervous system involvement in early-PD without OH. Our results suggest that sympathetic dysfunction is an early manifestation of autonomic dysfunction in patients with PD.

Disclosure: Nothing to disclose.

EPO-028 | Longitudinal assessment of sudomotor dysregulation in amyotrophic lateral sclerosis: A multimodal functional study

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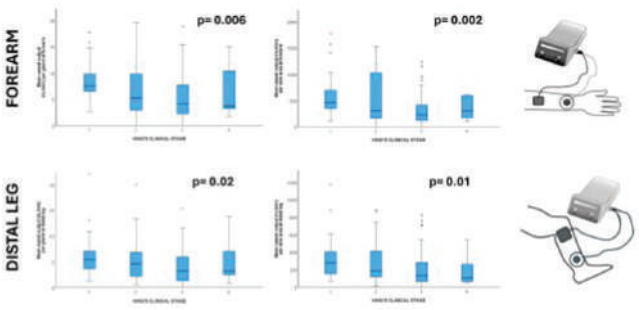
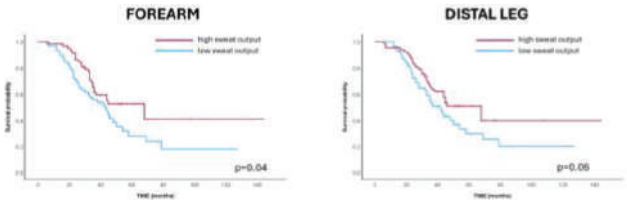
Background and Aims: Among autonomic complaints, sudomotor symptoms have been described in approximately one-quarter of patients with amyotrophic lateral sclerosis (ALS). However, no study has systematically investigated their correlations with the onset and severity of the disease, as well as progression over time. Here we used a multimodal approach to answer these questions in a large cohort of ALS patients

Methods: Patients underwent functional assessment of sudomotor dysfunction by clinical questionnaires and dedicated instruments, such as sympathetic-skin-response (SSR) and dynamic-sweat-test (DST) recorded at upper and lower limbs at recruitment, after 6 and 12 months.

Results: ALS patients ($n=125$), compared with HC ($n=30$), complained of more thermoregulatory symptoms ($p=0.001$), with a significant reduction in sweat output at DST and SSR amplitude at upper and lower limbs (all $p<0.05$). Across clinical stages, patients displayed a significant reduction in overall sweat output (all $p<0.02$), a result confirmed by longitudinal study ($p<0.001$). Bulbar onset patients showed more autonomic symptoms and thermoregulatory disturbances than spinal onset patients, interestingly functional study disclosed significant difference for SSR, but not for DST between the two groups, suggesting an impairment of central-brainstem circuits underlying thermoregulatory dysfunction in the bulbar phenotype. Finally, survival analysis showed that reduction of total sweat output at upper limb was significantly associated with poor prognosis ($p=0.04$).



DYNAMIC SWEAT TEST ACROSS CLINICAL STAGES IN ALS PATIENTS



Kaplan-Meier curves of survival probability of ALS patients stratified according to the total sweat output at the dynamic sweat test

Conclusion: Sudomotor disturbance is part of the non-motor symptoms of ALS patients, worsening in parallel with motor disability and being more pronounced in bulbar phenotype. Functional assessment of sudomotor dysregulation could be considered as a potential biomarker of disease progression in ALS.
Disclosure: None.

EPO-029 | Association of fibromyalgia severity with patients' mood, sleep quality, quality of life and autonomic dysfunction

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Background and Aims: Fibromyalgia syndrome is a musculoskeletal disorder characterized by widespread pain. Pain limits their daily activities, affecting their mood and quality of life. Autonomic derangements have also been shown to be associated with FMS. This study was done to explore the association of autonomic dysfunction, sleep quality and mood with increasing severity of fibromyalgia and its impact on their quality of life
Methods: Hundred adult fibromyalgia patients, as per ACR 2010 criteria, were evaluated for sleep quality, Quality of life, Pain, Mood, and FMS severity using validated questionnaires. They were also evaluated for autonomic functions using heart rate variability and Ewing's battery of tests.
Results: Pain scores on VAS were 6.80±1.58 and 54.10±14.33 on global pain scale. Mean FIQR score was 50.62±13.68, poor sleep quality. Mean depression, anxiety, and stress scores as assessed by DASS-21 were 10.04±4.59, 8.33±4.48, and 10.75±4.66, respectively. Autonomic dysfunction was observed in less than 50% of patients, but no significant correlation was found between FMS severity and level of AD. An increasing trend of depression, anxiety, stress, was observed with increase in FMS severity. Sleep quality and quality of life deteriorated with increasing severity of FMS.
Conclusion: Pain increased with increasing severity of FMS but there is no association of FMS severity with autonomic dysfunction. There is a deterioration in mood, sleep quality as well as quality of life of patients with increasing severity. The causal association of autonomic dysfunction observed in a few of the patients needs further exploration in a follow-up study.
Disclosure: Nothing to disclose.

EPO-030 | Autonomic function as predictor of cognitive impairment following deep brain stimulation in Parkinson's disease

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Background and Aims: Parkinson's disease (PD) affects over 4 million people older than 50. While deep brain stimulation (DBS) is an established treatment for motor complications in PD, mechanisms explaining cognitive dysfunction post-DBS remain incompletely understood. Our aim is to investigate whether baseline autonomic function is associated with cognitive impairment post-DBS in PD.
Methods: Prospective cohort study. STN-DBS surgery candidates were recruited between 2016 and 2019, and submitted to baseline neurological, autonomic (non-invasive Finometer device (Finapres) and 3-lead ECG), and comprehensive neuropsychological assessments. A follow-up autonomic and cognitive assessment was conducted 6–12 months post-surgery. An adaptation of the Ewing battery of autonomic tests was followed. The high frequency component of RRi variability (HFRR) (parasympathetic tone), the low frequency component of SAP variability (LFSAP) (sympathetic tone) and baroreceptor gain were used for analysis. Cognitive change scores (T1-T2) were computed and assumed as dependent variable in a regression model, using baseline demographics and quantitative scores on autonomic non-invasive tests as independent variables.
Results: 38 patients were included. Phonetic verbal fluency ($p=0.013$), Frontal Assessment Battery (FAB) ($p=0.008$) and Trail Making test part B ($p=0.035$) deteriorated post-DBS. LFSAP was associated with a worse FAB score post-DBS, even after adjustment for age and disease duration ($p=0.022$) (Figure 1). Both variables were correlated ($r=0.416$; $p=0.035$). This seems independent from a DBS effect on autonomic function.

Table 1. Analysis of cognitive impact of deep brain stimulation (DBS) in this PD patient group. Performance on a neuropsychological battery of tests (mean and SD) pre- and post-DBS is shown. Higher scores indicate better performance, except for Trail Making Test A and B, where higher scores (longer time to complete the task) indicate poorer performance. Bold indicates statistically significant *p*-value ($p < .05$).

	Pre-DBS	post-DBS	paired t-test
MoCA	24.2 (2.7)	25.4 (2.6)	p=0.385
Frontal assessment battery (FAB)	14.1 (2.1)	11.2 (3.2)	p=0.008
Semantic verbal fluency	15.6 (4.7)	12.6 (5.0)	p=0.207
Phonetic verbal fluency	33.0 (9.3)	26.9 (11.5)	p=0.013
Wechsler memory scale	12.1 (2.6)	21.4 (32.9)	p=0.046
Digit span memory test	9.6 (1.9)	8.6 (1.9)	p=0.276
Progressive matrices de raven (PM47)	25.4 (5.4)	26.0 (5.3)	p=0.338
Figure copy test	11.5 (1.8)	11.4 (1.7)	p=0.885
Trail making test part A	85.3 (43.8)	107.1 (69.1)	p=0.099
Trail making test part B	249.3 (222.7)	351.9 (235.4)	p=0.035
Boston naming test	43.5 (22.5)	53.8 (7.5)	p=0.059
Clock drawing	3.8 (1.5)	3.4 (1.3)	p=0.705

Table 2. Mean and SD of the autonomic parameters values pre-surgery and post-surgery. HFRR for high frequency RR variability, LFSAP for low frequency systolic arterial pressure, BRG for baroreceptor alpha-index gain and HR for heart rate. DBS – deep brain stimulation[surgery.

	HFRR (sec2)	LFSAP (mmHg2)	BRG	HR (bpm)
Pre-DBS	186.7 (236.8)	4.9 (5.5)	5.2 (3.6)	70.3 (10.8)
Post-DBS	111.1 (108.2)	3.4 (2.5)	3.7 (3.1)	71.3 (10.5)
Paired t-test pre- vs post-DBS	p=0.080	p=0.295	p=0.043	p=0.658

Conclusion: The identification of treatable targets and useful biomarkers of cognitive dysfunction after DBS helps identifying whose patients are specifically vulnerable for accelerated cognitive decline post-DBS, allowing for better patient selection and prognostic information.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 1

EPO-031 | Aetiology of index and recurrent ischemic events in patients treated with short-term DAPT: Data from the READAPT study

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Background and Aims: It is unclear whether the aetiology of minor stroke or TIA affects the effectiveness of short-term dual antiplatelet treatment (DAPT). This study aims to analyse the aetiology of first and recurrent events and their predictive value in a real-world population of patients treated with DAPT.

Methods: The real-life study on short-term DAPT in Patients with ischemic stroke or TIA (READAPT) prospectively included, from February 2021 to February 2023, patients with minor stroke or high-risk TIA receiving DAPT. We determined the aetiology of index and recurrent cerebral ischemic events. Cox regression analysis identified predictors of ischaemic recurrence.

Results: Among 1920 patients with ischaemic stroke or TIA (65.4% male, median age 72 years) the index event was undetermined in 830 cases (43.2%), lacunar in 534 (27.8%), atherothrombotic in 452 (23.5%) and other determined cause in 104 (5.4%). Sixty-four patients (3.3%) had a 90-day recurrent ischaemic stroke or TIA. There were no differences among the different aetiologic groups in recurrent events. Among the 64 patients with recurrences, the distribution of aetiologies was different for the recurrent event as compared to the index events (undetermined 46.9% vs 34.4% large vessel 29.7% vs 21.8%; lacunar 18.8% vs 31.2%; other 4.7% vs 6.3%; cardioembolic 0 vs 6.3%; $p=0.001$).

Conclusion: Our data suggest that there is no difference in the risk of recurrent events according to stroke aetiology of the index event in patients treated with short-term DAPT. Recurrent events have a different aetiological distribution of index events.

Disclosure: Nothing to disclose.

EPO-032 | Exploring the prognostic role of fibrinogen in ischemic stroke

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Background and Aims: Several biomarkers might play a prognostic role in stroke. We explored the prognostic role of plasma fibrinogen levels (PFL) at stroke onset on residual disability and risk of hemorrhagic infarction in incident patients with ischemic stroke (IS).

Methods: Historical cohort study design. Data on comorbidities, National Institutes of Health Stroke Scale (NIHSS) on admission, PFL at stroke onset (<300 mg/dL, >=300 mg/dL) and modified Rankin Scale (mRS) before and after 3 months were collected, as well as hemorrhagic conversion among patients treated with Intravenous Thrombolysis (IVT). 'mRS difference' was computed between mRS at 3-months after stroke and onset. ANCOVA and logistic regression were used.

Results: 241 men and 203 women aged 66.9 ± 13.1 and 72.1 ± 14.2 years, respectively, were enrolled. PFL directly correlated with age at stroke onset ($p=0.043$). No difference in the distribution of PFL by site of lesion, TOAST and Oxfordshire Community Stroke Project classification, indication to thromboarteriectomy and NIHSS were detected. Inverse association was found between PFL

and IVT indication [aOR=0.46 (95% CI: 0.30, 0.72, $p=0.001$)]. In IVT treated patients, mean mRS difference was higher in subjects with high PFL after adjusting for age, onset NIHSS, diabetes mellitus, smoking habit (1.39 vs 1.33, $p=0.000013$). No association of PFL with hemorrhagic infarct conversion was found.

Conclusion: In IS patients, high PFL are associated to reduced indication to IVT and increased disability at 3 months after stroke. The prognostic role of PFL at stroke onset may depend on age and NIHSS at onset. PFL was not associated with an increased risk of post-treatment hemorrhagic infarction.

Disclosure: Nothing to disclose.

EPO-033 | Diagnostic utility of Vessel Wall MR Imaging in patients with Acute Ischemic Stroke

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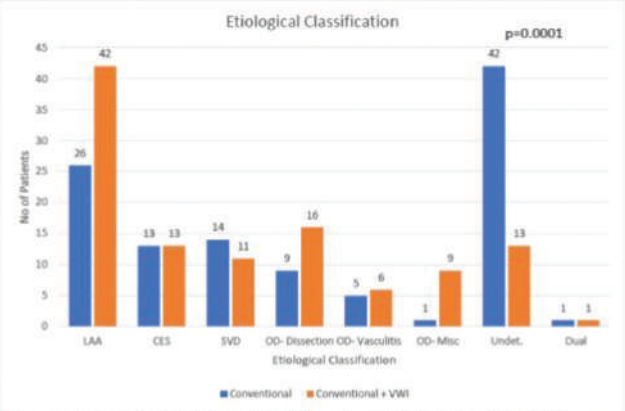
Background and Aims: There is a need for better investigations to elucidate the etiology of stroke. High-Resolution Vessel Wall MRI is emerging imaging technique used to help understand the etiopathogenesis of acute ischemic stroke (AIS). Studies describing various findings have not yet clarified the exact utility of VW-MRI to subtype AIS. Current study was undertaken to evaluate the diagnostic utility of VW-MRI in patients with AIS.

Methods: A single-centre, prospective study recruited patients with AIS within 30 days. A team of stroke neurologists classified the etiology of AIS before and after VW-MRI. Subsequent statistical analysis was done to look for the proportion of patients with a change in etiological classification before and after VW-MRI and factors associated with the same.

Results: A total of 111 patients were recruited with a median age of 50.5 years (IQR: 38–60 years) and 72.4 % of the study population were males. The incorporation of VW-MRI resulted in change in etiological classification in 38 out of 111 (34.3%) ($p=0.0001$) patients. A baseline etiological classification of undetermined as per traditional luminal imaging modalities was found to be a strong predictor of change in etiological classification post VW-MRI (OR: 38.7; 95% CI: 2.7–555.7)



Data represented as n(%); LAA : Large Artery Atherosclerosis; CES: Cardioembolic Stroke; SVD: Small Vessel Disease; OD: Other Determined.

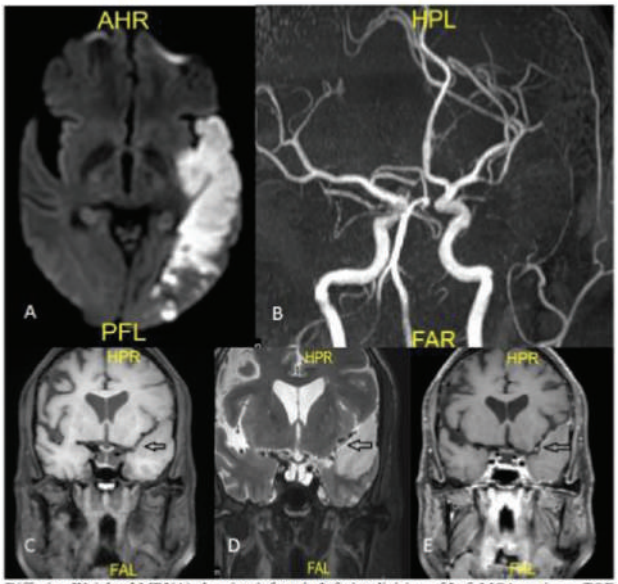
FIGURE Etiological Classification Before and After Vessel Wall MR Imaging

TABLE Univariate Logistic Regression for change in Etiological classification after VW- MRI

Factors	Change in Etiological Classification			
	No	Yes	OR (95% CI)	p-value
Sex				
Male	54	26	1.38 (0.55-3.51)	0.49
Female	23	8	**0.34 (0.15-0.77)**	**0.01**
Age		--	**0.97 (0.94-0.99)**	**0.047**
Time to VW		--	1.04 (0.99-1.09)	0.102
Stroke Territory				
Basilar	6	6	1 (0.32-3.1)	1
MCA	37	15	0.40 (0.11-1.45)	0.16
Multiple	10	3	0.3 (0.05-1.6)	0.16
PCA	4	1	0.25 (0.02-2.94)	0.27
Vertebral	10	3	0.3 (0.05-1.66)	0.16
ICA	10	6	0.6 (0.13-2.73)	0.51
Type of Infarct				
Mixed	15	4	**0.26 (0.08-0.80)**	**0.02**
Perforator	15	6	1.5 (0.35-6.41)	0.58
Territorial	42	17	1.52 (0.43-5.2)	0.51
Watershed	5	7	**5.2 (1.06-24.7)**	**0.04**
% Stenosis CTA				
<50 %/None	24	9	**0.38 (0.17-0.81)**	**0.012**
50-95	7	5	1.90 (0.48-7.57)	0.36
Critical Stenosis	6	2	0.88 (0.15-5.24)	0.90
Occlusion	19	5	0.70 (0.20-2.44)	0.58
% Stenosis MRA				
<50 %/None	36	16	**0.44 (0.24-0.80)**	**0.007**
50-95	13	7	1.21 (0.40-3.60)	0.73
Critical Stenosis	8	5	1.40 (0.40-4.97)	0.60
Occlusion	17	6	0.79 (0.26-2.39)	0.68
Conventional Etiological Classification				
LAA	25	1	**0.04 (0.005-0.29)**	**0.002**
CES	13	0	-	-
SVD	11	3	4.16 (0.34-50.61)	0.26
OD-Dissection	9	0	-	-
OD-Vasculitis	4	1	6.25 (0.32-121.33)	0.23
OD-Misc	0	1	-	-
Undetermined	13	29	**51.79 (6.35-422.08)**	**0.000**
Dual	1	0	-	-

Data represented as n(%);ICA: Internal Carotid Artery; MCA: Middle Cerebral Artery; PCA: Posterior Cerebral Artery; LAA : Large Artery Atherosclerosis; CES: Cardioembolic Stroke; SVD: Small Vessel Disease; OD: Other Determined

Conclusion: Vessel wall MRI can be an important additive investigation to help subtype AIS effectively, especially in the sub-group of the "Undetermined" Category.



Diffusion Weighted MRI(A) showing infarct in Inferior division of Left MCA territory. TOF MRA (B) showing severe irregular narrowing in inferior division of Left MCA. Sagittal T1 weighted VW-MRI (C) showing a focal eccentric thickening of the inferior division of Left MCA; corresponding Sagittal T2 weighted VW-MRI (D) demonstrating eccentric hyperintensity. Sagittal contrast enhanced T1 weighted VW-MRI demonstrating eccentric contrast enhancement in the same vessel consistent with a symptomatic high risk atherosclerotic plaque.

FIGURE Representative case with altered etiological classification post VW-MRI.

Disclosure: Nothing to disclose.

EPO-034 | **Perihematomal edema impact in the 3 years follow-up of lobar intracerebral haemorrhage**

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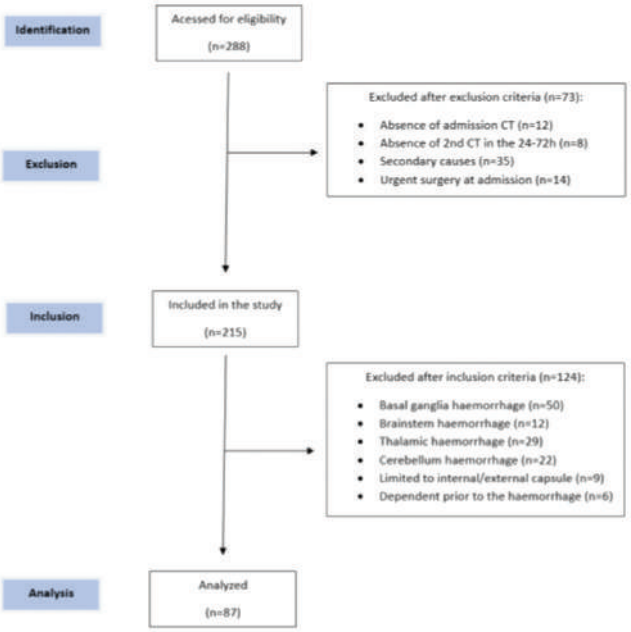
Background and Aims: Spontaneous intracerebral hemorrhage (ICH) is a leading cause of non-ischemic strokes with substantial impact on morbidity and mortality. While perihematomal edema (PHE) is recognized as indicator of secondary brain injury and has been linked to increased neurological disability, there is a paucity of long-term follow-up studies exploring these associations. This study aims to address this gap and evaluate the enduring impact of PHE on the outcomes of ICH patients.

Methods: A retrospective cohort study at Centro Hospitalar Universitário São João, Porto, Portugal, included 87 lobar primary ICH patients from 2014 and 2020. We evaluated absolute (PHE), relative (rPHE) perihematomal edema, and edema extension distance (EED) measured at admission computer tomography (CT) scan and 24–72 hours post-ICH. Primary outcomes were 3-year survival and favorable functional outcome (FO) defined as modified Rankin Scale 0–3.

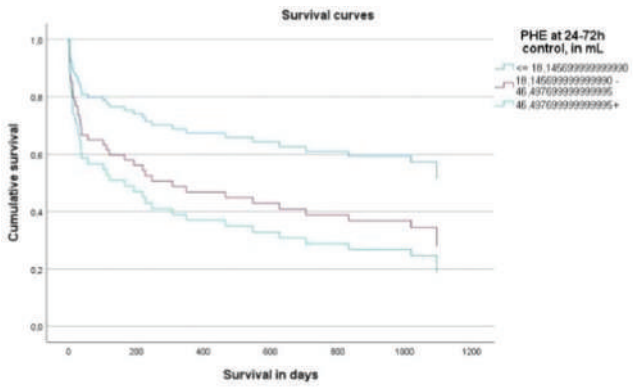


Patient selection flowchart

Results: Median age was 74.0 years (interquartile range 66–82), with 51.7% male. After 3 years, 40.2% were alive, 14.9% had a favorable FO. PHE at 24–72 h negatively correlated with survival in days (Cox regression hazard ratio 2.520, 95% CI 1.118–5.681, $p = 0.026$), but not rPHE or EED. An inverse correlation of EED at 24–72 hours to a better FO was also observed (OR 0.055, 95% CI 0.004–0.788, $p = 0.033$).

Variables	(n= 87)
Demographic and clinical	
Male sex – n (%)	45 (51.7)
Age, Years – median (IQR)	74 (66-82)
Previous mRS – median (IQR)	1 (1-2)
Hypertension – n (%)	59 (67.8)
Dyslipidemia – n (%)	43 (49.4)
Diabetes – n (%)	23 (26.4)
Smoker – n (%)	18 (20.7)
Previous alcohol abuse – n (%)	9 (10.3)
Antiplatelets – n (%)	26 (29.9)
Anticoagulant -n (%)	18 (20.7)
Statins – n (%)	37 (42.5)
Atrial fibrillation – n(%)	16 (18,4)
Hematoma characteristics	
Hematoma volume at admission, mL – median (IQR)	21.25 (6.89–35.95)
PHE at admission, mL – median (IQR)	25.40 (8.49-50.16)
PHE at control, mL – median (IQR)	33.99 (13.19-60.76)
rPHE at admission – median (IQR)	1.22 (0.66-2.72)
rPHE at control – median (IQR)	1.09 (0.67-2.32)
EED at admission, mL – median (IQR)	0.56 (0.29-0.80)
EED at admission, mL – median (IQR)	0.59 (0.30-0.83)
Follow-up outcomes	
Death at 3 years – n(%)	52 (59.8%)
Independence at 3 years (mRS 0-3) – n(%)	21 (24.1%)

Demographic characteristics and follow-up



Survival curve for PHE at control

Conclusion: PHE appeared to predict early mortality in lobar ICH. Given the observed tendency towards better functional outcomes (FO) in patients with low EED, recognizing PHE as an early death predictor emphasizes the necessity for further research to understand its role in influencing patient outcomes.

Disclosure: Nothing to disclose.

EPO-035 | Clonal hematopoiesis of indeterminate potential (CHIP) in ischemic stroke etiology

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Background and Aims: Clonal Hematopoiesis of Indeterminate Potential (CHIP) is characterized by the presence of somatic mutations in peripheral blood cells without evidence of a hematological neoplasm. Recent research has associated CHIP with cardiovascular disease and stroke. The objective of our study is to evaluate the relationship of CHIP with the etiology of the ischemic stroke and how its measurement could contribute to the study of stroke causes.

Methods: Prospective observational study of consecutive patients who suffered an ischemic stroke between September 2021 and August 2022. After complete work-up, patients were classified as cardioembolic (CE), atherothrombotic (AT) and cryptogenic (CRYP) stroke. Patients with double mechanism, incomplete study or active neoplasia were excluded. During hospital admission, 13 genes related to CHIP were analysed. A variant allele fraction of >1% was considered positive.

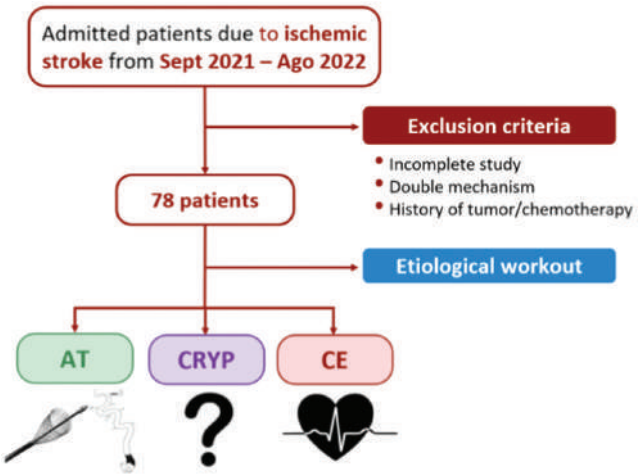

FIGURE 1 Methodology of the study with the corresponding exclusion criteria. AT = Atherothrombotic; CRYP = Cryptogenic; CE = Cardioembolic.

Results: Samples from 78 patients (50% women, mean age 73.4 years) were analysed and etiologically classified as: 37 CE (47.5%), 33 AT (42.3%) and 8 CRYP (10.3 %). Twenty-eight patients had CHIP (35.9%), of which the predominating mutations were: DNMT3A

(35.7%), TET2 (32.1%) and PPM1D (14.3%). Patients with CE stroke had a higher frequency of CHIP and less mutation heterogenicity (Figure 2). In the multivariate analysis, the TET2 mutation was associated with CE etiology after adjusting by age, coronary artery disease and classic cardiovascular risk factors (OR 20.9; $p=0.016$) (Figure 3).

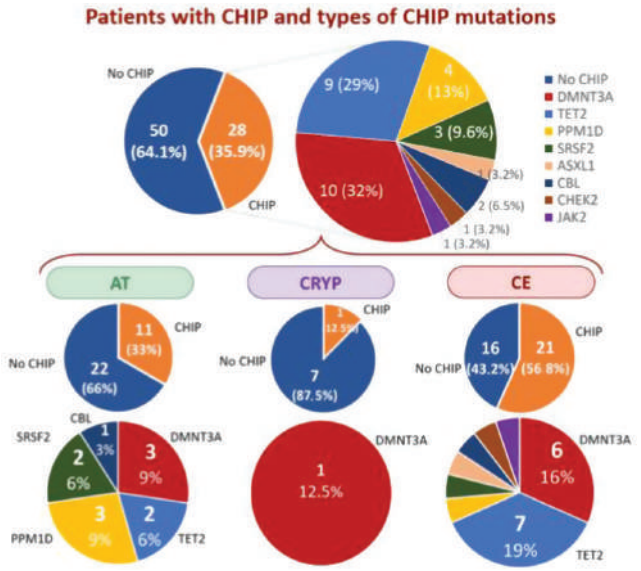

FIGURE 2 Frequency of CHIP and the different mutations according to the etiological diagnosis. It can be observed how patients with CE stroke had a higher frequency of CHIP and less mutation heterogenicity.

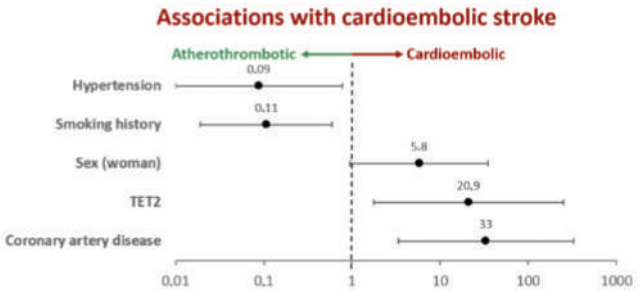

FIGURE 3 Forest plot of the multivariate analysis. In which it is shown the association between cardioembolic stroke and the presence of the TET2 mutation.

Conclusion: CHIP is frequently found in patients with ischemic stroke. The presence of the TET2 mutation was associated with CE stroke and could potentially facilitate the etiological diagnosis of stroke.

Disclosure: Nothing to disclose.

EPO-036 | Exploring sex disparities in ischemic stroke treatment and functional outcomes

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Background and Aims: Females face worse functional recovery after stroke. While poorer health, older age and greater stroke severity could explain this, some population studies have shown that accessibility and timeliness of treatment also play a role. We aimed to assess sex-related disparities in stroke treatment and functional outcomes within our population.

Methods: This retrospective, single-center study included acute ischemic stroke patients treated with thrombolysis and/or thrombectomy from January 2015 to December 2022 at our stroke center. The primary outcome was functional status at 3-month follow-up, while the secondary outcome was time from symptom onset to final reperfusion therapy (TSOFT). Bivariate analysis comparing female and male patients was followed by binary logistic and linear regression to identify predictors of functional outcome and TSOFT, respectively.

Results: 1219 patients were included (54% females, mean age 74 years). Females were older, had worse baseline functional status and higher NIHSS scores at admission. Bivariate analysis showed that females were more likely to have unfavorable functional outcomes (OR 1.367; 95% CI 1.092–1.713) and significantly longer TSOFT (228 versus 200 min; $p=0.002$). However, after adjusting for confounders, female sex itself did not correlate with worse functional outcomes (aOR 1.237; 95% CI 0.926–1.646), while longer TSOFT did (aOR 2.177; 95% CI 1.302–3.641). Additionally, linear regression analysis indicated a significant association between female gender and longer TSOFT, even after adjusting for confounders (B = −0.055, $p=0.003$, 95% CI [−0.091, −0.019]).

Conclusion: Our findings suggest female stroke patients experience delays in treatment, and that these contribute to worse functional outcomes.

Disclosure: Nothing to disclose.

EPO-037 | Factors associated with fast infarct growth and its impact on patients treated with Mechanical Thrombectomy

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Background and Aims: Infarct growth rate varies significantly between stroke patients. Fast infarct growth (FIG) is associated with more severe neurological deterioration within time lapse between

stroke onset and neurological procedures; that information may be crucial for Mechanical Thrombectomy (MT) decision-making process. We aimed to identify factors associated with FIG.

Methods: We retrospectively analyzed 641 consecutive patients with AIS in anterior circulation treated with MT in Comprehensive Stroke Center in University Hospital, Cracow (2019–2023). In all patients we obtained pre-stroke risk factors and performed computed tomography perfusion (CTP) followed by post-processing analysis with RAPID software. FIG was identified if ratio of CTP-derived cerebral blood flow <30% volume/time from last known well to imaging exceeded 10ml/h. We included 151 (23.56%) patients with FIG and 490 (76.44%) without.

Results: Patients with FIG were more frequently males (58.3% vs 46.9%, $p=0.015$), had significantly lower time from last known well to imaging (135 [84–213]min vs 249.5 [189–302]min, $p<0.001$), higher NIHSS on admission (18 [15–21] vs 15 [10–19], $p<0.001$) and higher hypoperfusion intensity ratio (HIR, defined as T10max to T6max volumes ratio) (0.57 [0.47–0.68] vs 0.3 [0.15–0.44], $p<0.001$). After multivariate analysis, each increase of 0.1 in HIR increased odds for FIG 2.02 (1.76–2.33, $p<0.001$). Moreover, FIG was linked with 0.57 (0.35–0.93, $p=0.024$) lower odds for obtaining functional independency at day 90, after adjusting for confounders.

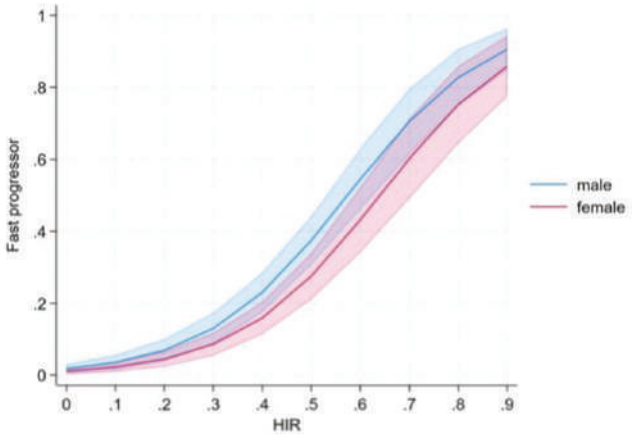

FIGURE 1 Association of hypoperfusion intensity ratio and probability of FIG (fast infarct growth) according to patient sex.

Conclusion: Higher HIR (denoting less robust leptomeningeal collaterals) and male sex are associated with FIG. Although patients with FIG may have lower time from last known well to admission, they present more severe neurological symptoms and worse long-term prognosis.

Disclosure: ERA-NET-NEURON/21/2020 iBioStroke grant.

TABLE 1 Comparison of patients with and without FIG.

	Patients without FIG (N=490)	Patients with FIG (N=151)	*P* value
Demographics			
Male, n (%)	**230 (46,9)**	**88 (58,3)**	**0.015**
Age, years, median [IQR]	72 [60-65]	69 [61-80]	0.203
Stroke risk factors			
Hypertension, n (%)	357 (72.9)	104 (68.9)	0.341
Diabetes Mellitus, n (%)	114 (23.3)	33 (21.9)	0.412
Hiperlipidemia, n (%)	102 (20.8)	33 (21.9)	0.784
Atrial fibrillation, n (%)	161 (32.9)	49 (32.5)	0.926
History of stroke/TIA, n (%)	63 (12.9)	19 (12.8)	0.93
History of myocardial infarction, n (%)			
Smoking, n (%)	108 (22)	36 (23.8)	0.114
Clinical characteristics			
Baseline NIHSS, median [IQR]	**15 [10-19]**	**18 [15-21]**	**<0.001**
Time from LKW to puncture, median [IQR]	**249.5 [189-302]**	**135 [84-213]**	**<0.001**
Intravenous thrombolysis, n (%)	289 (59)	96 (63.6)	0.313
Successful recanalization, (mTICI≥2b), n (%)	426 (86.9)	139 (92.1)	0.089
Stroke localization			0.384
ICA, n (%)	77 (15.7)	18 (11.9)	
M1, n (%)	273 (55.7)	92 (60.9)	
M2, n (%)	108 (22)	28 (18.5)	
Tandem, n (%)	32 (6.5)	13 (8.6)	
Stroke etiology			0.151
Cardioembolic, n (%)	224 (45.7)	55 (36.4)	
Large vessel disease, n (%)	76 (15.5)	22 (14.6)	
Undetermined, n (%)	173 (35.3)	67 (44.4)	
Rare, n (%)	17 (3.5)	7 (4.6)	
Stroke-related complications			
Pneumonia, *n* (%)	100 (20.4)	37 (24.5)	0.283
Urinary tract infection, *n* (%)	71 (14.5)	30 (19.9)	0.113
Recurrent stroke *n* (%)			
No hemorrhagic transformation, *n* (%)	358 (73.1)	114 (75.5)	0.553
Outcomes			
90 functional independency (mRS≤3), n(%)	**318 (64.9)**	**79 (52.3)**	**0.005**
Radiological examination			
Baseline ASPECTS, median [IQR]	8 [7-9]	7 [6-9]	**<0.001**
Penumbra, ml, median [IQR]	89 [53-126]	96 [55-127]	0.798
Infarct (CBF<30%), ml, median [IQR]	**5 [0-14]**	**54 [33-80]**	**<0.001**
HIR, median [IQR]	**0.3 [0.15-0.44]**	**0.57 [0.47-0.68]**	**<0.001**

*FIG – fast infarct growth; TIA – transient ischemic attack; LKW - last known well; ASPECTS - Alberta Stroke Program Early CT Score; CBF – cerebral blood flow; HIR – hypoperfusion intensity ratio

EPO-038 | **Admission blood pressure: Causes and consequences in large vessel occlusion stroke**

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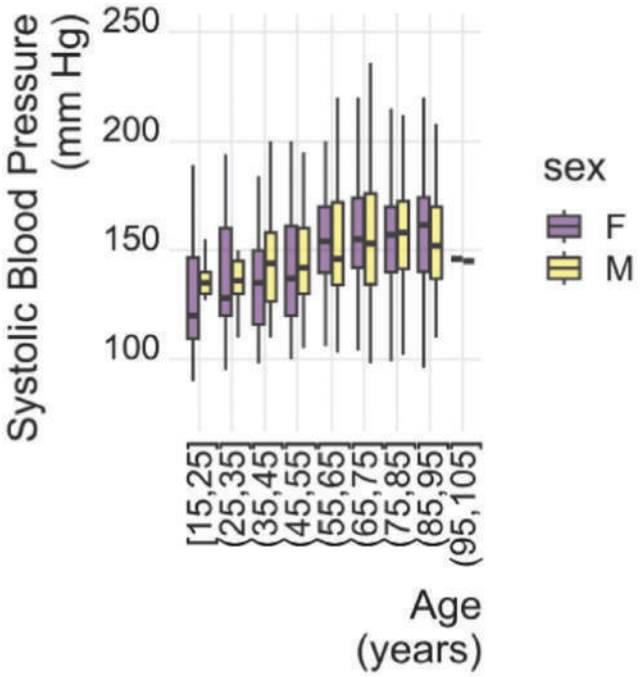
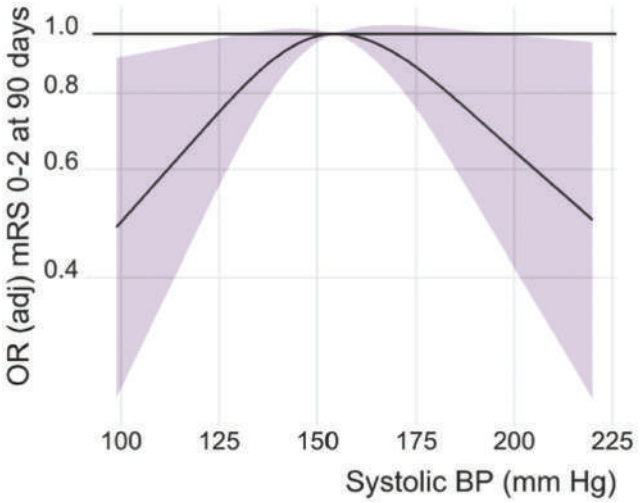
Background and Aims: The influence of sex and age on admission blood pressure and how admission blood pressure relates to clinical outcome (modified rankin score at 90 days – mRS-90) in stroke patients treated with endovascular thrombectomy is unclear.

Methods: Retrospective analysis was performed on patients with stroke receiving clot retrieval. Systolic blood pressure was assessed as the first recorded value. Outcome was assessed by the modified Rankin scale (mRS) score with mRS of 0 to 2 denoting functional independence. A multivariable binary logistic regression was created.

Results: In a cohort of 1079 stroke patients treated with clot retrieval, systolic blood pressure was dependent on age ($p<0.0001$) and there was a significant interaction of sex with females less than 50 years old presenting with lower blood pressure. Multivariable logistic regression revealed a quadratic relationship with both low and high admission systolic blood pressure associated with decreased odds of functional independence.



Relationship between age, sex and admission systolic blood pressure in stroke patients treated with endovascular thrombectomy



Adjusted odds ratio of admission systolic blood pressure in predicting functional independence in stroke patients treated with endovascular thrombectomy

Conclusion: Further investigation into sex differences in blood pressure control and early stroke pathophysiology is required.

Disclosure: Nothing to disclose.

EPO-039 | Renal function and Neurofilament Light chain serum concentrations in ischemic stroke

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Background and Aims: Neurofilament Light chain (NfL) is a leading biomarker of long-term stroke patients' prognosis. Next step is to evaluate if NfL could be effectively employed as candidate surrogate end-point in stroke studies. An accurate identification of potentially confounding factors is required. This longitudinal prospective observational study investigates the correlations between NfL serum concentrations and renal function in ischemic stroke patients.

Methods: We included patients with stroke at neuroimaging, 18-80 years, onset <24h, NIHSS >1, pre-stroke mRS < 2. Exclusion criteria: TIA/previous stroke/TBI/other neurological disease, chronic immunosuppression, pregnancy, severe chronic kidney disease (eGFR < 30mL/min). Patients were treated as standard of care; serum creatinine was measured on admission blood tests. NfL serum concentrations were determined with Ella Automated-Immunoassay-System on samples collected within 24h from onset (T0), after 3–5 days (T1) and 7 ± 2 days (T2).

Results: At present, 43 patients have been enrolled (12 females, median age 64y[IQR18.5]. At onset, 53.5% had NIHSS 1–4, 39.5% NIHSS 5–15, 7% NIHSS>16. NfL median values were lower at T0

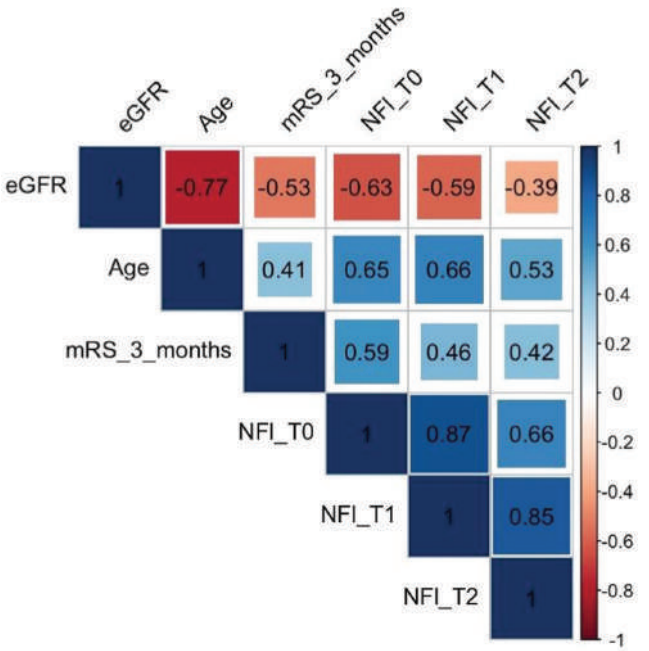

FIGURE 1 Correlation matrix between eGFR, age, mRS at 3 months, NfL.

(35.9pg/mL [IQR49.05]) vs T1 (66.1pg/mL [IQR97.25]; $p = 0.003$) and T2 (122pg/mL [IQR170.25]; $p < 0.001$). NfL at all time-points correlated positively with age and mRS at 3 months, and negatively with eGFR (T0 and T1 $p < 0.001$, T2 $p = 0.01$; Figure 1). Correlation analysis showed a negative linear relationship between eGFR and NfL at all time-points ($p \leq 0.01$; Figure 2).

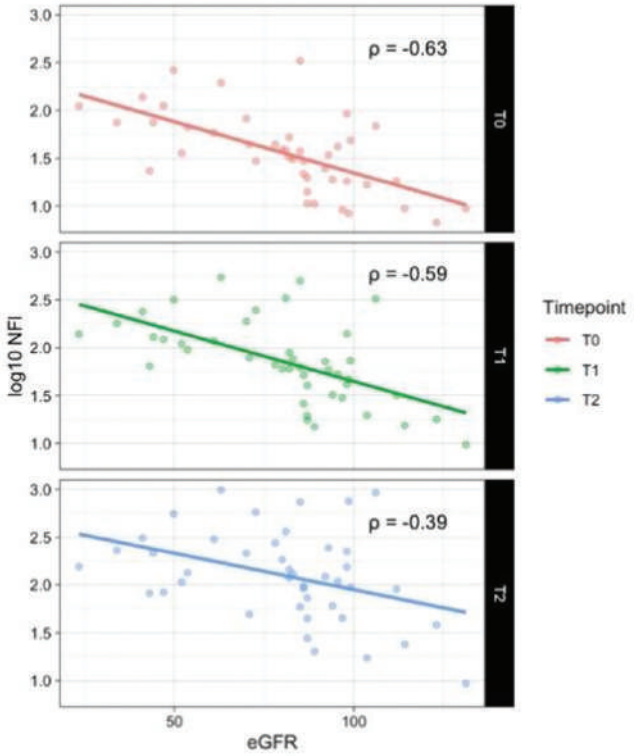

FIGURE 2 Correlations between eGFR and NfL at the three time-points.

Conclusion: NfL serum levels are inversely correlated with renal function in ischemic stroke patients and this variable should be considered in future studies as a potential source of bias in this population.

Disclosure: This study was supported by the Italian Ministry of Health "Ricerca Corrente 2022–2024" granted to IRCCS Mondino Foundation.

EPO-040 | New metrics of hypoxic burden predict recurrent cardio-cerebro-vascular events following ischemic stroke

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Background and Aims: Considering the limitations of conventional metrics of sleep-disordered breathing (SDB), novel physiologically informed metrics are needed to better predict the risk of cardio-cerebrovascular events (CCVE) associated with SDB. In this study, we suggest the use of new metrics of hypoxic burden to predict CCVE in stroke patients.

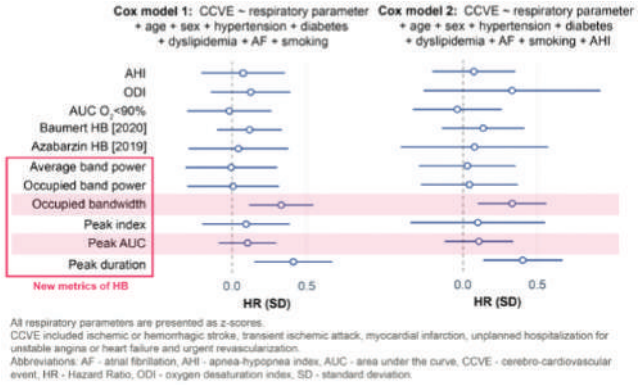
Methods: This is an exploratory analysis of the prospective observational longitudinal Sleep Deficiency & Stroke Outcome Study (ClinicalTrials.gov Identifier: NCT02559739). In acute ischemic stroke patients, hypoxic burden metrics were computed based on the oximetry signal from the respiratory polygraphy within the first week post-stroke. Recurrent CCVE were recorded over a 3-year follow-up. Cox regression with adjustment for vascular risk factors was used to investigate the prognostic value of 48 cardiovascular parameters regarding CCVEs.

Results: Out of 447 recruited patients, 347 were included in this analysis (Figure 1). 15% developed a future CCVE (mean observation time is 648 days). The 99% occupied bandwidth and negative peak duration significantly predicted vascular risk, whereas no associations were significant for apnea-hypopnea index (AHI), oxygen desaturation index (ODI), area under curve following non-specific desaturation <90%, or hypoxic burden parameters according to Azarbarzin and Baumert (Figure 2). The 99% occupied bandwidth and negative peak duration were not significantly associated with AHI or ODI (Figure 3).

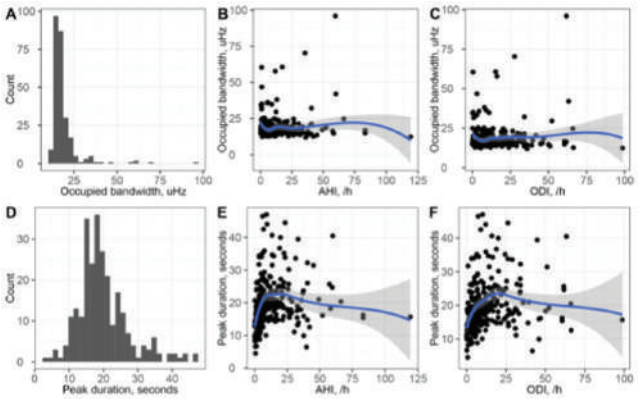
Parameter	Value
Age, years	65.10 [56.10, 73.70]
Sex (female)	125 (36.0%)
TIA	56 (16.1%)
NIHSS at admission, points	2.00 [0.00, 4.00]
NIHSS at discharge, points	0.00 [0.00, 2.00]
mRS at subacute stroke	0.00 [0.00, 1.00]
Intravascular stroke treatment	79 (22.8%)
Hypertension	200 (58.3%)
Diabetes	46 (13.3%)
Dyslipidemia	200 (59.3%)
Obesity	67 (19.5%)
Atrial fibrillation	33 (9.7%)
Current smoking	85 (24.8%)
AHI, /h	7.30 [3.50, 18.40]
AHI≥20/h	73 (22.7%)

Abbreviations: AHI – apnea-hypopnea index, NIHSS – National Institute of Health Stroke Scale, mRS – modified Rankin Scale, TIA – transient ischemic attack.

Patient characteristics.



Coefficient plots of Cox regression models showing the association of respiratory parameters at acute stroke with the vascular risk.



Properties of hypoxic burden metrics: histograms and associations with AHI and ODI.

Conclusion: Among investigated parameters, 99% occupied bandwidth and negative peak duration emerge as the most robust predictors of CCVE after stroke. Future studies should further validate the predictive ability of these markers.

Disclosure: Swiss National Science Foundation grant #320030_149752.

EPO-041 | Endovascular treatment in medium vessel occlusion: Experience from a stroke unit

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Background and Aims: Medium vessel occlusion (MeVO) accounts for 25–40% of ischemic strokes with visible vessel occlusion. The endovascular treatment's (EVT) efficacy and safety hasn't been confirmed in MeVOs. We aim to evaluate the functional outcome of MeVOs that received EVT.

Methods: One-year retrospective study, with descriptive and comparative analysis.

Results: From 40 patients admitted, 10 (25%) received EVT (all with M2 occlusion). The median age was 76.5 years ([Q3-Q1]: [85.75–61.5]). The median time from symptom onset to admission was 442.5 ([Q3-Q1]: [840–117.5]) minutes with a median NIHSS at admission of 7 ([Q3-Q1]: [11.75–3]). Median ASPECTS was 9 ([Q3-Q1]: [10–8]) with Tan collateral score of 3 in 10 patients. 15 patients received acute revascularization treatment: 7 EVT, 5 iv thrombolysis (rtPA) and 3 rtPA plus EVT. The median door-in-door-out time was 86 ([Q3-Q1]: [139.5–71]) minutes and the median door-to-needle time was 136 ([Q3-Q1]: [193–133]) minutes. After EVT, 8 (20%) patients had a TICI 2b. At discharge, the median NIHSS was 2 ([Q3-Q1]: [5.75–0]). The median mRS at 90 days was 3 ([Q3-Q1]: [4–1]). EVT isn't related with mRS at 90 days (p 0.920). EVT is related with a greater variation between NIHSS at admission and at discharge (p 0.014). A favourable mRS at 90 days was significantly related with a lower NIHSS at discharge (p 0.032).

Conclusion: Despite the absence of direct correlation between EVT and favourable functional outcomes at 90 days, EVT is significantly correlated to a greater variation between NIHSS at admission and at discharge suggesting a possible efficacy of this procedure in MeVOs.

Disclosure: Nothing to disclose.

EPO-042 | Dynamic outcome prediction of alteplase-treated acute ischemic stroke patients: A machine learning approach

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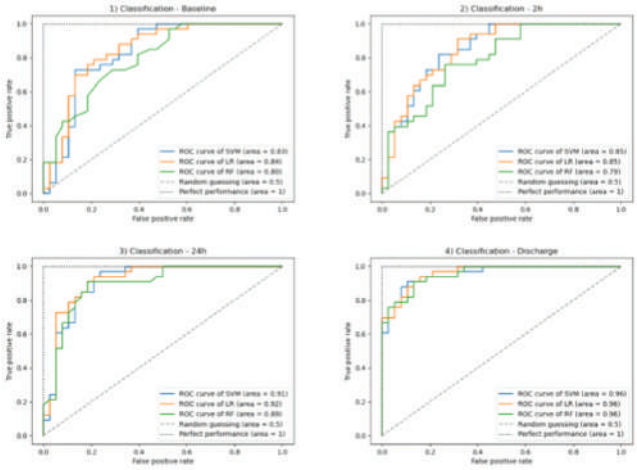
Background and Aims: Numerous factors impact the functional outcomes of acute ischemic stroke (AIS) patients treated with intravenous thrombolysis (IVT). Currently, there is a lack of predictive models incorporating clinically relevant features at various time points. This study aimed to develop a machine-learning model for dynamic prediction of functional outcomes.

Methods: Retrospective analysis involved alteplase-treated AIS patients at the University Neurology Clinic of Vojvodina (Novi Sad, Serbia) from December 2008 to December 2022. Clinical data were categorized into four groups based on collection time: Baseline, 2-h, 24-h, and Discharge features. These were utilized as input for the model. The 90-day modified Rankin scale (mRS), as an outcome measure, determined favorable (mRS ≤2) and unfavorable outcomes (mRS ≥3). The main classifier evaluation parameter was the area under the receiver operating characteristic (AUC-ROC) curve.

Results: The study comprised 355 patients (average age 66.4 years, 64% male), with 55% achieving a favorable outcome. Models demonstrated good discrimination on the testing set (AUC = 0.80–0.96), with the highest values in the 24-h (AUC = 0.89–0.91) and discharge models (AUC = 0.96).

Models and Selected Features								
Baseline		2-hour		24-hour		Discharge	
1. Age 2. Baseline Systolic Blood Pressure 3. ASPECTS 4. Baseline NIHSS 5. Baseline Hemoglobin 6. Baseline Glycemia 7. Platelet count 8. Usage of Acetylsalicylic acid 9. Onset to treatment time 10. Door to CT time 11. Type of hyperlipidemia 12. OCSP type of stroke		1. Age 2. ASPECTS 3. Baseline NIHSS 4. Baseline Hemoglobin 5. Baseline Glycemia 6. Platelet count 7. Usage of Acetylsalicylic acid 8. Onset to treatment time 9. Door to CT time 10. 2-hour NIHSS 11. Type of hyperlipidemia 12. OCSP type of stroke		1. Age 2. Baseline Glycemia 3. Platelet Count 4. Door to Needle time 5. 2-hour NIHSS 6. 24-hour NIHSS 7. Post-tPA Diastolic Blood Pressure 8. OCSP type of stroke		1. Age 2. Baseline glycemia 3. 24-h NIHSS 4. 24-h NIHSS 5. Door-to-needle time 6. OCSP type of stroke 7. Discharge NIHSS 8. Discharge treatment 9. Length of hospitalization	
Classifier	Evaluation metrics							
	AUC	Accuracy	AUC	Accuracy	AUC	Accuracy	AUC	Accuracy
SVM	0.83	0.76	0.85	0.78	0.91	0.87	0.96	0.90
Logistic Regression	0.84	0.79	0.85	0.76	0.92	0.85	0.96	0.89
Random Forest	0.80	0.72	0.79	0.75	0.89	0.83	0.96	0.87

Selected features and Evaluation metrics



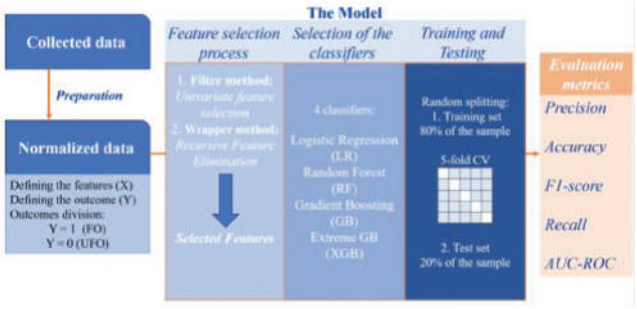
AUC-ROC curves

Conclusion: The baseline model is applicable for predicting clinical outcomes before IVT, aiding in decision-making for its initiation, while other models enhance predictive accuracy for post-IVT clinical outcomes, allowing timely adaptations in treatment approaches.
Disclosure: Nothing to disclose.

EPO-043 | The outcome prediction of ischemic stroke patients with atrial fibrillation: An interpretable machine learning study

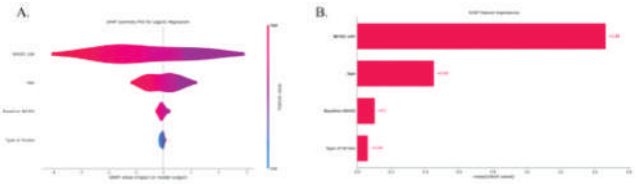
I. Petrović[1]; M. Ivanišević[2]; A. Balenović[1]; I. Milosavljević[1]; S. Rajić[1]; D. Vlahović[1]; Z. Božić[3]; Ž. Živanović[1]
[1]*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia;* [2]*Faculty of Medicine, University of Belgrade, Belgrade, Serbia;* [3]*Neurology Clinic, University Clinical Center of Vojvodina, Novi Sad, Serbia*

Background and Aims: Considering that patients with atrial fibrillation (AF) can also achieve favorable outcomes, there is a noticeable literature gap in identifying contributing factors and prediction possibilities for this group. The aim was to utilize interpretable machine learning (IML) to analyze the functional outcomes of stroke patients with admission AF.
Methods: We included 381 alteplase-treated acute ischemic stroke (AIS) patients, out of which AF was registered in 29% during admission. Based on the 90-day modified Rankin Scale (mRS) value, two groups were made: a favorable outcome group (mRS ≤2), and an unfavorable outcome group (mRS ≥3). 63 features were used as input for the analysis and model build-up. The decision-making process was better understood through the interpretation packages.

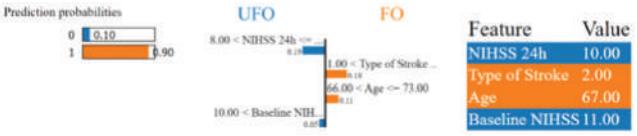


Machine Learning Model Build-Up Process

Results: In the AF group ($n = 109$), a favorable outcome was achieved in 55% of patients, and 4 selected distinguishing variables were: the patient's age, the baseline and 24-h value of NIHSS (National Institutes of Health Stroke Scale), and the type of stroke determined by OCSP (Oxfordshire Community Stroke Project). Logistic regression showed high predictive power (AUC = 0.922), and the interpretation packages revealed a 24-h NIHSS value as the most influential factor.



SHAP analysis results – the whole group-level interpretation



LIME analysis results – the individual-level interpretation

Conclusion: By focusing on alteplase-treated ischemic stroke patients with admission AF, this study identified younger age, lower baseline and 24-h NIHSS values, and OCSP types of AIS other than TACI as important predictors of a favorable 90-day functional outcome. IML can enhance trust and aid in understanding the decision-making 'black box' of machine learning.
Disclosure: Nothing to disclose.

EPO-044 | Endovascular treatment in ischemic stroke with isolated anterior cerebral artery occlusion

J. Mayol[1]; M. Rodrigo-Gisbert[1]; M. Olivé-Gadea[1]; F. Rizzo[1]; F. Diana[2]; M. Rubiera[1]; C. Molina[1]; A. Tomasello[2]; M. Ribó[1]; M. Requena[1]
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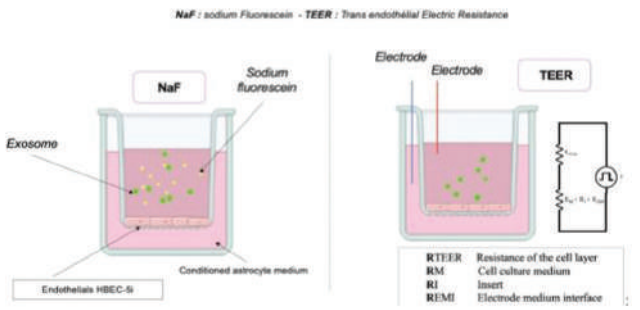
Background and Aims: Limited data exist on endovascular treatment (EVT) for anterior cerebral artery (ACA) occlusion-associated ischemic stroke, leading to variability in therapeutic decisions. Therefore, we aim to evaluate EVT safety and efficacy in patients with ACA occlusions compared with best medical treatment (BMT).
Methods: Retrospective cross-sectional study involving consecutive patients presenting with isolated ACA occlusion stroke from November-2015 to November-2023. The study delineated baseline clinico-radiological characteristics and treatment-related factors. Primary safety outcomes included symptomatic intracerebral hemorrhage (sICH) and 90-day mortality. Secondary outcome was functional independence (90-day mRS = 0–2).
Results: Among the 68 patients, 41 (60.3%) underwent EVT. Median age was 78 (IQR 73–84) years [EVT 77, IQR 68–84 vs BMT 84, IQR 73–89; $p = 0.137$]. Median NIHSS score was 9 (IQR 5–16) [EVT 9, IQR 7–17 vs BMT 7, IQR 4–16; $p = 0.478$]. No statistically significant differences were observed between patients undergoing EVT or BMT in sICH rate (EVT 10.5% vs BMT 4.5%, OR 1.179, 95% CI 0.078–17.84; $p = 0.905$), 90-day mortality (EVT 26.3% vs BMT 29.3%, OR 1.874, 95% CI 0.372–9.443; $p = 0.447$), or functional independence (EVT 36.4% vs BMT 25.0%, OR 0.774, 95% CI 0.078–7.634; $p = 0.826$). Among patients undergoing EVT, cardioembolic stroke showed higher odds of functional independence than other etiologies (OR 5.54, 95% CI 1.095–27.99; $p = 0.038$).



Method for permeability testing when exosomes are in contact with the BBB model

Conclusion: In our series, EVT for isolated ACA occlusion stroke was safe, although it did not significantly modify outcomes. Within EVT patients, cardioembolic stroke showed greater benefits. Ongoing randomized clinical trials will determine EVT efficacy for ACA occlusions.
Disclosure: Nothing to disclose.

EPO-045 | Obstructive sleep apnea syndrome: A cerebrovascular risk factor, linked to Alzheimer's disease

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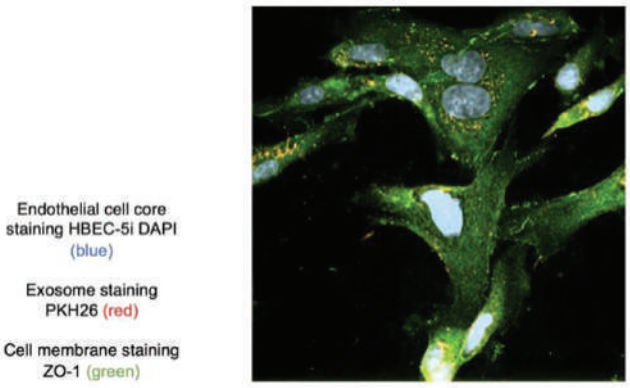
[1]*Université Jean Monnet, Saint-Etienne, France;* [2]*CHU, Saint-Etienne, France;* [3]*INSERM, U1059, SAINBIOSE, Université de Lyon, Saint-Etienne, France;* [4]*Gérontopôle AURA, 25 boulevard Pasteur, Saint-Etienne, France*

Background and Aims: Some studies have shown a link between obstructive sleep apnea syndrome (OSA) and Alzheimer's disease (AD). Our aim is to show that OSA is associated with cognitive disorders and has biological similarities with AD.
Methods: Isolation, characterization and quantification of exosomes from blood sera of non-AD apneic elderly subjects ($n = 15$); non-AD non-apneic elderly controls ($n = 15$) and AD elderly subjects (in progress, currently $n = 10$). Establishment of an in vitro BBB model whose permeability will be measured in contact with exosomes from each group.
Results: After isolation by precipitation and chromatography, characterization of exosomes by Western blot (WB) and ELISA using anti-CD81, CD63 and CD9 antibodies showed that apneic subjects had a high level of exosomes similar to AD patients. In addition, the exosomes of apneic subjects contained TAU and beta-Amyloid proteins in almost the same quantities as those of AD patients. The in vitro BBB model (monoculture of endothelial cells in astrocyte-conditioned medium) showed an increase in permeability of the model in contact with exosomes from apneic subjects similar to AD subjects. However, patients with very severe apnea induced a greater alteration of the BBB than AD patients.



Imaging exosomes in contact with endothelial cells

Conclusion: Analysis of exosomes from the 3 groups showed similarities between the apneic and AD groups compared with controls, suggesting that OSA may be a factor in the development of AD.
Disclosure: Nothing to disclose.

Clinical neurophysiology

EPO-046 | A new way to modulate somatosensory cortex: High frequency tACS matching individual evoked HFOs frequency

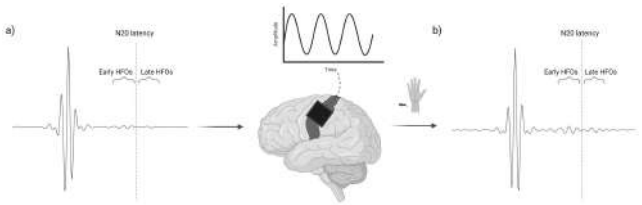
A. Cruciani[1]; G. Pellegrino[2]; A. Todisco[1]; F. Motolese[1]; M. Sferruzzi[1]; D. Norata[1]; F. Santoro[1]; G. Musumeci[1]; M. Rossi[1]; F. Pilato[1]; V. Di Lazzaro[1]; F. Capone[1]

[1]*Department of Medicine and Surgery, Unit of Neurology, Neurophysiology, Neurobiology, and Psychiatry, Università Campus Bio-Medico di Roma, Roma, Italy*; [2]*Epilepsy program, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada*

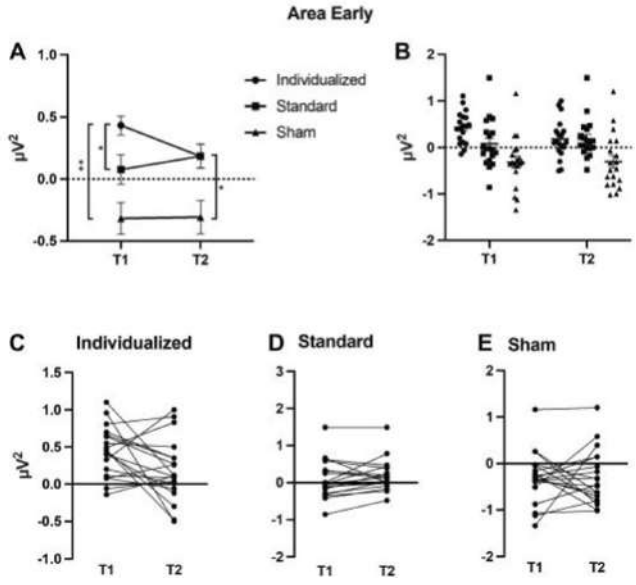
Background and Aims: Transcranial Alternating Current Stimulation (tACS) modulates brain activity non-invasively through electrical currents, with established effects on the primary motor cortex. This study explores the entrainment effects of tACS on the somatosensory system, particularly on evoked high-frequency oscillations (HFOs), comparing individualized, standard (600 Hz), and sham settings in healthy subjects.

Methods: The study involved three blocks, each a week apart and randomized among participants: Individualized tACS at the individual's HFOs rhythm, Standard tACS at 600 Hz, and Sham stimulation. Nineteen healthy participants underwent median nerve stimulation, and somatosensory evoked potentials (SEPs) were recorded before tACS (T0), immediately after tACS (T1), and 10 minutes after tACS (T2). High-frequency oscillations (HFOs) were identified and analyzed using a customized MATLAB pipeline. tACS was administered. Statistical analysis assessed differences across stimulations in delta values (T1-T0, T2-T0) using one-way repeated measure ANOVA and post-hoc comparisons.

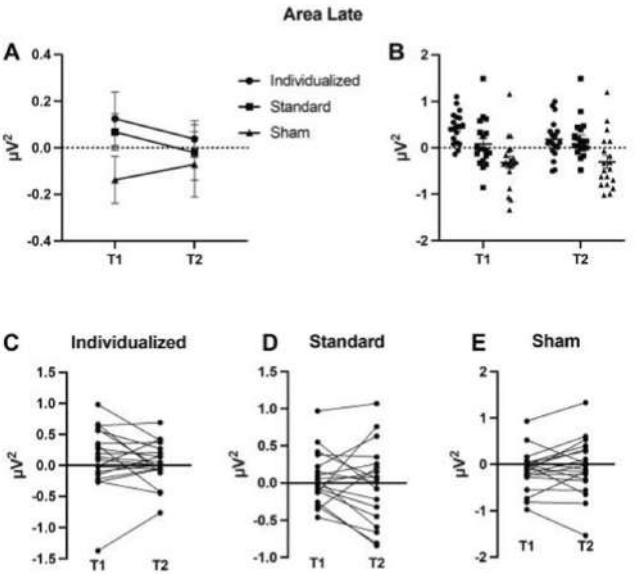
Results: Comparing T0 to T1 and T0 to T2 we found that Individualized tACS significantly increased Area Early compared to Standard and Sham, but no differences were observed between Standard and Sham. Area Late, N20 amplitude, and N20 latency showed no significant effects across stimulations at both time points (T1, T2).



Schematic representation of tACS delivered over left S1. Representative HFOs from subject 7: a) HFOs before tACS (T0); b) HFOs immediately after individualized tACS (T1)



Effects of different tACS stimulations on Area Early



Effects of different tACS stimulations on Area Late

Conclusion: Concluding, we here provide the first evidence that tACS tuned to the individual HFOs frequency modulates the thalamocortical activity in a frequency- and time-specific manner. Multiple studies have demonstrated dysregulation of HFOs in various pathological conditions. Accordingly, the evidence of individualized tACS capacity to influence somatosensory system could potentially pave the way for novel therapeutic applications.

Disclosure: Nothing to disclose.

EPO-047 | EEG and brain MRI alterations in transient global amnesia: The impact of time and gender

C. Ferrazzoli[1]; A. Castelli[1]; V. Ferrazzoli[2]; A. Pagano[1]; G. Di Mauro[1]; C. Liguori[1]; N. Mercuri[1]; F. Placidi[1]; F. Izzi[1]
[1]*Epilepsy Center, Neurology Unit, Department of Systems Medicine, University of Rome Tor Vergata, Rome;* [2]*Diagnostic Imaging Unit, Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome*

Background and Aims: The aim of the study is to evaluate the prevalence and characteristics of EEG and Brain MRI findings in patients with transient global amnesia (TGA).
Methods: This single-center observational retrospective study examined adult inpatients admitted at Policlinico Tor Vergata (2013–2023) with transient global amnesia (TGA), diagnosed according to Hodges and Warlow criteria. Only patients who underwent both EEG and brain MRI were included.
Results: Of 69 patients meeting criteria (41 females, 28 males; mean age 62.38 ± 9.20 years), TGA symptoms lasted 5.46 ± 6.14 hours. EEG abnormalities occurred in 68.1% of patients, predominantly bilateral (38.3% left, 51% bilateral, 10% right, $p = 0.002$). Focal slowing was observed in 33.3%, and interictal epileptiform abnormalities in 34.8%. Epileptiform changes were more frequent in females than males (46.3% vs. 17.86%, $p < 0.05$). EEG latency from TGA was shorter in the epileptiform group (47 ± 22.63 vs. 61.86 ± 36.6 hours, $p = 0.013$). Brain MRI revealed DWI positive lesions in 23.2% (left prevalence 11/16, bilateral 4/16, right 1/16, $p = 0.007$). DWI-positive patients had a shorter time interval from attack to MRI (82 ± 27.66 vs. 101.43 ± 45.54 hours, $p < 0.05$). No significant correlation existed between DWI positivity and EEG alterations or lateralization.
Conclusion: The study affirms timing importance, with shorter intervals correlating with increased EEG and MR-DWI findings in TGA. Left-sided DWI lesion dominance was noted, consistent with prior studies. No lateralization of EEG abnormalities was found, and MRI and EEG results showed no significant association. Additionally, a significant correlation between gender and paroxysmal EEG abnormalities suggests a potential gender-specific etiology in TGA, warranting further investigation.
Disclosure: Nothing to disclose.

EPO-048 | Investigating the working mechanism of transcranial direct current stimulation

E. Lescrauwaet[1]; M. Sprengers[1]; E. Carrette[1]; C. Algoet[1]; A. Mertens[1]; D. Klooster[2]; R. Raedt[1]; P. Boon[1]; K. Vonck[1]
[1]*4brain, Department of Neurology, Reference Center for Refractory Epilepsy, Ghent University Hospital, Ghent, Belgium;* [2]*Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands*

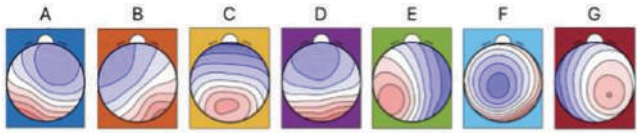
Background and Aims: Transcranial Direct Current Stimulation (tDCS) is used to modulate neuronal activity but its exact mechanism of action (MOA) is unclear, hampering its clinical applicability. This study investigates tDCS modulation of the corticospinal neurotransmission and its MOA. By anesthetizing the scalp before applying tDCS and by applying tDCS to the cheeks, we investigated whether stimulation of peripheral and/or cranial nerves substantially contributes to the effects of tDCS.
Methods: In a randomized cross-over study, 4 conditions were compared in 19 healthy volunteers: (1) anodal tDCS (a-tDCS) over the motor cortex, (2) a-tDCS over the motor cortex with a locally applied anesthetic on the scalp, (3) a-tDCS over the cheek region and (4) sham a-tDCS over the motor cortex. Motor evoked potentials (MEPs) were measured before and up to 1 h after a-tDCS. A questionnaire was used to assess the tolerability of a-tDCS.
Results: A significant MEP amplitude increase compared to baseline was found from 30 to 60 min after motor cortex a-tDCS. When applying a-tDCS over the motor cortex with a local anesthetic applied, only a non-significant small increase in MEP amplitude compared to baseline was observed. The questionnaire demonstrated that side effects are significantly lower when the local anesthetic was applied before a-tDCS administration.
Conclusion: The significant MEP amplitude increase observed post a-tDCS supports the modulatory effects of tDCS. The absence of significant modulation when a local anesthetic was applied suggests that effects of tDCS are not solely established through direct cortical stimulation, but stimulation of peripheral and/or cranial nerves might contribute to tDCS-induced modulation
Disclosure: Nothing to disclose.

EPO-049 | Exploring brain network dynamics in parkinson's patients with visual hallucinations: An EEG microstate approach

E. Toplutaş[1]; R. Uysal Kaba[2]; B. Güntekin[3]; L. Hanoğlu[1]
[1]*Department of Neurology, Istanbul Medipol University, Istanbul, Turkey;* [2]*Institute of Neuroscience, Istanbul Medipol University, Istanbul, Turkey;* [3]*Department of Biophysics, Istanbul Medipol University, Istanbul, Turkey*

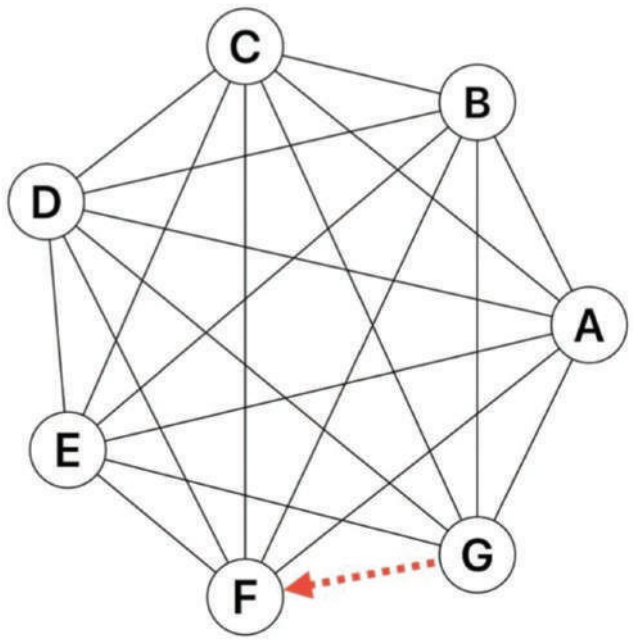
Background and Aims: In this study, we explore the realm of Parkinson's disease (PD), focusing on the manifestation of visual hallucinations (VH), a symptom often overshadowed yet critical in understanding the disease's complexity. Our aim is to elucidate the alterations in brain networks among PD patients experiencing VH, utilizing EEG microstate analysis. This approach offers a window into the neurophysiological processes underpinning these hallucinatory experiences.
Methods: Our cohort consisted of 19 PD patients reporting VH and a matched group of 20 PD patients without such symptoms. The matching criteria included age, gender, educational level, cognitive performance, and PD motor scores. We captured the brain's electrical activity through 5-min EEG recordings in a resting state with eyes

closed. The analysis of EEG microstates was conducted using templates derived from healthy controls, segmented into seven distinct topographical maps.



The analysis of EEG microstates was conducted using templates derived from healthy controls, segmented into seven distinct topographical maps.

Results: Between the two groups, statistical analysis revealed no significant differences in demographics, cognitive assessments, or motor scores. When examining the EEG microstate parameters, including duration, occurrence, and coverage, the results were consistent across all seven microstates, showing no notable variations. However, a significant finding emerged in the transition probabilities, with the VH group exhibiting a markedly lower frequency of transitions from microstate G to microstate F ($p < 0.001$).



The probabilities of microstate transitions are illustrated here, with the VH group exhibiting a significantly lower frequency of transitions from microstate G to microstate F ($p < 0.001$).

Conclusion: This study explores at EEG microstate alterations in PD patients who have VH, providing information on the neurophysiological processes that underpin these phenomena. The findings give a more advanced understanding of the disease's neural origins than just symptomatology.

Disclosure: There are no conflicts of interest.

EPO-050 | Neurophysiological consequences of network degeneration in Alzheimer's disease

F. Freri[1]; E. Canu[1]; G. Bertazzoli[2]; V. Castelnovo[1]; M. Marizzoni[3]; C. Bagattini[4]; C. Fracassi[4]; M. Bulgari[4]; M. Delai[4]; E. Ferrari[4]; A. Stango[4]; A. Geviti[5]; N. Bonfiglio[5]; M. Pievani[3]; D. Brignani[6]; V. Romei[7]; V. Nicolosi[3]; F. Agosta[8]; M. Filippi[9]; M. Bortoletto[4]

[1]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy; [2]Neurophysiology Lab, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy; and Center for Mind/Brain Sciences CIMeC, University of Trento, Rovereto, Italy; [3]Laboratory Alzheimer's Neuroimaging & Epidemiology, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy; [4]Neurophysiology Lab, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy; [5]Unit of Statistics, IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy; [6]Department of Clinical and experimental Sciences, University of Brescia, Brescia, Italy; [7]Centro Studi e Ricerche in Neuroscienze Cognitive, Dipartimento di Psicologia, Alma Mater Studiorum-Università di Bologna, Campus di Cesena, Cesena, Italy; Facultad de Lenguas y Educacion, Universidad Antonio De Nebrija, Madrid, Spain; [8]Neuroimaging Research Unit, Division of Neuroscience, and Neurology Unit, IRCCS San Raffaele Scientific Institute, and Vita-Salute San Raffaele University, Milan, Italy; [9]Neuroimaging Research Unit, Division of Neuroscience, Neurology Unit, Neurorehabilitation Unit, and Neurophysiology Service, IRCCS San Raffaele Scientific Institute, and Vita-Salute San Raffaele University, Milan, Italy

Background and Aims: Aim of this study is to demonstrate that TMS-evoked potentials (TEPs) can track neurodegeneration within cortical networks in Alzheimer's disease (AD).

Methods: We collected TEPs, resting state functional MRI (rs-fMRI), diffusion tensor imaging (DTI), and an extended neuropsychological evaluation in AD cases at various stages of the disease and healthy controls. TEPs were elicited by stimulating the parietal nodes of the default mode network (DMN) and the frontal nodes of the executive control network (ECN). We tested for differences in cognition, WM microstructural tract integrity and early TEP amplitudes (<50 ms) across groups.

Results: Two early TEP components generated for DMN stimulation, i.e., P20P and N20F, showed significantly higher amplitude after left stimulation than after right stimulation in mild cognitive impairment (MCI) due to AD, and not in other groups. Moreover, the N20F following a left DMN stimulation was stronger in MCI patients compared to healthy controls and to AD patients in dementia stage.

Conclusion: In the early stages of the disease, AD is associated with asymmetric alterations of neurophysiological responses in the DMN, in line with previously reported vulnerability of this network and of the left hemisphere in AD cases. The increased TEP responses only in the MCI group indicate that neurophysiological alterations within the DMN are not linearly related with the disease staging. Early TEP components from DMN stimulation have the potential to differentiate MCI due to AD from healthy individuals. Funding: Italian Ministry

of Health (GR-2016-02364132). Foundation Research on Alzheimer Disease.

Disclosure: F Freri, G Bertazzoli, V Castelnovo, C Bagattini, C Fracassi, M Bulgari, M Delai, E Ferrari, A Stango, A Geviti, NS Bonfiglio, D Brignani, V Romei,V Nicolosi have nothing to disclose. E Canu received research supports form the Italian Ministry of Health (IMH). M. Marizzoni receives research support from IMH. M Pievani received research supports form IMH. M. Bortoletto receives research support from IMH. M. Filippi received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi, speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA, participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda, scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme, he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, the Italian Ministry of University and Research, and FISM. F. Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and receives or has received research supports from IMH, the Italian Ministry of University and Research, AriSLA, the European Research Council, the EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease.

EPO-051 | Repetitive transcranial magnetic stimulation of the supplementary motor complex: What is known?

K. Germanova[1]; K. Panidi[1]; M. Nazarova[2]
[1]*Institute for Cognitive Neuroscience, Centre for Cognition and Decision Making, HSE University*; [2]*Department of Neuroscience and Biomedical Engineering, Aalto University, Finland*

Background and Aims: The supplementary motor complex (SMC), consisting of the pre-SMA and SMA-proper, contributes to a wide variety of brain functions. Non-invasive brain stimulation over both pre-SMA and SMA-proper areas effectively modulated different aspects of neurological and psychiatric disorders. In this review, we focused on studies with repetitive transcranial magnetic stimulation (rTMS) applied to these regions in both healthy individuals and clinical populations.

Methods: We collected original studies in English from the PubMed, Cochrane, and Scopus databases (PROSPERO ID – CRD42020141289) categorizing them into (1) studies on healthy volunteers and (2) studies on patients. From each study, we extracted: demographics, the function investigated, stimulation parameters including TMS coil targeting approach, and the primary outcomes.

Results: The final sample included 129 articles: 68 studies performed on healthy and 61 studies on clinical populations. Notably, the majority of studies focused on the SMA-proper rather than the pre-SMA. In the healthy participants, the SMA-proper was stimulated aiming to influence both motor (65% of papers) and cognitive processes (25% of papers), 10% of the article reported only neurophysiological findings. The pre-SMA stimulation was also applied aiming to modulate primarily motor function (79%). In the clinical population, both regions were stimulated to mitigate motor impairment symptoms. The SMA-proper was mostly stimulated in patients with Parkinson's disease (>40% of papers), while the pre-SMA – in patients with obsessive-compulsive disorder.

Conclusion: We suggest that SMA-proper/pre-SMA is a promising target for TMS for various neuropsychiatric conditions. Nevertheless, further research is needed to understand the interhemispheric and SMA/pre-SMA effect differences.

Disclosure: Nothing to disclose.

EPO-052 | Dopaminergic therapy and swallowing physiology in patients with Parkinson's disease: An electrophysiological study

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Background and Aims: Though dopaminergic therapy is the gold-standard treatment for PD, its effects on the swallowing function are still debated. Objective of the study is to assess the swallowing function through an electrokinesigraphic approach in a group of non-dysphagic PD patients with motor complications evaluated both in off- and on-therapy.

Methods: the repeated swallowing of a liquid bolus was performed while recording the following parameters: i) surface electromyographic activity of the submental-suprahyoid muscles (sh-EMG), involved both in the oral and pharyngeal phases of swallowing); ii) intraswallowing apneic pause (AP); iii) pharyngo-laryngeal mechanogram (PLM). Amplitude, duration and area of the recorded signals and time intervals were calculated using the Matlab platform. All patients were assessed both in on- and off-medication state.

Results: 11 patients (64 ± 6.4, 4F/7M) were enrolled and completed the experimental assessments. A significant ($p < .05$) shortening of the interval between the inspiratory and expiratory peaks following the swallowing act and the end of the AP was observed in the on- vs. off-medication state. Better but not statistically significant swallowing performances were also observed in patients when on-medication, in particular we observed a shorter oro-pharyngeal delay ($p = .11$) and a larger area of the PLM ($p = .017$)

Conclusion: dopamine therapy can improve the synergy between breathing and swallowing in accordance to previous findings that dopaminergic treatment can improve pulmonary function tests. However, based on these preliminary results in a small group of non-dysphagic PD patients, no significant changes in the other aspects of the oral and pharyngeal phases of swallowing were observed.

Disclosure: None.

EPO-053 | Neurophysiological evidence on the intravenous methylprednisolone use in spinal surgery

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Background and Aims: Research suggests corticosteroids post-spinal injury might increase side effects without benefits, highlighting a lack of symptom or electrophysiological controls. The hypothesis is that intravenous methylprednisolone (IVMP) could restore surgery-induced MEP amplitude reduction in a range-dependent manner, potentially improving postoperative motor scores.

Methods: This study reviewed spinal surgery patients with neurophysiological monitoring at a tertiary hospital, 2017–2023. Patients with over 50% MEP reduction were categorized into steroid and non-steroid groups upon surgeon's decision. MEP monitoring occurred at set intervals post-event, with examining MEP restoration and its correlation with motor recovery across defined MEP decline ranges. Statistical methods like T-tests and Pearson's correlation evaluated the effect of MEP recovery on motor outcomes.

Results: The analysis included 100 patients (71, steroid; 29, non-steroid group), with 807 muscles examined (524, steroid; 183 non-steroid group) (Table 1). The steroid group demonstrated higher MEP amplitudes (%) compared to the non-steroid group exclusively in the −100% to −80% MEP reduction range (Figure 1). A significant correlation was identified between the recovery of MEP amplitude and motor score improvement within the −80% to −50% reduction range (Table 2). For cases with complete MEP loss (-100%), no recovery in MEP or motor function was observed (Figure 1 and Table 2).

TABLE 1 Basic characteristics

Table 1. Basic characteristics

Variables	Steroid (N = 71)	Non-steroid (N = 29)	*P*
Demographics			
Age, mean (SD), y	53.7 (15.4)	55.8 (14.8)	0.535
Gender, No.(%)			0.073
Male	36 (50.0)	20 (71.4)	
Female	36 (50.0)	8 (28.6)	
Underlying systemic disease, No.(%)			
Hypertension	24 (33.3)	8 (28.6)	0.812
Other cardiovascular disease	3 (4.2)	2 (7.1)	0.617
Diabetes mellitus	10 (13.9)	5 (17.9)	0.756
Peripheral neuropathy	0 (0.0)	0 (0.0)	1.000
Main diagnosis, No.(%)			
Spinal cord tumor	37 (51.4)	7 (25.0)	
Ossification of posterior longitudinal ligament	23 (31.9)	8 (28.6)	
Herniated cervical disc	5 (6.9)	5 (17.9)	
Ossification of ligament flavum	2 (2.8)	4 (14.3)	
Spinal stenosis	1 (1.4)	0 (0.0)	
Other	4 (5.6)	4 (14.3)	
Lesion occupying spinal level, mean (SD)	3.4 (1.7)	3.7 (1.9)	0.372
Lesion level category, No.(%)			0.434
Cervical	41 (56.9)	12 (42.9)	
Cervico-thoracic	9 (12.5)	4 (14.3)	
Thoracic	17 (23.6)	11 (39.3)	
Thoraco-lumbar	3 (4.2)	0 (0.0)	
Lumbar	2 (2.8)	1 (3.6)	
Preoperative characteristics			
Preoperative motor score, mean (SD), score	91.1 (8.6)	94.3 (7.4)	0.263
Preoperative motor deficit, No.(%)			0.110
Motor deficit	49 (68.1)	14 (50.0)	
No motor deficit	23 (31.9)	14 (50.0)	
Perioperative characteristics			
Main operation type, No.(%)			
Tumor removal	37 (51.4)	7 (25.0	
Posterior spinal fusion	3 (4.2)	5 (17.9)	
Anterior cervical discectomy and fusion	3 (4.2)	4 (14.3)	
Laminectomy	21 (29.2)	7 (25.0)	
Laminoplasty	6 (8.3)	4 (14.3)	
Other	2 (2.8)	1 (3.6)	
Operation level, No.(SD)	4.5 (2.2)	3.9 (1.8)	0.249
Intraoperative motor eveked potentiall (MEP)			
MEP_{amp} reduction, mean (SD), %	-57.55 (33.17)	-59.78 (32.63)	0.531
MEP_{amp} reduction, muscle No.(%)			
Total	524 (100.0)	183 (100.0)	
-100%	24 (4.6)	10 (5.5)	
-100% ~ -80%, -80%	83 (15.8)	32 (17.5)	
-80% ~ -50%, -50%	59 (11.3)	30 (16.4)	
-50% ~ 0%	130 (24.8)	50 (27.3)	
No reduction	228 (43.4)	61 (33.3)	
MEP_{amp} at the end, mean (SD), %	-4.34 (104.04)	-20.75 (97.01)	0.133
Hemodynamic characteristics			
Bleeding amount, mL, mean (SE)	949.4 (124.3)	752.5 (157.7)	0.079
BP after induction, mmHg, mean (SD)			
SBP	130.4 (16.3)	122.8 (17.1)	0.237
DBP	76.3 (10.9)	71.1 (15.2)	0.298
MAP	94.4 (11.7)	88.3 (14.7)	0.156
Postoperative characteristics			
Motor score in POD1, mean (SD), score	86.5 (11.3)	89.3 (11.7)	0.280
ΔMotor, mean (SD), score	-4.6 (9.6)	-5.0 (8.3)	0.835
Motor change in POD1			0.386
Motor improvement	10 (13.9)	1 (3.6)	
No motor change	26 (36.1)	11 (39.3)	
Motor deterioration	36 (50.0)	16 (57.1)	

ΔMotor = Motor score of postoperative day 1 - Motor score of preoperative day 1; SD, standard deviation.
Student's t-test, Mann-Whitney test, or Fisher's exact test; $P < 0.05$, statistically significant.

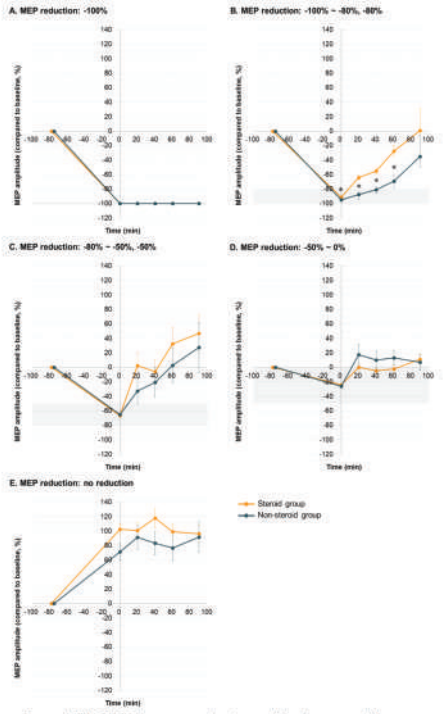

Figure 1. The MEP change over time in steroid and non-steroid group
MEP, motor evoked potential. Student's t-test was applied to compare the MEP amplitude between groups at each timepoint. $P < 0.05$, statistically significant. *, $P < 0.05$.

FIGURE 1 The MEP change over time in steroid and non-steroid group

TABLE 2 Correlation between MEP change and postoperative motor outcome

MEP reduction	Group	ΔMEP, %, mean (SD)				ΔMotor
		0 min – 20 min	0 min – 40 min	0 min – 60 min	0 min – 90 min	mean (SD)
-100%	Steroid	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.19 (0.67)	-6.25 (5.56)
	r (P)	-	-	-	-0.332 (0.268)	
	Non-steroid	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	-13.90 (5.36)
	r (P)	-	-	-	-	
-100% ~ -80%, -80%	Steroid	27.37 (61.31)	36.20 (45.54)	63.83 (74.27)	92.41 (108.41)	-1.70 (3.36)
	r (P)	0.175 (0.113)	0.237 (0.033)*	0.252 (0.037)*	0.234 (0.077)	
	Non-steroid	7.28 (17.56)	14.19 (23.52)	25.78 (38.44)	58.94 (101.62)	-1.03 (2.58)
	r (P)	0.111 (0.547)	0.078 (0.670)	0.076 (0.720)	0.213 (0.506)	
-80% ~ -50%, -50%	Steroid	68.92 (137.77)	61.05 (130.58)	99.55 (160.92)	112.84 (176.74)	-1.92 (3.51)
	r (P)	0.259 (0.048)*	0.241 (0.071)	0.325 (0.023)*	0.349 (0.018)*	
	Non-steroid	32.55 (94.57)	44.72 (100.77)	67.17 (105.63)	90.98 (124.96)	-2.57 (4.42)
	r (P)	0.207 (0.273)	0.300 (0.145)	0.305 (0.178)	0.399 (0.158)	
-50% ~ 0%	Steroid	24.07 (61.80)	18.39 (59.47)	19.12 (61.41)	36.60 (69.79)	-0.78 (2.41)
	r (P)	0.059 (0.502)	-0.062 (0.498)	0.093 (0.343)	0.025 (0.821)	
	Non-steroid	46.67 (105.85)	42.27 (89.12)	46.53 (76.51)	36.80 (59.38)	-0.76 (3.38)
	r (P)	-0.003 (0.982)	0.051 (0.738)	0.005 (0.974)	0.040 (0.853)	
No reduction	Steroid	-1.78 (166.52)	14.26 (173.13)	0.77 (155.38)	-6.79 (155.28)	-0.38 (2.34)
	r (P)	-0.105 (0.114)	0.025 (0.720)	0.029 (0.708)	-0.073 (0.378)	
	Non-steroid	19.91 (105.67)	18.62 (96.91)	10.98 (95.09)	18.79 (95.09)	-1.05 (2.96)
	r (P)	0.055 (0.673)	-0.028 (0.834)	0.192 (0.185)	0.193 (0.299)	
Total	Steroid	17.29 (127.17)	23.77 (128.11)	127.57 (127.57)	139.08 (139.08)	-1.04 (3.05)
	r (P)	0.202 (0.016)*	0.211 (0.013)*	0.274 (0.003)**	0.291 (0.003)**	
	Non-steroid	26.00 (91.71)	26.74 (83.67)	83.84 (83.84)	92.35 (92.35)	-1.51 (4.17)
	r (P)	0.137 (0.287)	0.192 (0.153)	0.190 (0.206)	0.287 (0.156)	

MEP, motor evoked potential; ΔMotor = Motor score of postoperative day 1 - Motor score of preoperative day 1; SD, standard deviation. Pearson's correlation analysis was applied. $P < 0.05$, statistically significant.

r, Pearson's correlation coefficient between ΔMEP and ΔMotor. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.

Conclusion: This current study is the first to investigate the effects of IVMP on the deterioration degree of MEP waves, and it further explores the impact of IVMP on postoperative motor outcomes in relation to the degree of MEP deterioration.

Disclosure: Nothing to disclose.

EPO-054 | Detection of electrophysiological markers indicating neuropathy in children and adolescents diagnosed with type 1 DM

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Background and Aims: We aimed to investigate the temporal changes and patterns of involvement in nerve conduction studies and autonomic tests in children and adolescents diagnosed with type 1 diabetes mellitus (T1DM).

Methods: We conducted nerve conduction studies and autonomic tests twice, with a one-year interval, on 63 patients aged between 8 and 18, with a minimum disease duration of 2 years, all diagnosed with T1DM. Demographic and clinical findings were assessed, and the study design is summarized in Figure 1.

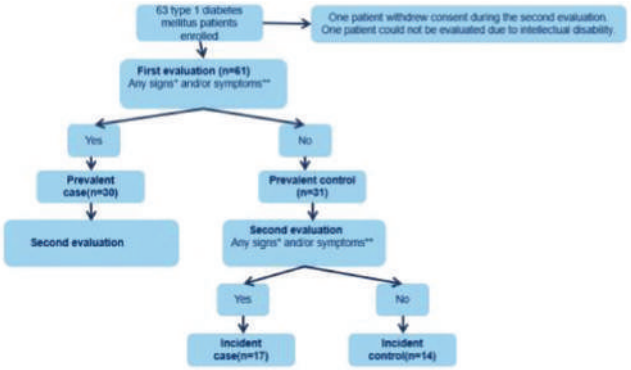

FIGURE 1 Diagram of the study design *associated with polyneuropathy, **according to Diabetic Neuropathy Symptom Score (DNS)

Results: No pathological findings consistent with the classical signs of neuropathy were observed in the parameters of nerve conduction studies. The most frequently abnormal parameters were peroneal F persistence (38.1%) and minimum F latency (30.2%), R-R interval variability (RRIV) (21%), and tibial minimum F latency (11.1%). Sural sensory peak latency and peroneal motor distal latency were found to be longer in both prevalent and incident case groups compared to the incident control group ($p < 0.05$). When the prevalent case group was compared with the prevalent control group, RRIV was lower, and sympathetic skin response (SSR) latency was longer in both upper and lower extremities ($p < 0.05$).

Conclusion: Monitoring latencies and conduction velocities in sensory and motor nerves may be more guiding in understanding the development of polyneuropathy. In addition, it seems useful to include SSR and RRIV examinations, which are parameters not frequently evaluated, in polyneuropathy research protocols in this group.

Disclosure: None of the authors has any conflict of interest to disclose.

EPO-055 | Difference in electromyographic features of dystonic and essential tremor: A pilot study

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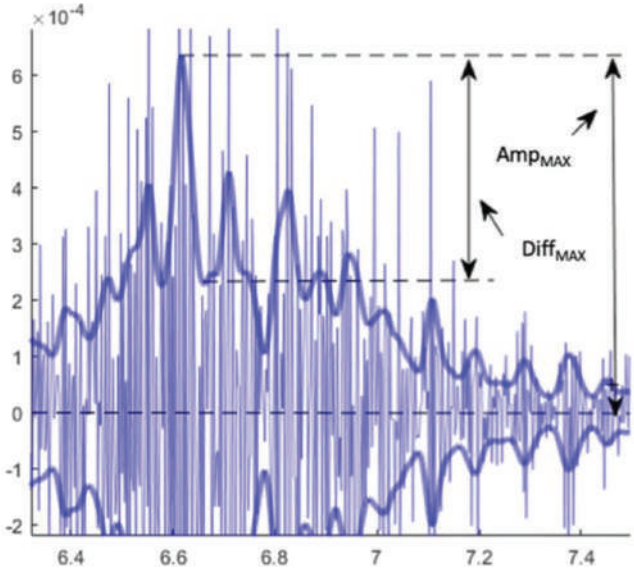
Background and Aims: Many patients with dystonic tremor (DT) – especially in the form of bilateral upper limb action tremor – are

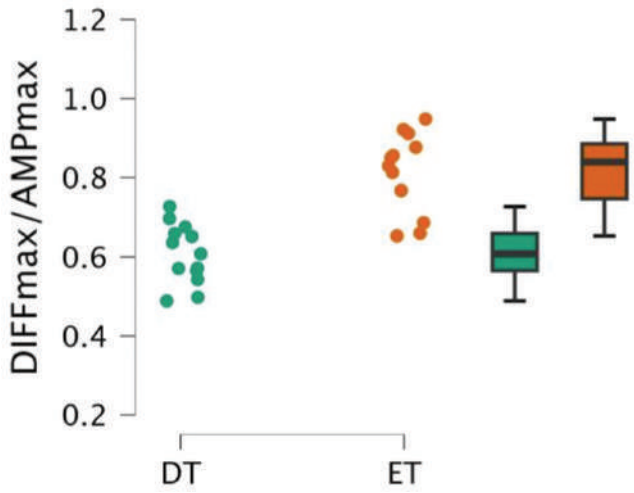
misdiagnosed as having essential tremor (ET). We aimed to find specific objective electromyographic (EMG) features of DT.

Methods: We examined 25 patients with upper limb tremor referred to our laboratory with a working diagnosis of ET. Surface EMG data were recorded from the extensor and flexor carpi radialis (ECR, FCR), first dorsal interosseus muscle and accelerometer placed on the index finger of a more affected limb by the Neurosoft®Neuro-MEP-8 EMG.

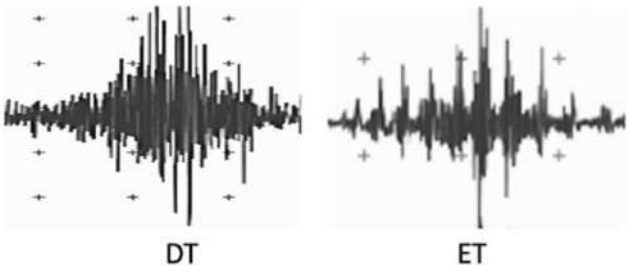
Results: None of the patients presented with obvious clinical features of dystonia. In 13 patients, we detected antagonist co-contraction, motor overflow, mirror dystonia, null point, and/or myoclonic jerks on EMG, thus suggesting the diagnosis of DT. From objectively measured parameters, these patients had a significantly lower ratio between maximum peak difference (measured between the highest and lowest point of discharge spike), and its maximum negative amplitude (DIFFmax/AMPmax; 0.607 ± 0.075, vs. 0.815 ± 0.102, $p < 0.001$, Cohen's $d = 2.333$). It indicates that isolated tremor bursts on EMG are less prominent in DT, perhaps due to rising from the background of sustained muscle contractions (dystonia). None of the other parameters differed significantly.



Measured parameters



Difference between ET and DT



Examples of patients with DT and ET

Conclusion: Surface EMG might help to verify subclinical dystonic activity and thus distinguish clinically similar tremors. In addition, measurable parameters might be used in the objective assessment of tremor types and they can become a part of the diagnostic process using deep learning methods.

Disclosure: This study was supported by the Grant of the Ministry of Education, Science, Research and Sport of the Slovak Republic (VEGA Nr. 1/0527/22).

EPO-056 | Reference values for near fiber EMG measures in upper and lower limb muscles

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Background and Aims: Near-fiber MUP (NF-MUP) analysis provides novel and useful information on motor unit potential (MUP) temporal dispersion (NFM-Dispersion) and instability (NF-MUP segment jitter (NFM-SJ)) from signals acquired during routine EMG protocols. NFM-Dispersion is the spread in the times with which muscle fiber action potentials (MFAP) pass the recording electrode, whereas NFM-SJ reflect the temporal inconsistencies in their generation.

Methods: NFM-Dispersion and NFM-SJ reference values were determined for six muscles (deltoid, biceps, triceps, vastus lateralis, tibialis anterior and medial gastrocnemius), based on a sample size of 20 control cases each with a minimum of 20 MUPs per muscle (age 23–79 y-o). The EMG signals used were acquired using a standard needle EMG examination protocol. DQEMG (Decomposition-based Quantitative EMG) software was used for the calculation of NF-MUP parameters. Reference values were defined using a method based on the e-norm (Jabre, 2015) and e-ref (Nandedkar, 2018) methods.

Results: The distribution of values by quartiles indicated a small variability between subjects, with low standard errors and narrow confidence intervals. The analysis of values above the defined reference values indicated that NF-MUP parameters are highly clustered and close to the reference values. Considering all of the MUPs for each respective group of control muscles, the percentage of unstable MUPs ranged between 4.9 and 11.2%, and the percentage of dispersed MUPs from 5.2 to 13.4%.

TABLE 1 NFM-SJ reference values.

Muscle	Q1 (μs) /SE	Mean (μs) /SE	Std	Q2 (μs) /SE	Q3 (μs) /SE	E-Ref (μs)	95th P (μs)
Deltoid	28.1/0.8	35.4/0.8	11.5	34.6/1	41.9/0.9	53	55
Biceps	27/0.4	34.1/0.5	10.9	32.7/0.5	40.5/0.7	50	52
Triceps	29.9/0.7	36.9/0.7	11.3	35.4/0.8	43.6/0.8	53	55
Vastus L	29/0.7	36.9/0.7	11.4	36/0.9	43.1/0.8	50	58
Tibialis A	32.3/0.9	39.1/1	12.9	38.3/0.7	46.4/1.1	60	62
M Gastroc	34.2/0.9	42.7/0.8	14.1	41.7/1	49.5/1	65	67

TABLE 2 NFM-Dispersion reference values.

Muscle	Q1 (ms)/SE	Mean (ms) /SE	Std	Q2 (ms) /SE	Q3 (ms) /SE	E-Ref (ms)	95th P (ms)
Deltoid	0.7/0.07	1.5/0.09	1.2	1.3/0.08	2.1/0.1	3	3.8
Biceps	0.6/0.06	1.2/0.08	1.2	1/0.06	1.7/0.08	3	3.1
Triceps	0.8/0.08	1.7/0.09	1.2	1.4/0.09	2.1/0.14	3	4.1
Vastus L	0.5/0.11	1.2/0.11	1.1	1/0.12	1.8/0.14	3	3.4
Tibialis A	0.4/0.08	1.3/0.09	1.5	1/0.09	1.8/0.14	3	4.1
M Gastroc	0.7/0.13	1.6/0.12	1.2	1.4/0.14	2.3/0.14	3	3.7

Conclusion: NFM-Dispersion and NFM-SJ stability measures, extracted from regular EMG signals, are useful and solid parameters that can augment the current understanding of neuromuscular disorders.

Disclosure: Nothing to disclose.

EPO-057 | Introduction to near fiber EMG, a novel way to measure motor unit electrophysiological properties

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Background and Aims: Motor Unit Potential (MUP) complexity and instability are key parts of EMG examinations, whose assessment can be time-consuming or subjective. We introduce a novel and semi-automated way of measuring MUP complexity and instability, based on Near Fiber (NF) EMG concepts. A NF-MUP is the summation of the muscle fibre potentials of fibers near the recording electrode (NF-MFPs). The temporal dispersion and instability of NF-MFPs are new clinically useful MU characteristics that can be quantified using NF-MUP parameters.

Methods: Aspects of novel signal processing algorithms used to extract MUP trains, estimate MUP and NF-MUP templates and select isolated NF MUPs for complexity and instability analysis as well as new quantitative measures to characterize sampled MUs will be described, demonstrated, and discussed.

Results: NFEMG has been used to study and assess several neuromuscular diseases. It has been used to detect increased MUP complexity and instability in CIDP, ALS, GBS, and diabetic neuropathy. In addition, it can be used to diagnose MG with similar accuracy as provided by SFEMG.

Conclusion: NF EMG offers an exciting new, rapid, and comprehensive evaluation of MUP complexity and instability that promises to significantly advance the diagnosis and monitoring of neuromuscular diseases.

Disclosure: Nothing to disclose.

EPO-058 | Sural-to-medial femoral cutaneous amplitude ratio in early diagnosis of uremic neuropathy

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Background and Aims: Chronic Renal Failure (CRF) is typically associated with length-dependent axonal polyneuropathy and secondary demyelination. This study aimed to clinically and electrophysiologically assess CRF patients experiencing polyneuropathy-related complaints before initiating dialysis. The sural-to-medial femoral cutaneous nerve action potential (NAP) amplitude ratio (SMFCAR) was evaluated for its sensitivity and specificity in early electrophysiological diagnosis.

Methods: The study included 32 CRF patients (mean age 60.0 ± 9.6 years) and 30 age and sex-matched controls (58.9 ± 6.6 years). Assessments encompassed neurological examination, Michigan Neuropathy Screening Instrument (MNSI) A-B, and Semmes-Weinstein monofilament (10 g–5.07 mm) test. Radial, median, ulnar, medial femoral cutaneous, sural, and superficial peroneal sensory; median, ulnar, tibial, and peroneal motor conduction studies were performed. Sural-to-radial amplitude ratio (SRAR) and SFMCAR were calculated, and their diagnostic sensitivities were compared.

Results: The patients were in the CRF stages of 3 (59.4%), 4 (34.4%), and 5 (6.3%). The average CRF duration was 54.3 ± 46.1 (8–276) months. MNSI-B indicated clinical polyneuropathy in 59% of the patients, while routine nerve conduction studies diagnosed it in 72%. Median SRAR and SMFCAR values were significantly lower in patients than controls ($p < 0.001$ for both). At 90% specificity, SMFCAR's cut-off was <2.8 with a sensitivity of 59%, while SRAR's was <0.77 with a sensitivity of 35%.

Conclusion: In some CRF patients with symptoms compatible with length-dependent polyneuropathy, peripheral nerve involvement might be in a stage that cannot be detected by routine examination and electrophysiology. SMFCAR may be a useful alternative to SRAR in the early diagnosis.
Disclosure: Nothing to disclose.

EPO-059 | Subclinical epileptic activity and cognitive decline in Parkinson's disease and atypical parkinsonisms

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Background and Aims: Subclinical epileptiform activity (SEA) are epileptic discharges that occur without clinical seizures. There is evidence that SEA might be associated with accelerated cognitive decline in Alzheimer's disease (AD). Its occurrence and clinical correlates in parkinsonian syndromes have not been studied yet. Our primary aim was to study the frequency of SEA in parkinsonian patients. The secondary aim was to compare clinical and demographic characteristics in patients with and without SEA and characterize SEA morphologically.
Methods: Retrospective cross-sectional study. We examined patients with parkinsonian syndromes who underwent level 1/2 polysomnography between 1/1/2018 and 31/05/2022. Demographic information, diagnosis, and presence of mild cognitive impairment/dementia were obtained by chart review. Electroencephalogram (8 channels) was manually analysed for SEA, defined as paroxysms that fulfilled ≥4/6 epileptic discharge criteria according to the International Federation of Clinical Neurophysiology, confirmed by 3 epileptologists/neurophysiologists. Non-parametric statistical analysis was performed.
Results: 26 polysomnographies were reviewed (15 Parkinson's disease, 6 Multiple system atrophy, 2 Dementia with Lewy bodies, 2 vascular parkinsonism and 1 progressive supranuclear palsy). 14 patients had SEA (54%). There were no statistically significant differences between patients with SEA (median age 72yrs, 64% women, 36% with cognitive decline) and without (median age 64yrs, 67% women, 25% with cognitive decline). SEA's main location was temporal and temporo-occipital.
Conclusion: Our SEA prevalence was similar to studies with AD patients, and higher than data published from healthy controls (5–25%). Although it is a small heterogenous sample, with few EEG channels, it suggests that SEA is frequent in other neurodegenerative disorders.
Disclosure: Nothing to disclose.

EPO-060 | New national reference limits for nerve conduction studies

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Background and Aims: Reference limits are important for correctly interpreting nerve conduction studies (NCS). Because reference limits for NCS are dependent of the examining procedure and the equipment settings used, laboratory-specific reference limits are needed. However, creating such reference limits with traditional methods is expensive and time-consuming. We present reference limits for NCS using a more practical approach – extrapolated norms (e-norms) – using historical measurements from the world's largest database of NCS.
Methods: We applied the e-norms algorithm on 2 143 280 Norwegian historical NCS measurements (conduction velocities, amplitudes, distal latencies) from 1998 to 2023 for the motor Peroneal, Tibial, Median and Ulnar nerves and the sensory Sural, Superficial Peroneal, Medial Plantar, Median, Ulnar and Radial nerves. Age was stratified into decades starting from the age of 20 up to the age of 99. Height was stratified into three brackets: 150–170 cm, 170–180 cm and 180–200 cm.
Results: The stratification gave in total 630 reference limits. In general, the reference limits decreased with age and height for conduction velocities and amplitudes, and increased for latencies. The values were close to the currently used limits derived by traditional methods. Ten references limits for nerves in the lower extremities could not be reliable calculated.
Conclusion: We have calculated new national reference limits for NCS in Norway (published at https://www.ous-research.no/digmine). Compared to the reference limits already in use, the reference limits produced by the e-norms algorithm are similar. In addition, the algorithm also produced reference limits for age groups where high quality reference limits are currently lacking.
Disclosure: Nothing to disclose.

Neuroimmunology 1

EPO-061 | COVID-19 vaccination response in participants receiving efgartigimod IV or Efgartigimod PH20 SC in ADAPT+ or ADAPT-SC+

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Background and Aims: Patients with generalised myasthenia gravis (gMG) experience greater risk of adverse outcomes from respiratory infections, including COVID-19. Some immunosuppressive therapies used in gMG management increase risk of infection and impair vaccine responses. We investigated the effect of treatment with efgartigimod [administered intravenously (IV) or subcutaneously (SC, coformulated with recombinant human hyaluronidase PH20), a human IgG1 antibody Fc-fragment that reduces total and pathogenic IgG levels through neonatal Fc receptor blockade, on humoral immune responses to COVID-19 vaccination in participants with gMG.

Methods: In ADAPT+ (completed) and ADAPT-SC+ (ongoing open-label extension), efgartigimod IV (10 mg/kg) or efgartigimod PH20 SC (1000 mg) were administered in cycles of 4 once-weekly infusions/injections. Among other COVID-19 receptor binding domain-specific IgGs, SARS-CoV-2-IgG-RBD responses were assessed, nominally, at prevaccination, ≥4 weeks after vaccination, and subsequently at 1 week after fourth efgartigimod PH20 SC injection (when total IgG levels were maximally reduced, Figure). One sample was collected if postvaccination time points coincided with each other.

Results: Eighteen participants in ADAPT-SC+ (Table) received a COVID-19 vaccine during or after a cycle. For 78% ($n = 14/18$) of participants, this was their second or third vaccine dose. A 35.9-fold increase in SARS-CoV-2-IgG-RBD levels occurred from prevaccination to ≥4 weeks postvaccination (Figure). Similarly, from prevaccination to 1 week after the fourth efgartigimod PH20 SC injection, a 33.8-fold increase emerged (Figure). Similar results were observed with efgartigimod IV during ADAPT+.

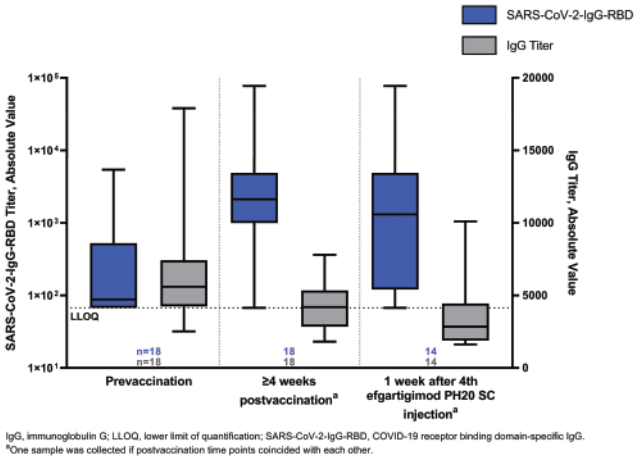

FIGURE Absolute Values of SARS-CoV-2-IgG-RBD Titer and Total IgG Titer

TABLE Participant Characteristics

Characteristic	Participants (N=18)
Age (y), mean (SD)	53.9 (11.7)
Age category, n (%)	
18-64 y	15 (83.3)
≥65 y	3 (16.7)
Sex, n (%)	
Female	10 (55.6)
Male	8 (44.4)
Body mass index (kg/m), mean (SD)	28.3 (6.2)

Conclusion: Consistent with efgartigimod IV results, participants receiving efgartigimod PH20 SC were able to mount antigen-specific IgG responses to COVID-19 immunisation, even when total IgG levels were maximally reduced.

Disclosure: Multiple relationships financial and non-financial nature for authors FS, JFH, JWS, FG, PD, BVH, SS, RM, JLDB, AA, and KW stated at point of presentation.

EPO-062 | Primary angiitis of the central nervous system: The experience of a tertiary center

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Background and Aims: Primary Angiitis of Central Nervous System (PACNS) is a rare inflammatory disorder affecting blood vessels in CNS without systemic involvement that exhibits a range of presentations. We aimed to characterize the population of patients with PACNS in a tertiary center.

Methods: Retrospective analysis of patients in Neuroimmunology outpatient clinic diagnosed according to Rice and Scolding (2020) criteria. Demographic, clinical, laboratory, imaging, and histological data were recorded.

Results: Twelve patients were included (male-to-female ratio 1:1.4) with an average age of symptom onset at 50.8 ± 16 years and diagnosis at 53.8 ± 13 years. Half were classified as definitive diagnosis, the remaining six as possible. Most frequent presenting symptoms were cognitive impairment (42%), stroke/focal neurological deficits (33%). Over the course of the disease, 66% also developed headache. MRI was abnormal in all 12 cases, with ischemic lesions (66%), microhemorrhages (33%) as the most frequent changes. Abnormalities in CSF were found in 82%, with lymphocytic pleocytosis in 54% (average 15.2 cells/μL), elevated protein levels in 45% (average 0.6 g/L), oligoclonal bands in 36%. Classical angiography was positive in 100% (5/5), and histological results in 75% (6/8) with prevalence of lymphocytic vasculitis. The treatments used were mainly corticosteroids (92%) and cyclophosphamide (75%). The patients were followed for an average of 8.4 ± 7 years, 33% with a Rankin scale ≥3. Despite treatment, gradual clinical deterioration was observed in 42% and sequelae cognitive impairment in 50%.

Conclusion: This analysis reveals a variety of clinical, radiological, and histological findings showing the complexity of the disorder. The severity of the condition despite treatment is also highlighted.

Disclosure: Nothing to disclose.

EPO-063 | CD20 T lymphocytes in multiple sclerosis: Impact on neuropsychological findings

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Background and Aims: Some T lymphocytes show molecular signature also for B lymphocytes (CD20)CD20 T lymphocytes may play a pivotal role in multiple sclerosis pathology, especially at progressive stages. This would suggest that CD20 T lymphocytes might be a marker of central nervous system (SNC) compartmentalized inflammation. We aim to investigate the correlation between CD20 T lymphocytes in peripheral blood in MS patients with neuropsychological features (i.e. cognition, depression, anxiety, fatigue and sleep quality).

Methods: We enrolled 90 MS patients. Each patient underwent cognitive assessment (BICAMS) and psychometric assessment (i.e. MFIS, BAI, BDI, PSQI). Cognitive status was defined through the cerebral functioning score (CSF). For each patient we performed blood sample collection to assess CD20 T lymphocytes and neurofilaments (NFL) levels.

Results: Forty-four out of 90 patients were relapsing-remitting (49%), 46 were progressive patients (51%). Seventy patients (18.9%) showed CD20 T lymphocytes in peripheral blood with a mean level of 0.38 ± 1.2. Patient with CD20 T lymphocytes were more likely to be in progressive patients (76.5% vs 23.5% of relapsing MS patients, $p = 0.02$), and showed a higher EDSS (3.5 vs 6, $p = 0.001$). Moreover, patients with CD20 T lymphocytes showed worse cognitive functioning ($p = 0.004$), higher global fatigue symptoms ($p = 0.02$) higher cognitive fatigue ($p = 0.01$), higher psychosocial fatigue ($p = 0.005$) and a trend toward worse sleep quality ($p = 0.06$). Conversely, NFL levels were not associated with CD20 T lymphocytes.

Conclusion: The presence of CD20 T lymphocytes in peripheral blood of MS patients, could possibly reflect an ongoing neurodegenerative process independent from inflammatory activity resulting in worse neuropsychological functioning.

Disclosure: MM has received research grants from the ECTRIMS-MAGNIMS, the UK MS Society, and Merck; honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. AC has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen and Novartis. MP has received research grants from Italian MS Foundation and Baroni Foundation, honoraria from HEALTH&LIFE S.r.l. and Biogen and sponsorship for travel/meeting expenses from Novartis, Roche and Merck. RL has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. VBM has received research grants from the Italian MS Society, and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. AE, ALS, CDM, VN, FN, FF, FL ME have nothing to disclose.

EPO-064 | Intravenous vs subcutaneous natalizumab in the treatment of multiple sclerosis, a cohort study

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Background and Aims: Subcutaneous (SC) natalizumab has been recently approved for multiple sclerosis treatment. There are few studies comparing clinical effectiveness and safety of subcutaneous and intravenous Natalizumab.

Methods: Retrospective study of multiple sclerosis patients followed at a Portuguese tertiary center, currently under treatment with Natalizumab (NTZ). Analysis of efficacy and safety of intravenous (iv) and subcutaneous (sc) formulations.

Results: Data were collected from 59 patients of which 12 were treated with iv NTZ (group 1), 36 with iv and then formulation was switched to sc NTZ (group 2), and 11 with sc NTZ (group 3). At baseline, patients from group 1, 2 and 3, had respectively a median

EDSS of 2.0 [IQR: 0–4.5], 1.5 [IQR: 0–6.0] and 1.0 [IQR: 0–2]. ARR (Annualized relapse rate) was 1.0 in all groups. Patients from group 1 (5/41.7%) group 2 (16/44.4%), and group 3 (6/54.5%) had disease activity on CE-MRI. Patients from group 1, 2 and 3, had respectively a median of 4 [IQR: 1.0–14.0], 3 [IQR: 1.0–13.0], and 1.0 [IQR: 1.0–2.0] years of treatment. After treatment, median EDSS was 2.0 [IQR: 0–4.5] in group 1 and 2, and 1.5 [IQR: 1–2] in group 3, and median ARR was 0 in all groups. One patient (8.3%) of group 1 (3 years of NTZ) and 2(18.1%) patients of group 3 (1 year of NTZ) had disease activity on CE-MRI. Both formulations were well-tolerated. Only two patients presented minor gastrointestinal side effects and discontinued sc formulation. Three patients refused to switch to sc NTZ.

Conclusion: Both formulations of NTZ seem to be comparable in safety and in stabilizing the disease.

Disclosure: All authors declare that they have no conflicts of interest related to the manuscript.

EPO-065 | Crohn-related CRION case report: When optic neuropathy is not synonymous with demyelinating disease

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Background and Aims: Among the extra-intestinal manifestations in Crohn's disease, Chronic Relapsing Inflammatory Optic Neuropathy (CRION) is an inflammatory optic neuropathy characterized by a strong responsiveness to steroids.

Methods: A 22-year-old woman suffering from Crohn's disease since 2014, undergoing multiple ileal resections, on Vedolizumab therapy. Since March 2023, during a flare-up of IBD (and Vedolizumab suspension) she began to experience bilateral eyelid edema, photophobia, and pain during eye movements. She underwent endocrinological examination suspecting Graves' disease (negative autoantibodies, no hormonal profile alterations) and Ophthalmic examination (chemosis, conjunctival hyperemia, tearing). Brain MRI showed bilateral edematous impregnation of periocular soft tissues, lacrimal glands, perisclera tissues, lateral rectus muscles, and a swollen (non-enhancing) appearance of the optic chiasm. Blood tests were normal. She went to the emergency department where a neurologist initiated high-dose steroid therapy, with symptoms remission. A flare was observed upon tapering the dose, prompting the resumption of steroid therapy. Cervical spine MRI was negative and cerebrospinal fluid analysis showed no oligoclonal bands, negative viral and bacterial meningitis panel, polyclonal immunoglobulins, and 106 mg/dL protein. Anti-AQP4, anti-MOG, complement factors, myositis-associated autoantibodies, ANA, AMA, LKM, and ENA were negative.

Results: In IBD, optic neuropathy may be ischemic (not detected during ophthalmic examination), reactive to anti-TNF drugs (unlikely due to Vedolizumab therapy), demyelinating (ruled out by diagnostic workup), associated with rheumatological disease (excluded), or CRION. The latter seems most likely in this patient.

Conclusion: Timely diagnosis of CRION leads to rapid reversal with steroid therapy, avoiding permanent visual sequelae.

Disclosure: No disclosures.

EPO-066 | Evaluation of parameters affecting sexual dysfunction in multiple sclerosis: A preliminary study

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Background and Aims: This study aimed to analyze the factors affecting sexual dysfunction (SD) in Multiple Sclerosis (MS) which is one of the most important causes of disability in young adults.

Methods: Volunteers diagnosed with MS were included in the study. The Arizona Sexual Experiences Scale (ASEX), Beck Depression Inventory (BDI) and Short-Form Health Survey (SF-12) were used to screen for possible SD, assess depression and evaluate quality of life (QoL) respectively. MS types and disease-modifying drugs (DMDs) used by patients were recorded. Disease durations were divided into four groups (1–3, 4–6, 7–9, ≥10 years).

Results: Socio-demographic information of 418 MS patients is shown in Table 1. A positive correlation was found between ASES and BDI scores and a negative correlation with SF-12. Multivariate variance analysis showed significant effects of BDI scores, gender and disease duration on SD. Women had higher ASES scores than men. As BDI scores increased, a significant increase in ASES was observed. SD was found in all disease duration groups, being more pronounced in the 1–3 and 4–6 year diagnosis groups. Age, MS type, DMD's used, education duration and SF-12 levels had no significant effect on ASES scores.

Parameter	Score
Age, mean (Years)	37.99 ± 10.01
Age range (Years)	(min: 18 - max: 66)
Female, n (%)	291 (69.6%)
MS diagnosis duration (years)	7.76 ± 6.64
(min: 1, max: 36)	
MS Type (n)	RRMS*: 133
	Progressive MS**: 285
Education (%)	Primary School (8.1%)
	Secondary School (6.2%)
	High School (26.8%)
	University (48.1%)
	Master's Degree (10.8%)

*RRMS: Relapsing-Remitting Multiple Sclerosis

**Progressive MS: Progressive Multiple Sclerosis

Sociodemographic Data of Patients

Conclusion: The study supports the literature in finding SD more common and associated with depression in women compared to men. SD and depression were more intense in patient groups diagnosed for up to six years, possibly due to changes in coping mechanisms over the years. Further studies are needed.
Disclosure: Nothing to disclose.

EPO-067 | The use of diffusion tensor tomography to assess the pyramidal system in patients with multiple sclerosis

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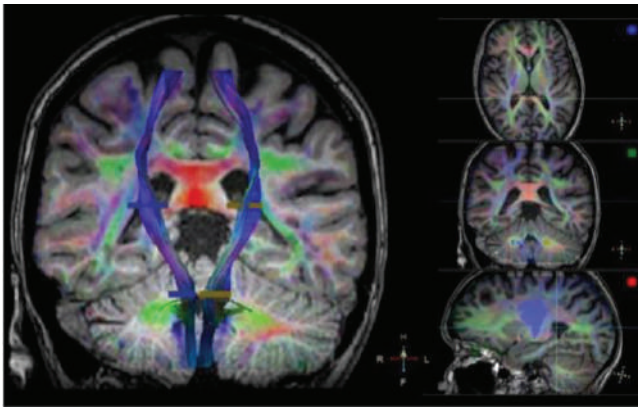
Background and Aims: The corticospinal tract (CSC) forms the basis of motor neurophysiology. The aim – to study CST in patients with highly active Multiple sclerosis (MS) during period of switching therapy.
Methods: 24 patients with MS were examined. Depending on severity of violations of pyramidal functional system (PFS) according to EDSS, patients were divided into 2 groups, group 1—17 patients with score of 0–2.5 points, group 2—7 patients with score of >=3 points. Diffusion tensor images (DTI) were processed using the DTI FiberTrak software.
Results: There was a decrease in the volume of pyramidal tract in patients of group 2 ($p < 0.001$), an asymmetry of indicator was found, in several patients – decrease on the clinically intact side, which may indicate visually undetectable signs of damage to pyramidal tract. There was a distinct tendency towards decrease in fractional anisotropy and a decrease in length of pyramidal tract as pyramidal deficit increases ($p < 0.001$). Negative correlations were found between indicators of neurological deficit and volume and length of the pyramidal tract, as well as a direct correlation of duration of course of MS with apparent diffusion coefficient (ADC) and the reverse – with fractional anisotropy.

Table 1.
Demographic indicators of the examined patients

Indicator	All patients n=24	1st group n=17	2nd group n=7
Sex M/F	7/17	6/11	1/6
Age M+/-σ	38,4+/-10,3	37,6+/-9,6	39,8+/-11,5
Duration of the disease M+/-σ	5,6+/-3,7	5,6+/-4,1	5,5+/-3,0
Type of MS	RRMS – 20 SPMS – 4	RRMS – 16 SPMS – 1	RRMS – 4 SPMS – 3
EDSS, score Me [Q1, Q3]	2,0 [1,5; 3,5]	1,5 [1,5; 2,0]	4,5 [3,5; 5,5]
Pyramidal functional system, score Me [Q1, Q3]	1,0[1,0; 3,0]	1,0 [0,0; 1,0]	3,0 [3,0; 3,0]

Patient data



Visualization of CST using DTI

Table 2.
Indicators of diffusion tensor examination of the pyramidal tract in patients with MS

Indicator	1st group n=17	2nd group n=7	Control group n=5
Volume of the pyramid tract (V), mm³	7414+/-1490 **p1-2<0,001**	5 650+/-1 828	7252+/-1025 p1-K=0,543 p2-K=0,018
Fractional anisotropy (FA)	0,515+/-0,031 p1-2=0,296	0,504+/-0,016	0,524+/-0,009 p1-K=0,045 **p2-K <0,001**
Apparent diffusion coefficient (ADC), 10^ (-3) mm²/sec	0,826+/-0,052 p1-2=0,113	0,857+/-0,065	0,807+/-0,02 p1-K=0,574 **p2-K=0,01**
The length of the pyramid tract (L), mm	123,5+/-12,4 p1-2=0,04	116,4+/-4,7	133,5+/-7,1 **p1-K=0,001** **p2-K<0,001**

Note: p1-2 is an indicator of the statistical significance of differences between groups 1 and 2, p1-K is an indicator of the statistical significance of differences between 1 and control groups, p2–K is an indicator of the statistical significance of differences between 2 and control groups. Statistically significant indicators are indicated in bold.

DTI results

Conclusion: The revealed decrease in volume and length of pyramidal tract, an increase in ADC, the asymmetry of these indicators, correlations with level of pyramidal insufficiency, EDSS and duration of the course of MS, obviously, can serve as additional criteria for assessing dynamics of disease and effectiveness of therapy.
Disclosure: Nothing to disclose.

EPO-068 | Characterizing double-negative neuromyelitis optica spectrum disorder: A systematic review and meta-analysis

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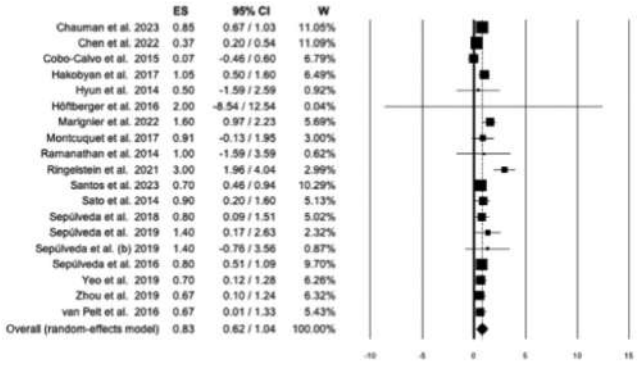
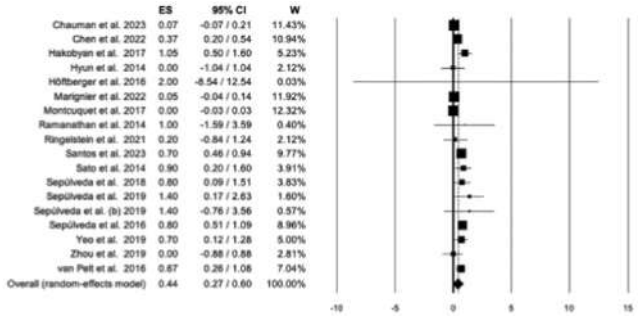
Background and Aims: Neuromyelitis-optica spectrum disorders (NMOSD) usually associate with aquaporin-4 (AQP4) or myelin oligodendrocyte glycoprotein (MOG) antibodies. Seronegative-NMOSD (SN-NMOSD) has been described, but the clinical-therapeutic profile is poorly defined.

Methods: We searched PubMed, Scopus and Google Scholar databases for studies reporting SN-NMOSD patients, on which anti-MOG-Abs and AQP4-Abs were tested. PRISMA guidelines and methodological quality control were assessed. Fixed or random-effects models were used to pool results across studies.

Results: We included 36/1027 articles screened and analyzed 591 SN-NMOSD patients (mean age: 30.3 [range 6–78]; female:male ratio; 2:1). Disease course was relapsing in 66% of cases. Brain MRI at onset showed brain abnormalities in 165/241 patients (69%) including tumefactive brain lesions in 19/241 (8%). Spinal cord MRI showed cervicothoracic lesions (99/241, 41%) and LETM (89/241, 37%). CSF analysis showed OCBs in 58/300 patients (19.3%). Mean annualized relapse ratio (ARR) was 0.77 (95% CI 0.10–1.8), and was higher in patients with late onset (>50 years, $p<0.001$). Mean EDSS and late-onset were associated with a relapsing course ($p<0.05$). Relapsing SN-NMOSD patients had a higher ARR and a worse outcome compared to AQP4-NMOSD or MOG-NMOSD. Among relapsing patients, 147/247 (60%) received a disease-modifying treatment (DMT). The administration of any DMT led to a reduction of ARR (pre-treatment: 0.83 ± 0.21 [95% CI 0.62–1.04, $I^2=66.19\%$, $p<0.0001$]; post-treatment: 0.44 ± 0.17 [95% CI 0.27–0.60, $I^2=85.81\%$, $p<0.0001$]).



Forest plot with random-effects models used to pool results of pre-treatment ARR across studies, including early and late-onset NMOSD.



Forest plot with random-effects models used to pool results of post-treatment ARR across studies, including early and late-onset NMOSD.

Conclusion: DN-NMOSD is a severe condition with distinctive features compared to AQP4-NMOSD. The administration of DMTs seems to be effective in this group of patients, but randomized clinical trials are needed.

Disclosure: The authors declare no conflicts of interest.

EPO-069 | Characterization of EEG patterns in a cohort of patients with autoimmune encephalitis

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Background and Aims: Variable EEG features associated with autoimmune encephalitis (AIE) have been reported in the literature, the diagnostic/prognostic value of which remains unknown. We aim to describe the EEG features from an institutional AIE cohort.

Methods: Retrospective review of the clinical and EEG features of AIE patients (according to Graus criteria) diagnosed between 2000 and 2023.

Results: In total, 49 AIE cases were identified (57.1% male) including 30.6% anti-NMDAr, 26.5% anti-GAD65 and 26.5% seronegative. EEG abnormalities were present in 81.6%: 71.4% had slow activity and 46.9% had focal epileptiform activity. These mostly involved the temporal region (59.6% and 69.6%, respectively). The extreme-delta brush pattern was present in 3 EEGs. Two patients presented with non-convulsive status epilepticus. An abnormal EEG was present in 78.6% of patients with normal brain MRI (49.0%), corresponding to

44.8% of the cohort. The presence of any EEG abnormality was associated with seizures at presentation ($p=0.022$). Even in patients without seizures, the EEG was abnormal in 65.0%. We found no significant difference in the EEG features when comparing serogroups, including seropositive vs. seronegative and intracellular vs. surface antibodies. The presence of slow activity was associated with an increased recurrence rate ($p=0.027$) in AIE with intracellular antibodies, when diffuse, and with increased disability after 6.0 (3.0–8.0) years in AIE with intracellular antibodies ($p=0.042$), when focal temporal.

Conclusion: EEG abnormalities are common in AIE, even in cases with normal brain MRI or without clinical seizures. The presence of slow activity may be a prognostic factor, depending on the antibody type.

Disclosure: The authors have nothing to disclose.

EPO-070 | The familiarity of romanian psychiatrists with anti-*N*-methyl-D-aspartate receptor encephalitis: A web-based study

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Background and Aims: Psychiatrists are often the first to be consulted in patients with anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. Thus, they need to be aware of clinical features, differential diagnoses, and treatment options for patients affected by this condition. In this study, we aimed to investigate the familiarity of Romanian psychiatrists with anti-NMDAR encephalitis.

Methods: We recruited psychiatrists from Romania and conducted a cross-sectional observational study by using a web-based survey.

Results: 111 psychiatrists completed the survey, of whom 47 (42.34%) were specialists, while 64 (57.66%) were trainees. The median length of training for specialists was ten years (IQR 9.5), while for trainees was 2.5 years (IQR 3). In total, 31 (27.93%) psychiatrists encountered a case of anti-NMDAR encephalitis, with no significant difference between specialists and trainees. 31 (27.93%) psychiatrists were either unaware of the disorder or only knew its name, while 77 (69.37%) had knowledge of an outline of it. Only 3 (2.7%) psychiatrists had comprehensive knowledge of the disorder. Respondents with a higher awareness level had undergone significantly longer training ($p=0.014$). Unsurprisingly, having encountered a case significantly influenced awareness levels ($p<0.001$). There were no significant differences between specialists and trainees regarding specific knowledge about anti-NMDAR encephalitis. However, higher awareness levels and having encountered a case significantly influenced answer accuracy for questions regarding psychiatric presentation and epidemiological features.

Conclusion: Our study indicates that Romanian psychiatrists have suboptimal knowledge of anti-NMDAR encephalitis, highlighting the need for improved awareness of this disorder.

Disclosure: Nothing to disclose.

EPO-071 | Neural antibodies in first-episode psychosis patients with warning signs for autoimmune encephalitis

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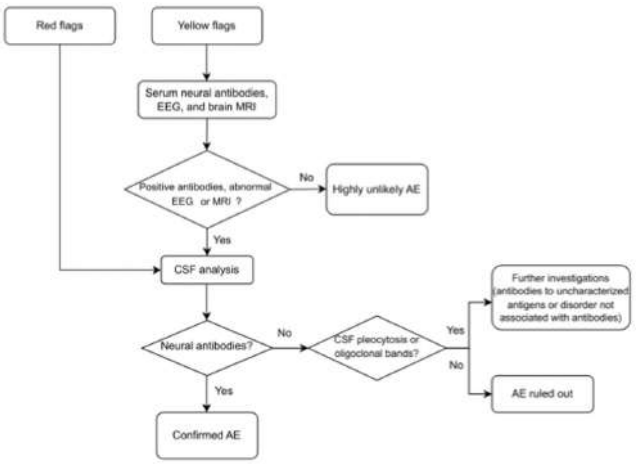
Background and Aims: While autoimmune encephalitis (AE) remains an essential differential diagnosis in first-episode psychosis (FEP), testing all FEP patients for neural antibodies is not feasible in real-world clinical practice. Thus, some researchers suggest selective testing in patients with warning signs of AE. Moreover, criteria have been proposed for a category of so-called autoimmune psychosis (AP). Here, we aimed to determine the prevalence of AE in a cohort of patients with FEP.

Methods: To achieve our objective, we used a phenotype-driven algorithm. Initially, we screened patients for "yellow" and "red flags" indicating low or high pre-test probability warning signs for AE, respectively. We also evaluated patients for previously proposed warning signs and AP criteria. Next, patients with red flags underwent cerebrospinal fluid analysis (including neural antibodies), while patients with yellow flags underwent tests for serum neural antibodies, EEG, and brain MRI.

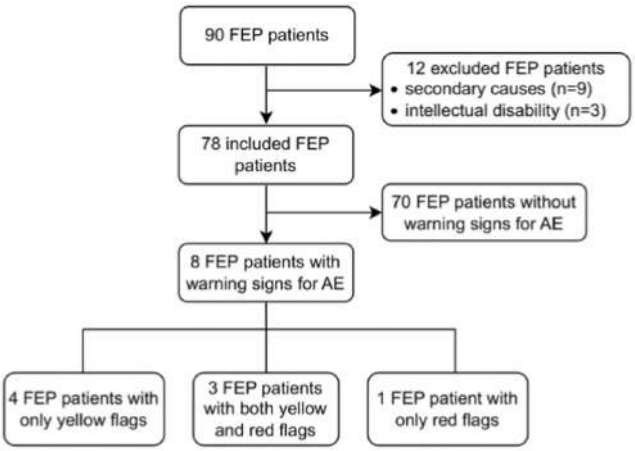


A phenotype-driven algorithmic approach for detecting autoimmune encephalitis in patients with first-episode psychosis. Abbreviations: AE, autoimmune encephalitis; CSF, cerebrospinal fluid.

Yellow flags (↓ pre-test probability for autoimmune encephalitis)	**Red flags** (↑ pre-test probability for autoimmune encephalitis)
• Rapid progression of psychosis (despite antipsychotic treatment) • Insufficient response to antipsychotics • Persistent hyponatremia (not explained by side-effects of medication) • Other autoimmune disorders (such as systemic lupus erythematosus or autoimmune thyroiditis)	• Altered level of consciousness • Severe or disproportionate cognitive dysfunction • Movement disorder (catatonia, dyskinesia, and/or dystonia) • Autonomic dysfunction • Focal neurological signs • Aphasia, decreased verbal output and/or unexplained dysarthria • Persistent headache • Seizures • Intolerance to antipsychotics or neuroleptic malignant syndrome
	Comorbidities: • Viral prodrome (mild fever, malaise, anorexia, and/or headache) • Recently diagnosed or active tumor (such as ovarian teratoma or thymoma) • Recent (<3 months) history of viral encephalitis
	History of autoimmune encephalitis

Warning signs for autoimmune encephalitis in patients with first-episode psychosis were defined as "yellow" (low pre-test probability) and "red flags" (high pre-test probability).

Results: We screened 78 patients with FEP and found that eight (10.3%) had at least one warning sign for AE: four (5.13%) patients had at least one red flag, while four (5.13%) had only yellow flags. Four (5.13%) patients met the criteria for possible AP. Two patients (2.56%) had anti-NMDAR encephalitis, while the remaining six (7.69%) received a primary psychiatric disorder diagnosis. The AP criteria failed to identify patients with definite AP due to a lack of paraclinical criteria.



Selection and inclusion of patients with first-episode psychosis and warning signs for autoimmune encephalitis.

Conclusion: Our study emphasizes the significance of including AE in the differential diagnosis of FEP.

Disclosure: This work was supported by the Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania (grants no. 881/41/12.01.2022 and 772/32/11.01.2023).

EPO-072 | Update of the treatment of pediatric neuromyelitis optica spectrum disorders

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Background and Aims: Neuromyelitis Optica Spectrum Disorders (NMOSDs) is a collection of inflammatory and demyelinating disorders affecting the central nervous system. Given the severity and recurrence nature of the attacks, effective and safe treatment modalities are crucial. This study aims to provide an update on the current and emerging therapies for NMOSDs in the pediatric population.
Methods: We conducted a comprehensive analysis of the existing medications utilized in the treatment of pediatric NMO, encompassing both those currently being investigated in clinical trials for pediatric NMO on clinicaltrials.gov and the NIH website, as well as articles published on PubMed and Embase since 2008.
Results: A total of 15 studies have been conducted to examine the effects of 7 distinct drugs. A total of 231 patients were enrolled / anticipated to be enrolled, with 139 receiving Azathioprine, 21 receiving rituximab, 24 receiving mycophenolate mofetil, 12 receiving eculizumab, 15 receiving Inebilizumab, 12 receiving Ravulizumab, and 8 receiving Satralizumab. Azathioprine, mycophenolate mofetil, and rituximab are commonly utilized and generally regarded as safe. Various monoclonal antibodies, such as eculizumab, Inebilizumab, Ravulizumab, and Satralizumab, are currently undergoing testing to determine their effectiveness and safety.
Conclusion: Pediatric NMO treatment is still challenging, further clinical trials and research are warranted.
Disclosure: None.

EPO-073 | Characterization of neuropeptide cortistatin in multiple sclerosis patients

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Background and Aims: Multiple sclerosis (MS) diagnosis is based on clinical, radiological and biochemical criteria. However, it is necessary to find specific and reliable biomarkers to assess disease activity. We hypothesize that endogenous neuroimmune mediators could

be a new type of molecules which address the progression of this autoimmune disorder.

Methods: To assess the potential of cortistatin (CST), an anti-inflammatory and neuroprotective neuropeptide crucial in neuroimmune interactions, as a peripheral biomarker, blood samples were taken from patients with relapsing-remitting MS. CST levels were analyzed in plasma and serum. We also evaluated by a microfluidic qPCR the gene expression of CST and specific receptors as well as the relationship of CST and the immune response in peripheral mononuclear blood cells isolated from MS patients.

Results: We observed that, although CST levels were unchanged in plasma they were significantly reduced in serum from MS patients compared to healthy controls. Of note, we found that CST was highly susceptible to degradation in serum. We also demonstrated that immunomodulatory therapies did not affect CST plasma levels, except for patients treated with beta interferon, they showed increased plasma CST. Interestingly, we found that the gene expression of CST and related peptides were similar between patients and controls, while expression for the GPR107 receptor, a recently discovered receptor in the somatostatin system, was significantly downregulated in MS patients.

Conclusion: Our results suggest that the CST system could be altered in MS patients. However, further studies are needed to determine its role during the pathogenesis of MS and its relationship with current treatments.

Disclosure: The author declares no conflicts of interest.

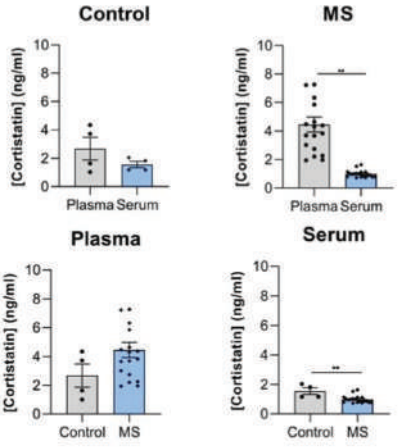

Figure 1. Variation of CST levels in plasma and serum. The comparison between plasma and serum CST levels of healthy **controls** and patients with **MS**, and between healthy controls and MS in **plasma** and **serum** is shown. Data are presented as mean ± SEM. **P < .01

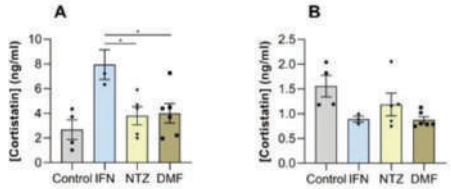

Figure 2. Levels of CST in the different therapies. The comparison between plasma **(A)** and serum **(B)** CST levels of MS patients distributed according to their disease modifying therapies is shown. IFN: interferon-β1a; NTZ, natalizumab; DMF: dimethyl fumarate. Data are presented as mean ± SEM. *P < .05

FIGURE 1

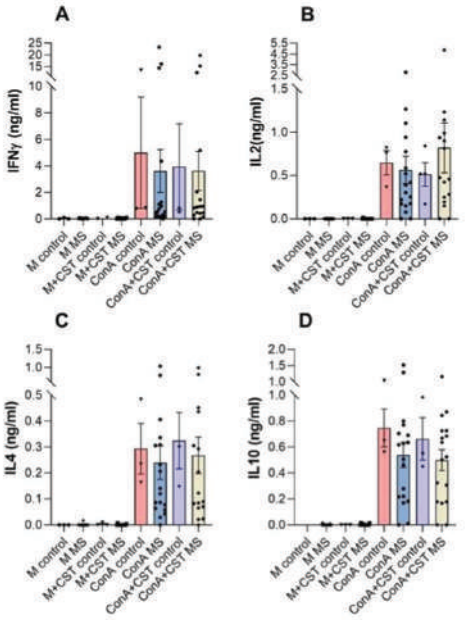

Figure 3. Cortistatin administration does not influence the polyclonal response of PBMCs in MS. The levels of IFNγ **(A)**, IL2 **(B)**, IL4 **(C)** and IL10 **(D)** are shown. The groups include healthy controls and MS patients treated respectively with medium (M), medium+CST, concavalin A (ConA), and ConA+CST. The administration of CST in MS does not influence the levels of IFN, IL2, IL4 or IL10 compared to healthy controls, nor does it modify the cellular response when administered together with ConA. Data are presented as mean ± SEM.

FIGURE 2

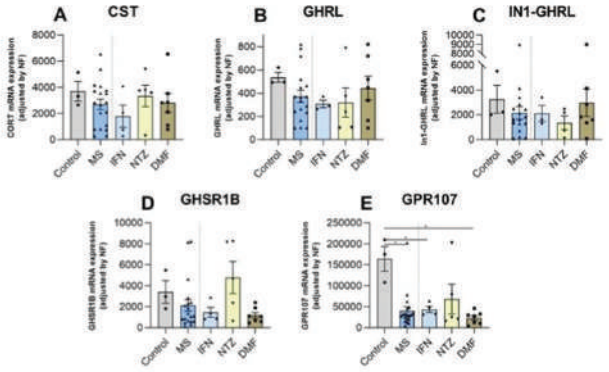

Figure 4. Determination of gene expression of molecules related to CST-ghrelin axis by fluidic qPCR. Normalization factor-adjusted mRNA expression levels are shown in controls, MS patients, and in the three most common treatments. Data are presented as mean ± SEM. MS, multiple sclerosis IFN: interferon-β1a; NTZ, natalizumab; DMF, dimethyl fumarate; GHRL: ghrelin In1-GHRL: In-1-ghrelin; GHSR-1b, R1b growth hormone secretagogue receptor; GRP107: G protein-coupled receptor 107. * P< 0.05 ** P< 0.01 *** P<0.001

FIGURE 3

EPO-074 | The role of innovative therapies in refractory myasthenia gravis: Are they interchangeable and safe? A case-series

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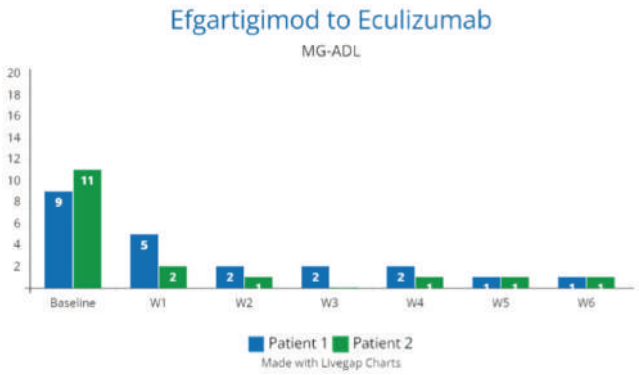
Background and Aims: Myasthenia Gravis (MG) therapies have dramatically changed in the last few years with the introduction of complement inhibitors and neonatal Fc receptor blockers. There are no data available on retreatment options in non-responder patient. We performed a case-series including four patients treated with innovative therapies that underwent a switch from anti-complement to FcRn blockers and viceversa.

Methods: We enrolled 4 patients with refractory MG treated with Efgartigimod (Pt. 1 and Pt. 2) and Ravulizumab (Pt. 3 and Pt. 4).They all underwent major clinical deterioration and switched to therapies with a different mechanism of action. We performed MG-ADL at the baseline and weekly, QMG at the baseline and after induction period of Eculizumab and cycle 1 of Efgartigimod and then every 3 months.

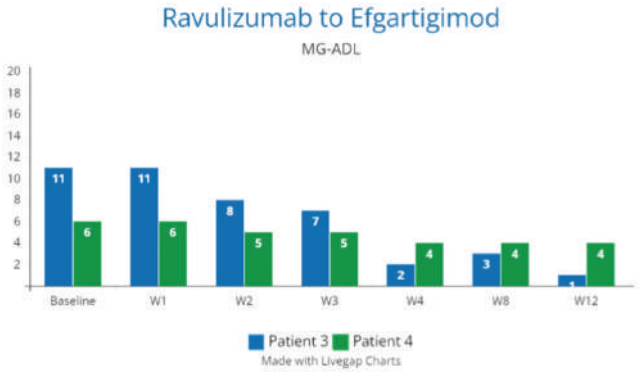
	AGE	SEX	AGE ONSET	DISEASE DURATION	MFGA	THERAPY SWITCH
Patient 1	46 y.o.	F	36 y.o.	10 years	IIIb	Efga -> Ecu
Patient 2	47 y.o.	F	26 y.o.	21 years	IIIb	Efga -> Ecu
Patient 3	33 y.o.	F	23 y.o.	10 years	IIIb	Ravu -> Efga
Patient 4	51 y.o.	F	28 y.o.	23 years	IIIb	Ravu -> Efga

Patients' characteristics description

Results: In the group of patients switching from Efgartigimod to Eculizumab we observed a mean MG-ADL reduction of 9 and a QMG reduction of 8.5 points after the induction period. Patients remained in the Minimal Symptom Expression for all the maintenance period. Ravulizumab to Efgartigimod switching group observed a MG-ADL global reduction of 5.5 points and a QMG reduction of 4 points after cycle 1. No major adverse events were observed except for Pt .4 who suffered from systemic infection. Efgartigimod was suspended and readministered after the resolution of the infection.



Efgartigimod to Eculizumab Group MG-ADL



Ravulizumab to Efgartigimod Group MG-ADL

Conclusion: Switch between innovative treatments with different mechanism of action proved to be a successful strategy in non-responders. Both Eculizumab and Efgartigimod succeeded in improving clinical status after few weeks of treatment. Further data collection is needed to assess the long-term efficacy of therapeutic switches.

Disclosure: Nothing to disclose.

EPO-075 | Cerebrospinal fluid interleukin-6 as a potential biomarker in CNS neuroinflammatory diseases: A real world analysis

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Background and Aims: Interleukin-6 (IL-6) pathways have recently been described in the pathogenesis of neuromyelitis optica spectrum disorder (NMOSD). Some data suggest that CSF IL-6 may be a short-term prognostic biomarker in NMOSD. However, whereas various cytokines would be involved in the pathogenesis of inflammatory disease, the differences in cerebrospinal fluid (CSF) cytokines between different inflammatory diseases remain unclear. We aimed to compare CSF IL-6 levels among various neurological inflammatory disorders and to explore the relationship between CSF IL-6 and various intrathecal immunoglobulin (Ig) indexes.

Methods: From May 2023 we prospectively obtained IL-6 levels in consecutive CSF samples in patients suspected of an inflammatory disease of the CNS. IL-6 has been tested by commercially available ECLIA Kit. We also collected CSF cell count, protein levels, quantitative IgG indexes such as Link Index and Kappa-free-light-chain Index using nephelometry, and oligoclonal band (OB) status using isoelectrofocusing on agarose gel.

Results: So far, 20 patients (13 female, 10MS, 4 NMOSD/MOGAD, 2 clinically isolated syndrome and 4 non-inflammatory controls), with a mean age of 42.5 years (SD 13.4) were enrolled. Patients with NMOSD/MOGAD showed higher IL-6 levels compared to MS (35.25 ± 33.14 vs 4.98 ± *p*: 0.05 pg/ml). An inverse correlation of IL-6 levels was observed with Link Index (*r*: −0.56 *p*: 0.01), Kappa-Index (*r*: −0.29 *p*: 0.2) and patients without OB displayed higher levels of CSF IL-6 (17.15 ± 23.21 vs 4.93 ± 2.15 *p*: 0.05 pg/ml).

Conclusion: Our preliminary data support the potential of CSF IL-6 as a diagnostic biomarker in CNS inflammatory diseases. We plan to confirm our observation on a larger sample size.

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology 1

EPO-076 | Prevalence and pattern of cognitive impairment in patients awaiting kidney and liver transplantation

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Background and Aims: Cognitive impairment (CI) is common in both end-stage kidney disease (ESKD) and end-stage liver disease (ESLD). The goal of the study was to assess the prevalence and pattern of CI in patients awaiting kidney and liver transplantation.

Methods: In this cross-sectional, prospective study, 27 consecutive patients with ESKD and 27 consecutive patients with ESLD due to alcoholic liver disease, all currently on transplant waiting lists, were screened for cognitive decline using the Addenbrooke's Cognitive Examination. Medical history, demographics and laboratory test results were also collected.

Results: The prevalence of CI among patients with ESKD and ESLD was 27% and 88%, respectively. In both groups, the most impaired cognitive domain was memory and additionally verbal fluency in patients with ESRD and visuospatial abilities in patients with ESLD. The most statistically significant increase in the prevalence of CI was found in patients with fewer years of schooling, in both ESLD and ESKD populations, and in elderly patients, but only in the ESLD group. Additionally, better cognitive functioning in ESKD patients was associated with higher levels of total lymphocyte count and alanine transaminase (ALT), and in ESLD patients with higher levels of ALT and aspartate transaminase.

Conclusion: The prevalence of CI, especially in patients with ESLD, is high and may negatively affecting the transplantation process. Routine screening tests in this group would contribute to the implementation of effective treatments and facilitate the provision of specialized health care.

Disclosure: Nothing to disclose.

EPO-077 | A case of phonagnosia in a patient carrying C9orf72 gene mutation

E. Stanitsa; L. Apostolakopoulou; E. Angelopoulou; V. Konstadinides; R. Antonellou; G. Velonakis; G. Karadima; G. Koutsis; L. Stefanis; S. Papageorgiou

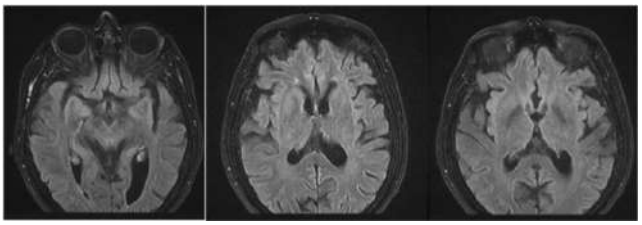
Department of Neurology, Eginition University Hospital, Athens, Greece

Background and Aims: Phonagnosia is a rare selective impairment of familiar voice recognition, with relative intact comprehension and recognition of faces. Compared to prosopagnosia, phonagnosia has been infrequently described in neurodegenerative diseases, and relative genetic evidence is scant.

Methods: We describe a case of a 56 years-old female patient, a primary school teacher, mainly presenting with progressive difficulty in recognizing familiar voices through the telephone, with intact recognition of familiar faces. Difficulties in concentration, visuospatial abilities, low information processing speed and apathy were also reported by her husband. Family history was positive for amyotrophic lateral sclerosis.

Results: Neurological examination was normal. MMSE was 26/20, and FAB was 13/18. The extensive neuropsychological examination revealed deficits in attention, executive function, visuospatial perception and memory, as well as impaired phonological and semantic verbal fluency. Brain MRI showed mild generalized cortical and hippocampal atrophy. Routine blood tests and electroencephalogram were normal. Audiological and ophthalmological evaluation was normal. CSF examination revealed normal TAU, p-tau and β-amyloid levels. Genetic analysis revealed C9orf72 expansion mutation. Phonagnosia was confirmed experimentally, by examining familiar voice recognition in a small sample of cognitively normal individuals

of similar age. Recently, another case of progressive phonagnosia was described in a patient with a C9orf72 expansion and frontotemporal dementia.



Brain MRI (FLAIR) of our patient demonstrating mild generalized cortical and hippocampal atrophy

Conclusion: To our knowledge this is the second case report of a patient with C9orf72 mutation presenting with phonagnosia. This might be partially explained by the overload of the neural network processing voices – due to her professional activity, combined with genetic mechanisms.

Disclosure: None.

EPO-078 | Unveiling constructional apraxia in huntington's disease through neurophysiological markers

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Background and Aims: This study investigates constructional apraxia (CA) in HD, a feature insufficiently explored. Our aim is to unravel CA's cognitive underpinnings within the HD population, shedding light on potential associated cognitive markers.

Methods: Seventy HD patients from the Enroll-HD study were recruited, meeting specific inclusion criteria including a positive molecular HD test, clinically evident neurocognitive disease, ≥2 years of formal education, and the absence of other cognitive-impairing neurological disorders. Comprehensive assessments encompassed neuropsychological, psychiatric, motor, and functional evaluations. CA presence and type were determined via a copying task.

Results: Unexpectedly, 32 HD participants exhibited constructional apraxia (CA), yet no significant differences emerged between CA and no-CA groups in demographic, clinical, motor, or functional aspects (all $p > 0.05$). MANOVA revealed overall non-significant neuropsychological differences, but AC participants scored significantly lower on Symbol digit modality test, Stroop-color word – reading, Stroop-color word – interference, and Phonological verbal fluency tests (all $p < 0.05$). Logistic regression, statistically significant (X^2 [8] = 7.625, $p = 0.006$; Cox & Snell $R^2 = 0.057$), linked AC only to Stroop-color word – interference test (Wald: 7.166, $p = 0.007$, OR: 0.955, 95% CI: 0.924–0.988).

		no-CA group		CA group		
	Score range	Mean	SD	Mean	SD	*p*
Demographic data						
Age (years)	-	49.54	12.47	51.10	12.47	.24
Clinical data						
CAG repeats	-	45.02	3.51	44.92	3.66	.80
Disease duration	-	4.06	2.51	4.48	2.30	.34
Motor functions						
UHDRS-motor	0-124	32.96	24.78	33.00	26.46	.99
Functional abilities						
TFC	0-13	6.92	4.64	7.11	4.52	.81

Note: no-CI group (HD patients not showing Closing-in); CI-group (HD patients showing Closing-in); UHDRS-motor (Unified Huntington Disease rating scale – motor score); TFC (total function capacity.

Means and SDs on demographic data, clinical data, motor functions, and functional abilities in HD patients showing or not showing CA

		no-CA group		CA group			
	Score range	Mean	SD	Mean	SD	*p*	η_p^2
Neuropsychological measures							
Mini Mental State Examination	0-30	22.94	4.80	21.59	5.10	.13	.01
Symbol digit modality test	-	18.69	11.53	13.73	11.07	**.01**	**.04**
Category fluency	-	10.87	5.49	8.99	6.04	.07	.02
Stroop-color word - naming test	-	35.73	18.64	30.81	18.64	.14	.01
Stroop-color word - reading test	-	52.42	26.76	42.21	23.58	**.02**	**.03**
Stroop-color word - interference test	-	20.60	11.43	15.15	10.36	**.006**	**.05**
Trail making test (part A) – time (sec)	0-240	79.94	39.32	97.47	43.98	**.02**	**.04**
Trail making test (part A) – correct responses	0-25	24.88	9.32	24.51	9.67	.82	<.001
Trail making test (part B) – time (sec)	0-240	194.56	66.41	215.42	49.37	**.04**	**.03**
Trail making test (part B) – correct responses	0-25	14.73	8.01	12.22	7.43	.07	.02
Phonological verbal fluency	-	15.25	12.77	11.18	8.79	**.03**	**.03**

in bold the significant values (significant at $p < .05$)

Means and SDs on neuropsychological measures in HD patients showing or not showing CA

		no-CA group		CA group			
	Score range	Mean	SD	Mean	SD	*p*	η_p^2
Psychiatric features							
Depressed mood	0-16	3.38	4.07	3.79	4.32	.58	.002
Suicidal ideation	0-16	0.51	1.36	0.94	2.56	.27	.009
Anxiety	0-16	3.50	4.24	2.76	3.73	.29	.009
Irritability	0-16	2.73	4.09	3.12	4.60	.61	.002
Aggressive behaviour	0-16	2.00	3.36	2.30	4.69	.68	.001
Apathy	0-16	3.55	4.96	3.55	4.60	.99	.001
Perseverative thinking	0-16	2.09	3.34	2.47	4.34	.59	.002
Obsessive-compulsive behaviour	0-16	2.76	4.95	1.92	3.90	.28	.009
Delusion	0-16	0.92	2.50	0.39	1.55	.14	.01
Hallucination	0-16	0.32	1.74	0.24	1.81	.79	.001
Disoriented behaviour	0-16	1.67	2.79	1.37	2.46	.51	.003

in bold the significant values (significant at $p < .05$)

Means and SDs on psychiatric features in HD patients showing or not showing CA

Conclusion: The Stroop-color word – interference test emerges as a predictor for constructional apraxia (CA), indicating its potential role in early detection and intervention for HD. These findings deepen our understanding of cognitive manifestations in HD, guiding future research and clinical strategies.

Disclosure: Nothing to disclose.

EPO-079 | Cognitive rehabilitation effects on grey matter volume and Go-noGo activity in progressive MS: Results from CogEx study

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Background and Aims: CogEx (ClinicalTrials.gov, NCT03679468) was a randomized, sham-controlled trial determining effectiveness of cognitive rehabilitation (CR) and aerobic exercise (EX) in progressive multiple sclerosis (PMS). We present volumetric MRI and task-related functional MRI (fMRI) findings.

Methods: Participants were randomized (1:1:1:1) to "CR-plus-EX", "CR-plus-sham-EX (EX-S)", "EX-plus-sham-CR (CR-S)", and "CR-S-plus-EX-S" and attended 12-week intervention. Physical/cognitive assessments were performed at baseline, immediately after intervention (week-12) and 6 months post-intervention (month-9). MRI sub-study participants underwent volumetric MRI and fMRI (Go-NoGo task).

Results: 104 PMS participated in the MRI sub-study ("CR-plus-EX": $n=25$; "CR-plus-EX-S": $n=28$; "CR-S-plus-EX": $n=25$; "CR-S-plus-EX-S": $n=26$); 88 (85%) completed baseline and week-12 volumetric MRI and 84 (81%) completed Go-NoGo fMRI. At week-12 and month-9, no differences were found among interventions for symbol-digit modalities test (SDMT) correct responses, nor for SDMT, California verbal learning test (CVLT) and brief visuospatial memory test *Z*-scores ($p=$ range 0.12–0.94). Time-by-treatment interactions for changes at week-12 vs baseline of normalized grey matter (NGMV) ($p=0.10$) and cortical GM (NcGMV) ($p=0.10$) volumes were not significant. However, they became significant ($p=0.04$; $p=0.02$, respectively) when comparing all patients performing CR vs those performing CR-S. "CR-plus-EX-S" patients exhibited Go-NoGo-related fMRI activity increase ($p<0.05$, corrected) at week-12 vs baseline in bilateral insular regions. In all CR patients, increased NGMV ($r=0.42$, $p=0.004$) and NcGMV ($r=0.36$, $p=0.01$) at week-12 vs baseline correlated with increased CVLT Z-score.

Conclusion: Conclusions. CR modulated GM volumes and insular fMRI activity in PMS. Funding. Funded by the MS Society of Canada (grant #EGID3185). Ancillary funding from CMSC, Danish MS Society, and National MS Society.

Disclosure: Nothing to disclose.

EPO-080 | Altered cognition in Parkinson patients with depression compared to major depressive individuals

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Background and Aims: The interaction of depression heralding PD and incidental depression after the diagnosis of PD is complex requiring a unified pathophysiological model of depression in PD. Here we explored the connectivity and cognitive differences between PD patients (with and without depression), Control and MDD patients. Our results indicate considerable cognitive and connectivity differences between PD and MDD patients suggesting a compensatory phase specific to PD, regardless of the pathophysiology of depression.

Methods: 38 Parkinson's outpatients (aged 49–86 years; 23 depressive (PDD) and 15 non depressive (PND)) and 46 healthy controls (aged 20–81 years; 22 depressive (MDD) and 24 non depressive (ND)) were recruited by their clinicians. We applied MMSE, MOCA and HDRS test to all the participants for cognitive and depression assessment.

Results: There was significant difference in terms of age ($p < .001$), education years ($p = 0.009$) and HDRS scores ($p < .001$). After adjusting age and education years, our findings revealed significant differences in orientation ($p = 0.050$) and abstraction ($p = 0.005$) scores which are subtests of MOCA without any difference in MOCA scores between PDD and MDD groups. We also observed that the MDD patients were clearly impaired on tests known to assess non-verbal primary memory, as well as verbal and non-verbal episodic memory compared to non-demented PD, a finding that has been confirmed both in non-depressed and depressed PD compared to MDD ($p < .005$).

Conclusion: Our study revealed valuable findings considering cognitive impairment in PD patients with depression compared to major depressive disorder (MDD). We believe that our results hold a clinicaş value for the literature.

Disclosure: Nothing to disclose.

EPO-081 | The affective and cognitive theory of mind and associated brain functional alterations in patients with PPA

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Background and Aims: We aimed to investigate cognitive and affective theory of mind (ToM) abilities in semantic (svPPA) and nonfluent (nfvPPA) variants of primary progressive aphasia, compared to other frontotemporal lobar degeneration (FTLD) cases, such as behavioral (bvFTD) and right temporal variants (rtvFTD). Moreover, this study explored the neural correlates of affective and cognitive ToM alterations in these FTLD syndromes.

Methods: Sixty-seven FTLD patients (14 nfvPPA, 17 svPPA, 23 bvFTD and 13 rtvFTD) and 98 healthy controls underwent neuropsychological evaluation, structural and resting-state functional MRI. Based on literature, two regions of interest (medial prefrontal cortex-lmPFC and right supramarginal gyrus-rSMG) were created as main nodes for affective and cognitive ToM, and RS functional connectivity (RS-FC) networks were obtained. Using graph analysis and connectomics, global and regional functional brain connectivity were assessed and compared between groups. Patients underwent the affective (SET-EA) and cognitive (SET-IA) ToM subtests of the Story-Based Empathy Task (SET), and their performances were compared across groups.

Results: Affective and cognitive ToM abilities as measured by the SET appeared similarly impaired in all patients' groups, including PPA. Significant regional RS-FC alterations within both affective and cognitive networks were observed in each group of patients as compared with healthy controls.

Conclusion: These findings suggest a deterioration of affective and cognitive ToM skills in FTLD patients, including PPA, which seems to be related to similar functional connectivity alterations. The present study emphasizes the importance of socio-cognitive features in the early detection of FTLD conditions. Funding. European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease.

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EPO-082 | Improving cognitive functions in healthy subjects using tACS and individual theta frequency

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Background and Aims: Transcranial Alternating Current Stimulation (tACS), a non-invasive method, aims to enhance cognitive abilities in healthy individuals and those with cognitive challenges by replicating brain activity. Beyond cognitive neuroscience, it shows promise for psychiatric issues like schizophrenia. This study explores tACS effects on eight healthy individuals aged 26 to 34.

Methods: Cognitive assessments (MMSE, MoCA, STROOP test, trail making parts A and B, short-term memory, Recall, Wechsler memory scale), EEG scans, and depression level evaluations conducted before and after tACS stimulation. Personalized tACS stimulation was administered to the dorsolateral prefrontal cortex (DLPFC) area, utilizing individual theta frequency (ITF) determined with MetLab. The 20-minute sessions, spanning five days, employed a 2 mA sinusoidal oscillating current at minus one ITF (4–8 Hz) to enhance cognitive functions. Post-stimulation, participants underwent the same battery of cognitive tests and EEG scans.

Results: The statistical analysis, utilizing paired samples T-test with a significance threshold of $p < 0.005$, revealed no significant change in depression levels ($p = 0.439$). While Wechsler memory scale, MoCA, MMSE, and STROOP tests exhibited no noteworthy differences, there were significant improvements in short-term memory ($p = 0.041$) and trail making part B ($p = 0.008$) (Table 1).

Conclusion: In conclusion, tACS, a well-established non-invasive brain stimulation technique, has demonstrated cognitive benefits in various conditions. This study reinforces existing literature, indicating notable enhancements in short-term memory and executive function (trail making) after five days of tACS stimulation. Further investigations should involve larger participant groups to consolidate and expand upon these findings.

Disclosure: Nothing to disclose.

EPO-083 | Effects of episodic and chronic tension type headache on cognition and empathic neural responses: A fMRI study

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Background and Aims: This study delves into tension-type headache (TTH), emphasizing its prevalence and impact on health and daily life. The evolving understanding of TTH's neurological basis, particularly altered central pain perception, prompts a need for comprehensive studies on mood, cognitive function, and pain empathy. The study aims to evaluate cognitive and empathic neuroimaging correlates of TTH, addressing the lack of integrated studies in this area.

Methods: The enrollment comprised 102 participants (46 TTH patients, 41 healthy controls) from Alanya University, diagnosed following International Headache Committee criteria. Exclusion criteria covered various conditions, and ethical approval was obtained. Structural and resting-state fMRI scans were conducted with specific parameters.

Results: Analyzing demographic and clinical data, age differences were nonsignificant ($p > 0.05$), while education years significantly varied ($p < 0.001$). MOCA scores exhibited a significant difference ($p < 0.05$), with tension-type headache patients scoring lower. Subgroup analysis of episodic and chronic patients revealed no significant differences in neurocognitive tests, volume, or connectivity ($p > 0.05$).

Conclusion: The study proposed a potential reverse causal relationship, suggesting individuals with higher empathy levels might be more susceptible to developing TTH. The decline in cognitive scores correlated with increased headache intensity, indicating a complex interaction between acute headache episodes, pain processing, and cognition. fMRI results demonstrated changes in brain regions associated with acute pain, impacting executive functions and highlighting the cost of cognition during acute pain episodes. It provides valuable insights into the intricate relationship between TTH, cognitive function and pain empathy, contributing to the understanding of the neurological underpinnings of TTH and its broader implications.

Disclosure: Nothing to disclose.

EPO-084 | Neurocognitive correlates of awareness of everyday functioning in middle-aged and older adults with HIV

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Background and Aims: People living with HIV (PLWH) are vulnerable for cognitive decline and are at greater risk for impaired everyday functioning; however, they may lack self-awareness of such impairments. We examined neuropsychological correlates of self-awareness of everyday functioning in PLWH.
Methods: In this cross-sectional study, 260 PLWH (40+ years) completed a comprehensive assessment including neuropsychological tests as well as self-report (i.e., Lawton and Brody IADL Questionnaire) and performance-based measures of everyday functioning (i.e., Timed Instrumental Activities of Daily Living). Self-awareness of functional status was calculated in the domains of medication management, financial management, telephone use, and grocery shopping. An algorithm was developed to classify accurate reporters, under-reporters, and over-reporters using cut-offs between actual performance vs self-reported performance. Multinomial and binomial logistic regression equations were used.
Results: For financial management, participants with higher scores in executive function/attention were less likely to be under-reporters, while participants with higher depression were more likely to over-report difficulties. For medication management, word-reading emerged as the only significant predictor of inaccurate vs accurate reporting. For telephone use, participants who scored higher on executive function/attention and word-reading were less likely to under-report difficulties. For grocery shopping, those of non-white race had increased risk for inaccurate reporting.
Conclusion: Factors that impact self-awareness of deficits may vary based on the functional domain and factors beyond cognitive function, such as mood and social factors, and should be included when examining awareness of functional difficulties. These results support the use of a domain level approach to examining awareness of functional difficulties in PLWH.
Disclosure: Nothing to disclose.

EPO-085 | From vision to language: Neuropsychological profile in a cohort of patients with Posterior Cortical Atrophy

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Background and Aims: The aim of this study was to analyze the neuropsychological profile of a group of patients with Posterior Cortical Atrophy (PCA) due to Alzheimer's disease (AD). Unlike typical AD, memory, insight and judgement are relatively preserved until latter stages but patients commonly report early language difficulties. However, some inconsistencies exist among the cognitive features described.
Methods: Clinical features and neuropsychological profile of 22 subjects (13 females) aged between 49 and 73 years (61.13 ± 7.04) with PCA due to AD have been analyzed. Each patient underwent a battery of neuropsychological tests, brain MRI, brain [18F]FDG-PET and alternatively amyloid-PET or research for AD biomarkers on CSF. A voxel-based analysis of [18F]FDG-PET compared with normal control subjects has been performed for 14 patients.
Results: All patients showed impairment in visual-perceptual, visual-spatial abilities and visuospatial memory. Variable language impairment was detected in 68% of patients. At voxel-based analysis of [18F]FDG-PET the evaluation of semantic fluency positively correlated with hypometabolism in the left angular gyrus ($p < 0.001$) and Progressive Matrices Test positively correlated with hypometabolism in inferior and superior left parietal gyrus ($p < 0.001$).
Conclusion: A considerable variability in the language profile was found: specifically, in some patients an impairment of semantic verbal fluency was observed, while in others a logopenic phenotype was detected, in agreement with the literature. The positive correlations found for semantic fluency and Progressive Matrices Test are consistent with the existing literature. Further studies are needed to characterize the progressive evolution of the neuropsychological profile of PCA.
Disclosure: The authors have nothing to disclose.

EPO-086 | Sex differences in neuropsychological profile in behavioural frontotemporal dementia

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Background and Aims: Behavioral variant (bvFTD) is the most common form of frontotemporal dementia (FTD), presenting with executive deficits and behavioural changes. Sex differences in prevalence, clinical characteristics, and biomarkers, have been described in several neurodegenerative diseases, including FTD. A previous study reported worse executive and language performances in FTD females than males, but these findings are still sparse and need further characterization.

Methods: We included 20 patients (12 females, 8 males, age-matched) diagnosed with bvFTD at the Memory Clinics of Novara and Vercelli, Piedmont, Italy. All patients underwent a neurological and neuropsychological evaluation at baseline, to characterize the clinical presentation. Patients also underwent a brain MRI and FDG-PET scan, and a lumbar puncture to support clinical diagnosis. In familial cases, mutations in genes frequently associated with FTD were investigated.

Results: In our cohort, sex did not influence global cognition, evaluated with the Mini Mental State Examination and the Montreal Cognitive Assessment (MOCA). When considering specific cognitive domains, we observed better performance in females compared to males in working memory (i.e., corrected Reverse Digit Span, $p=0.0198$), and language (i.e., MOCA denomination subscore, $p=0.03$).

Conclusion: From our preliminary data, sex might have a role in determining the type of neuropsychological impairment in bvFTD, with females performing better than males in language and working memory tests. These results confirm that sex may play a role in influencing clinical phenotype in bvFTD, supporting the hypothesis of sex as a pivotal variable for biological and clinical differences in neurodegenerative diseases.

Disclosure: Nothing to disclose.

EPO-087 | QEEG connectivity markers to predict post-stroke cognitive impairment: A pilot study

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Background and Aims: Post-stroke cognitive impairment (PSCI) occurs in about 20% of acute ischemic stroke (AIS) patients within the first months and is associated with poor long-term prognosis. AIS lesion seems to cause a change in the low-frequency resting state networks, resulting in increased local connectivity, associated with a global disconnection and a disruption of subcortical-cortical or cortico-cortical interactions. This study aimed to develop a predictive model incorporating quantitative EEG connectivity markers to accurately predict PSCI six months after AIS.

Methods: Data were collected from 30 patients with symptomatic supratentorial AIS confirmed by brain MRI without a history of cognitive impairment or dementia. Resting-state EEG was recorded within the first seven days after AIS onset. Relative power for delta, theta, alpha, and beta bands, delta/alpha ratio, coherence, and phase-locking value were computed. Neuropsychological assessments consisting of the Montreal Cognitive Assessment test, Digit Symbol, Digit Backward, Stroop Color-Word Test, and Rey Auditory Verbal Learning test were performed one and six months after AIS.

Results: Delta/alpha ratio and relative theta frequency power were independent predictors for PSCI, suggesting the association between post-stroke alpha slowing and PSCI, which may be mediated by attentional dysfunction.

Conclusion: QEEG markers seem to be a useful tool to inform early prognostication of PSCI, particularly when cognitive function cannot be adequately assessed.

Disclosure: Nothing to disclose.

EPO-088 | Indicators of cognitive status and quality of life in patients with dystrophic myotonia (DM)

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Background and Aims: Dystrophic myotonia (DM) is a rare multisystem autosomal dominant disease. This is the most common genetic form of muscular dystrophy in adults. Clinical manifestations are varied. Intellectual impairments are observed in all forms of DM. Purpose. Study of the characteristics of cognitive status and quality of life (QoL) in patients with DM.

Methods: 21 patients with a genetically confirmed diagnosis of DM: 3 male and 18 female, ME 45.0[39.0;52.0] years (14 – type DM1, 7 – type DM2). 33 healthy controls (HC): 11 male, 31 female. ME 45.0[38.0;53.0] years.

Results: According to the MoCA, a decrease in scores was found in patients with DM (Me 27.0[25.0;29.0]) compared to the HC (Me 30.0[28.5;30.0]), (U, $p=0.007$). When studying the MoCA subtests, patients with DM revealed a decrease in "attention" indicators (U, $p=0.04$); "delayed reproduction" (U, $p=0.054$). The SF-36 assessment showed that in patients with DM there is a dominant decrease in the general indicator of the physical component of health (Me 34.0[29.1; 38.5]) compared to the HC (Me 30.0[45.1; 56.1]), (U, $p=0.013$). A defect was identified in the subscales "physical functioning" (U, $p=0.0025$), "general health" (U, $p=0.048$) and "vital activity" (U, $p=0.046$).

Conclusion: Patients with DM have cognitive impairment with a predominance in the "attention" and "delayed recall" subtests. A decrease in QoL indicators was revealed in terms of physical functioning", "general health" and "life activity". The data obtained reflect the importance of cognitive testing and the study of QoL in patients with DM for the correction of identified disorders.

Disclosure: The authors have nothing to disclose.

EPO-089 | Cognitive decline in patients with diabetes mellitus type 2: The validity of PS-test

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Background and Aims: The objective of the study was to determine the validity of the tool for the early detection of cognitive impairment in patients with type 2 diabetes mellitus (DM).
Methods: The study group (SG) involved 102 patients (67 women, 35 men) with diabetes mellitus type 2, average age 67.5±8.1. The comparison group (CG) included 89 respondents aged 64.3±9.5 years (51 women, 38 men). Both groups were assessed by Montreal Cognitive Assessment (MoCA) test and by the specific tool for cognitive assessment in DM (PS-test) worked out by the authors. Statistic methods: nonparametric statistical estimation methods suitable for samples that do not follow a normal distribution; the Mann-Whitney test; Spearman test.
Results: The MoCA test results revealed statistically significant difference (SSD) between SG and CG. The average MoCA test score in SG was 21.07±0.36, in CG – 28.75±0.15 ($p<0.001$). SSD was revealed also as a result of PS-test performing. The average paremiological test score in SG was 14.46±0.38, in CG – 19.84±0.04. According to the Chaddock scale, the obtained correlation coefficient $r=0.8858$ corresponds to a high degree. The level of significance of the correlation is confirmed by the p value <0.0001. Thus, the developed test correlates well with the MoCA test chosen as an external reference criterion, which proves the validity of this tool.
Conclusion: PS-test can be used in clinical practice for early reveal of cognitive decline in patients with DM type 2.
Disclosure: The reported study was funded by Russian Foundation for Basic Research (RFBR) according to the research project no. 20-312-90044.

EPO-090 | Deciphering the decline in dementia diagnoses: A 2015–2022 analysis in Sweden

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Background and Aims: This study investigates age-standardized rates of dementia diagnoses in Sweden among individuals aged 65 and older from 2015 to 2022, focusing on three primary diagnoses—F00 (Alzheimer's disease), F01 (Vascular dementia), and F03 (Unspecified dementia). The primary objective is to analyze trends, emphasizing the significant decrease post-2019.
Methods: Data sourced from national healthcare records includes age-standardized rates measured as dementia diagnoses per 100,000 inhabitants for individuals aged 65 and older. Gender-specific trends for F00, F01, and F03 are analyzed using descriptive statistics and Poisson regression.
Results: For F00 dementia diagnoses, both males and females exhibit a consistent decline from 2015 to 2019, followed by a substantial reduction post-2019. Males experience a decline from 7.4 to 6.6, while females have a notable drop from 7.3 to 3.9. Similarly, F01 vascular dementia diagnoses demonstrate a substantial decrease in both genders post-2019. Males witness a decline from 110.6 to 78.3, while females see a drop from 91.1 to 63.9. Additionally, F03 unspecified dementia diagnoses portray a consistent decline from 2015 to 2019, with a further reduction post-2019. Males decrease from 161.1 to 135.3, while females drop from 138.0 to 115.6.
Conclusion: Findings reveal a substantial post-2019 decrease in dementia diagnoses, possibly impacting healthcare planning and resource allocation. Adaptability in healthcare systems is crucial for addressing the evolving needs of the aging population due to COVID-19 infection. One conclusion could be that demented persons did not get satisfactory assessment and care during the COVID period. Further research is needed to explore contributing factors.
Disclosure: The authors declare no conflicts of interest or financial relationships that could bias the study's results or interpretation.

Neurogenetics 1

EPO-091 | Autosomal dominant SPG18: A large Italian family

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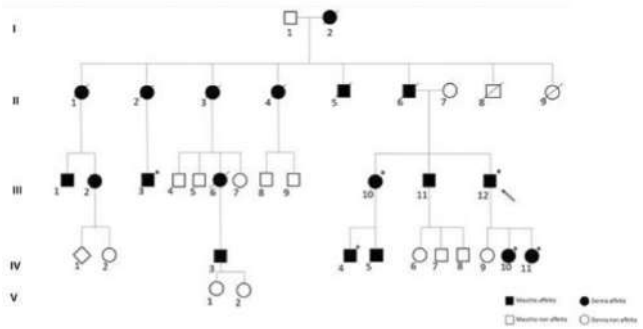
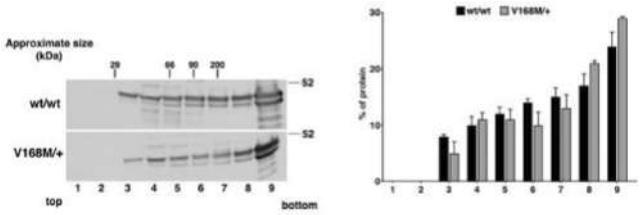
Background and Aims: Hereditary Spastic Paraplegias (HSP) are classified as "pure", when spastic paraplegia is the only symptom or "complex" when other clinical features are present. SPG18 is due to ERLIN2 AD or AR gene mutations.
Methods: We describe clinical and molecular findings of a large Italian AD SPG18 family. Whole exome sequencing. Sanger sequencing was performed to verify the genetic variation in the proband and family members. Velocity gradient assay on proband's fibroblasts was performed to investigate propensity of the mutated ERLIN2 to form oligomers.



SPG18 pedigree

Results: Five affected family members showed progressive spastic paraplegia. Neuropsychological evaluation pointed out a slight mental retardation in two patients. One patient reported generalized epilepsy. The proband's father died at 58 years old with a diagnosis of amyotrophic lateral sclerosis (ALS). Some of his siblings also died around 60 years old with an anamnestic history ascribable to ALS. Genetic analysis revealed the heterozygous missense mutation, c.502G>A (p.V168M), in ERLIN2 gene, which cosegregated with the disease in the affected patients and was not present in healthy subjects. Velocity gradient assay indicated no differences in oligomerization between mutated and wild-type protein.



velocity gradient essay

Conclusion: We report a large Italian SPG18 kindred supporting AD transmission pattern with a broad phenotypic variability. Our data strength p.V168M more frequent association to ALS while biochemical assays unravelled that V168M does not affect the ability of erlin-2 to oligomerize, excluding a dominant negative effect.
Disclosure: Nothing to disclose.

EPO-092 | Findings from the ILLUMINATE prospective Natural History Study (NHS) in individuals with ALSP

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Background and Aims: Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) is a rare, autosomal-dominant, neurodegenerative microgliopathy caused by a CSF1R gene mutation characterised by brain white matter demyelination and atrophy, swollen axons, pigmented glial cells, and clinical symptoms of cognitive, neuropsychiatric, and motor dysfunction. ALSP symptoms typically develop around 40–50 years of age, leading to death within ≈6–8 years; no approved therapies exist.
Methods: ILLUMINATE, the first NHS in ALSP (NCT05020743), is a prospective, multicentre study of individuals with definitive (satisfying full radiological, genetic, clinical criteria) or prodromal (satisfying genetic, radiologic criteria only) ALSP. Participants ($N \approx 50$) are followed for 24 months, with clinical assessments and MRI collected at screening and every 6 months and blood and cerebrospinal fluid (CSF) disease biomarkers collected at specific visits.
Results: As of Sept-2023, 24/42 enrolled participants were symptomatic and 18/42 prodromal. Ventricular volumes were higher at baseline and expanded over time, and baseline grey matter volumes were lower and declined over time, in symptomatic vs prodromal patients (Fig-1). Baseline soluble CSF1R in CSF was substantially lower in all participants (reflecting reduced microglial activity) than healthy individuals, whereas neurofilament light chain (NfL) in CSF and serum was elevated in symptomatic (indicating neuroaxonal injury) vs prodromal and healthy individuals (Fig-2). Cognitive impairment was greater in symptomatic than prodromal patients and correlated with MRI volume changes (Fig-3).

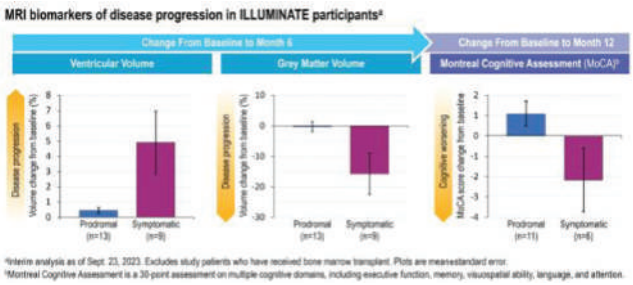

FIGURE 1

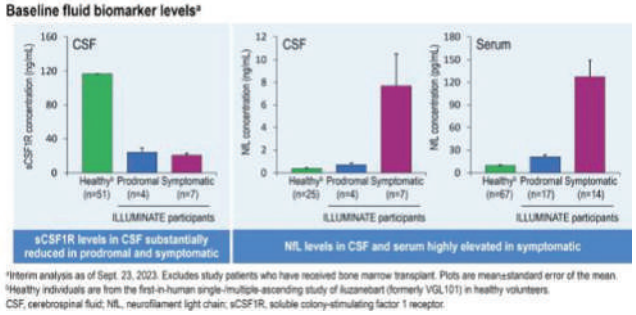

FIGURE 2

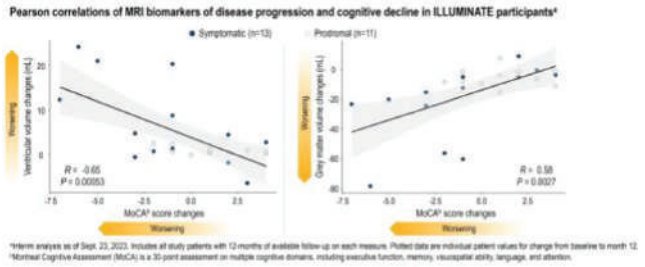

FIGURE 3

Conclusion: These findings demonstrate the sensitivity of MRI measures and NfL to ALSP pathophysiology, with potential to inform optimal clinical endpoints and interventional study design in ALSP and improve understanding of disease progression.

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EPO-093 | A recurrent homozygous deletion in MED22 leads to a progressive neurodevelopmental disorder and neurodegeneration

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Background and Aims: Proper neurodevelopment relies on gene expression programs influenced by signalling molecules, transcription factors (TFs), and epigenetic processes. In this study, we investigate an ultra-rare homozygous single amino acid deletion (p.Glu133del) in MED22, a component of Mediator, a key regulator of transcription, gene expression and posttranslational epigenetic modifications. Disruption of Mediator has been implicated in various neurodevelopmental and neurodegenerative disorders.

Methods: We analysed the variant's impact into the Mediator structure and function through cellular studies and computational simulations. We investigated MED22 protein function generating knock-out zebrafish model and knock-in Drosophila model. We performed scRNA-seq on zebrafish mutants.

Results: We identified eight affected individuals from six unrelated families with a severe progressive neurodevelopmental disorder, characterized by global developmental delay, microcephaly, dystonia, seizures, and microcephaly. In vivo models of Drosophila melanogaster and zebrafish demonstrate significant developmental disruption, mirroring major aspects of the human disorder. scRNA-sequencing data obtained from zebrafish mutants implicate MED22 in dopaminergic network dysfunction.

Conclusion: We establish the first association of MED22 with a human disorder, through integration of clinical, genetic and neuroradiological data. We provide insights in the molecular dynamics of Mediator dysfunction and in the neuronal pathways that might be affected by MED22 dysfunction.

Disclosure: Nothing to disclose.

EPO-094 | MicroRNA biomarkers of large vessel occlusion strokes in cross-sectional and longitudinal analysis

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Background and Aims: Exosomal microRNAs play an important role in developing disease biomarkers. Many microRNAs were associated with stroke in case-control studies on heterogeneous populations, but none had solid evidence to become a biomarker. In this pilot investigation, we analyzed the microRNA of stroke patients with large vessel occlusion (LVO) using a combination of cross-sectional and longitudinal study designs.

Methods: We performed a cross-sectional analysis of 2,632 serum exosomal microRNAs on 55 stroke patients and 53 non-stroke controls; and a longitudinal analysis in 10 stroke patients, collecting blood samples at <24 h, 3, 5, and 30 days after stroke. MicroRNAs were isolated using the mir VANA RNA isolation kit (Ambion, USA). We ran miRNA expression assays using TaqMan probes (Applied Biosciences, USA) on 384-well microplates using QuantStudio 6 available in our lab. Each assay was run in duplicates using endogenous (U6) and blank controls.

Results: We identified 51 microRNAs associated with ischemic stroke, however, only microRNA 9-3p and microRNA 233-3p survived stringent Bonferroni correction ($p < 0.01$). MicroRNA 9-3p had 9-fold higher levels in LVO stroke patients compared to controls ($p < 0.01$), and a strong correlation with the infarction volume ($r = 0.393$; $p = 2.98 \times 10^{-3}$). Both microRNAs significantly increased during longitudinal analysis from presentation to days 3–5 and then slowly declined at 90 days after stroke ($p < 0.01$).

Table 1. Significantly altered serum exosomal miRNAs in large vessel occlusion stroke and the correlation with the infarction volume (N= 55 stroke cases and 53 controls)

miRNA	Fold Change	Log fold change	p-value	FDR p-value	Bonferroni corrected p-value	Correlation with stroke volume/p-value
hsa-miR-9-3p	9.39	3.23	2.0×10^{-7}	5.6×10^{-5}	1.3×10^{-4}	↑*
hsa-miR-223-3p	-1.83	-0.87	1.1×10^{-7}	1.5×10^{-4}	7.1×10^{-4}	↓

*p- value =0.003

Significant microRNAs

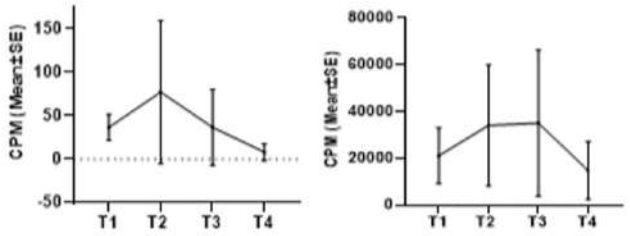

Figure 1. Longitudinal analysis of miRNA-9-3p (A), mi-RNA-223-3p (B) shows that they increase after presentation and decline at 90 days.

Longitudinal changes in microRNAS

Conclusion: Our study showed dysregulation of exosomal microRNAs 9-3p and 233-3p after ischemic stroke in cross-sectional and longitudinal analysis. If replicated in large-scale trials both microRNAs may be come ischemic stroke biomarkers

Disclosure: Nothing to disclose.

EPO-095 | Neurological symptoms in adults with Gaucher disease: A systematic review

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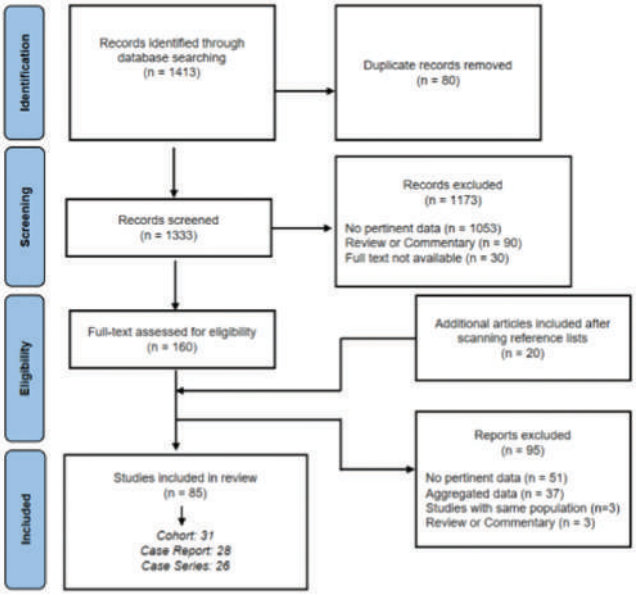
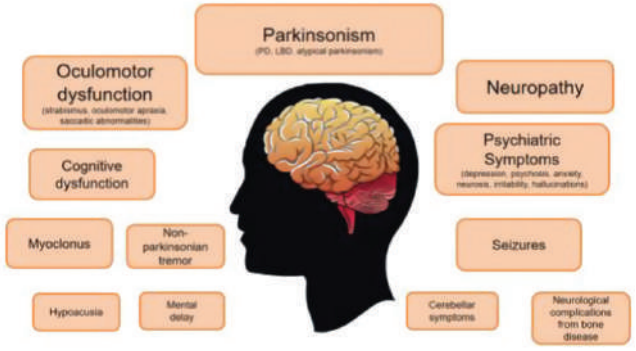
Background and Aims: Gaucher disease (GD) is traditionally classified into three types based on the presence or absence of neurological signs and symptoms, but their presentation can be highly variable in adulthood and they have not been adequately addressed in the literature so far. We performed a systematic literature review to analyze the entire spectrum of neurological manifestations in adult patients previously classified as GD type I, II or III, evaluating the role of variants in different neurological manifestations.

Methods: We searched databases for studies reporting clinical data of adult GD patients (age ≥18). Data extraction included GD types, GBA1 variants, age at disease onset and diagnosis, duration of GD and age at onset, and type of neurological symptoms reported.

Results: Among 4190 adult GD patients from 85 studies, 555 exhibited at least one neurological symptom. The median age at evaluation was 46.8 years (IQR 26.5), age at neurological symptoms onset was 44 years (IQR 35.1), and age at GD clinical onset was 23 years (IQR 23.4). Parkinsonism, including Parkinson's disease and Lewy Body dementia, was the most reported neurological manifestation. Other symptoms and signs encompassed oculomotor abnormalities, peripheral neuropathy, seizures, myoclonus, and cerebellar, cognitive and psychiatric symptoms. The genotype N370S/N370S mostly presented with Parkinsonism and the L444P variant with severe and earlier neurological symptoms.



The PRISMA flow diagram of the systematic review



Graphic summary of the principal neurological symptoms evaluated in adult patients with Gaucher Disease. The font size decreases based on the observed prevalence.

Conclusion: The findings of this systematic review highlight: (1) the relevance of a comprehensive neurological assessment in GD patients, and (2) the importance of considering possible undiagnosed GD in adult patients with mild systemic symptoms presenting unexplained neurological symptoms.

Disclosure: Nothing to disclose.

EPO-096 | **Description of a cohort of Primary Familial Calcification patients from a single centre in Italy: A systematic approach**

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Background and Aims: PFBC is a rare neurodegenerative disorder characterized by calcium deposition in the brain. Clinical manifestations include movement disorders, cognitive or psychiatric features; 50% of cases recognize a genetic cause, with an autosomal dominant (SLC20A2, XPR1, PDGFB, PDGFRB) or recessive inheritance (MYORG, JAM2, CMPK2). Almost 500 cases have been described from different centres with different clinical workup. We systematically describe a cohort from a single centre in Italy (Padova).

Methods: Clinical-neuropsychological examination, NGS genetic panel, blood test, CT scan

Results: We examined 78 PFBC subjects, 33 males and 45 females; 46% had a positive family history; secondary causes of calcium deposition were excluded. 21% were asymptomatic; mean age at onset was 55 years (min 23, max 90). The most frequent symptoms were movement disorders (Fig. 1): parkinsonism (58%), followed by tremor (56%). Dystonia was documented in 27% (with 2 cases of paroxysmal dystonia); cerebellar signs (21%) and chorea (13%) were less frequent; pyramidal signs were also present in 45% of cases. Psychiatric features were associated in 51%, and cognitive deficits in 38% (22 MCI and 4 dementias, mainly affecting executive domains). Pathogenic mutations were found in 55% of subjects (Fig. 2), mostly in SLC20A2 (45%) and MYORG (21%). Dentate nuclei were frequently involved besides basal ganglia (Fig. 3). DAT-Scan was positive in 21/32 (65.6%) of patients with parkinsonism.

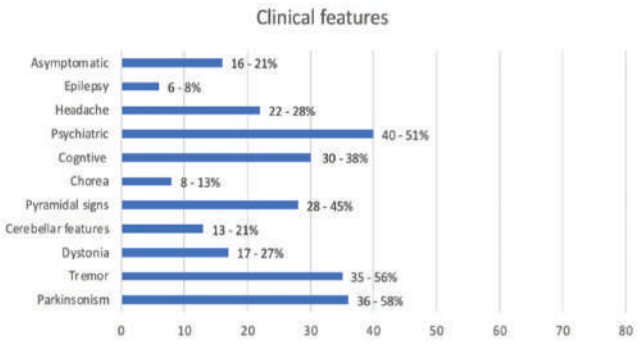

FIGURE 1 Clinical features of the cohort

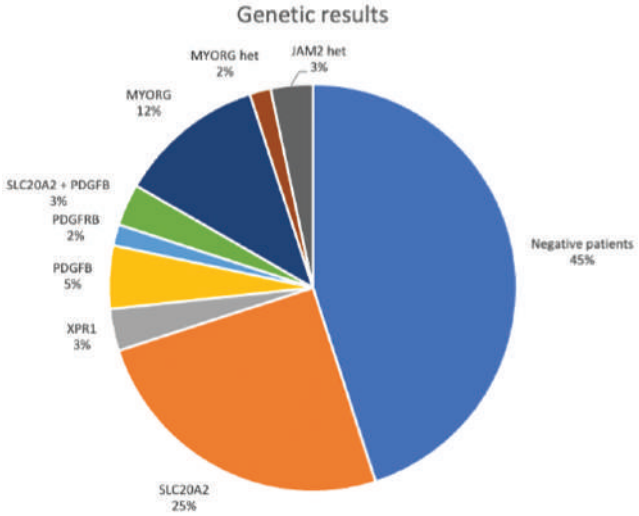

FIGURE 2 Genetic testing results in the cohort

CT brain site	%
Basal ganglia	100%
Dentate nuclei	65%
Thalami	45%
White matter	40%
Cortex	18%
Brainstem	8%

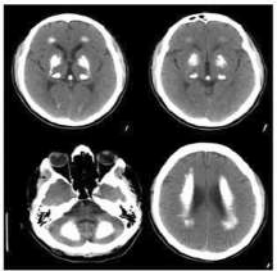

FIGURE 3 Radiologic features of the cohort and a CT example of a MYORG patient

Conclusion: Our work suggests a complete clinical, genetic and radiologic assessment to evaluate PFBC patients as a tool to obtain complete data to better understand this complex disease.

Disclosure: Nothing to disclose.

EPO-097 | Genetic study of SCA27B, CANVAS and other repeat expansion disorders in Greek patients with late-onset cerebellar ataxia

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Background and Aims: Late-onset cerebellar ataxia (LOCA) encompasses heterogeneous neurodegenerative disorders with symptom onset after 30 years of age. A genetic diagnosis is established in fewer than 30% of LOCA patients. Intronic tandem repeat expansions (TREs) in RFC1 and FGF14 have recently emerged as common causes of LOCA. This study screened Greek LOCA patients for the commonest causative TREs.

Methods: Over a 28-year period, 206 consecutive LOCA patients were referred for genetic testing. Based on clinical data and inheritance pattern, patients were screened for FRDA, SCA1,2,3,6,7 and FXTAS, followed by testing for CANVAS and SCA27B. PCR, RP-PCR, agarose gel electrophoresis and fragment analysis were performed, as appropriate, to detect the pathogenic TREs.

Results: A genetic diagnosis was reached in 60 of 206 cases (29.1%). Mean age was 60.1 ± 11.2 (35–87) years and mean age at onset 52.5 ± 11.4 (30–80) years. SCA27B accounted for 9.7% of LOCA cases ($n = 20$), CANVAS for 6.8% ($n = 14$) and FRDA for 4.4% ($n = 9$). The overall frequency of SCA1 ($n = 5$), SCA2 ($n = 6$) and SCA7 ($n = 3$) was estimated at 6.8%. No cases of SCA3 and SCA6 were identified. FXTAS ($n = 3$) contributed another 1.5% of cases.

Conclusion: Our study provides comprehensive data on the genetic basis of LOCA in the Greek population. SCA27B, followed by CANVAS, represent the commonest known genetic causes of LOCA. FRDA is also a relatively common cause of LOCA. SCA1,2,7 and FXTAS are rare, whereas SCA3 and SCA6 are virtually absent. We recommend prioritizing testing for FGF14 and RFC1 expansions in the diagnostic algorithm of LOCA.

Disclosure: Nothing to disclose.

EPO-098 | Mutational screening of greek patients with Charcot-Marie-Tooth disease using whole exome sequencing

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Background and Aims: Charcot-Marie-Tooth disease (CMT) is the most common cause of hereditary neuropathy, exhibiting extensive genetic heterogeneity, which can be addressed using whole exome sequencing (WES). This study screened previously undiagnosed Greek patients with CMT, using WES.

Methods: Over a 6-year period, 441 consecutive patients were referred for CMT molecular diagnosis. Following targeted testing for CMT1A and in selected cases for CMTX, 173 index-cases remained undiagnosed, of which 65 with a strong suspicion of hereditary neuropathy. To date, 32 of these, including 13 cases with demyelinating and 19 cases with axonal neuropathy, have been screened by WES using Ion Torrent technology and confirmed by Sanger sequencing.

Results: Causative variants were detected in 19 of 32 patients (59.4%) across 14 genes known to cause CMT, of which 3 were novel (in MPZ, SH3TC2 and KIF1A). In demyelinating forms the diagnostic yield was 76.9 % and in axonal forms 47.4%. Most causative variants were found in SH3TC2 (5 cases) and GJB1 (2 cases), all in demyelinating CMT. In patients with demyelinating CMT, single causative variants were found in EGR2, MPZ and NDGR1. In patients with axonal CMT, single causative variants were identified in HINT1, NEFH, BSCL2, NEFL, MORC2, GDAP1, KIF1A, SORD1 and MPV17.

Conclusion: The overall diagnostic yield of WES was comparable to other CMT populations. Our results contribute to the further mapping of gene variants associated with hereditary neuropathy and highlight the importance of WES in the diagnostic algorithm of disorders with high genetic heterogeneity, in the context of precision medicine.

Disclosure: Nothing to disclose.

EPO-099 | Phenotypical characterization of a cohort of SCA 27B patients

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Background and Aims: FGF14 intronic heterozygous GAA expansions have recently been identified to be a frequent cause of late onset cerebellar ataxia (LOCA) (SCA27B). We evaluated the frequency and phenotype of SCA27B in a cohort of patients with unsolved hereditary cerebellar ataxia (HCA).

Methods: We recruited 25 patients affected with HCA with no age limit who had negative results on testing for repeat expansions and ataxia gene panels and screened them for the FGF14-GAA repeat expansion.

Results: 4 of the 25 patients (16%) carried an FGF14 (GAA) ≥250 expansion. Median age at onset was 51.75 years (range 16–79). Episodic symptoms at onset were present in two patients with episodes of vertigo, sweating, gait imbalance in one case and ataxia, dysarthria, rigidity, diplopia and dysphagia in the other. On examination abnormal smooth pursuit movements, downbeat nystagmus, dysarthria and gait ataxia were present in all patients; appendicular ataxia was mildly present only in one patient. Other signs were hyporeflexia at lower limbs (¾), tremor of chin and hands (2/4), postural instability (¼). Other symptoms reported were diplopia (¼), cramps (2/4), urgency (¼), dysphagia (3/4), depression (2/4), hearing loss (2/4), chronic cough (¼). Alterations in BAEPs (¼), VEPs (2/4) and SEPs (¾) were present. Brain MRI revealed cerebellar atrophy (4/4), frontoparietal atrophy (2/4), superior cerebellar peduncle hyperintensities (¼).

Conclusion: Our results show the highly heterogeneity of SCA27B and support FGF14-GAA repeat expansion screening in patients with LOCA and MSA look-alikes. However, we suggest screening younger cohorts as well.

Disclosure: Nothing to disclose.

EPO-100 | Parkinsonism in primary mitochondrial disorders: Clinical characteristics and follow up

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Background and Aims: Primary mitochondrial disorders (PMDs) are a wide group of diseases characterized by a dysfunction of the mitochondrial respiratory chain, potentially involving the central and peripheral nervous system. Parkinsonism is described as a clinical feature of patients with PMDs. The objective of this study is to describe the clinical characteristics of parkinsonism in our cohort of patients affected by PMDs.

Methods: We revised the clinical records, including the extrapyramidal features, symptoms associated, the diagnostic investigations performed, genetic results, and response to therapy in all the patients presenting with parkinsonism in our PMDs cohort.

Results: 9/80 patients from our database presented characteristics of parkinsonism. Progressive external ophthalmoplegia (9/9), myopathy (9/9), ataxia (3/9), peripheral neuropathy (3/9), and optic atrophy (3/9) were the most frequent associated symptoms. Genetic analysis showed multiple mtDNA deletions with mutations in POLG1, TWNK and OPA1 nuclear genes. The most reported extrapyramidal symptom at onset was unilateral tremor. The age of onset was heterogeneous, ranging from 40 to 70 years old. Dopamine transporter imaging (DaTscan) showed a reduced or absent mostly asymmetrical striatal dopamine uptake. Overall, our cohort showed a good and sustained response to levodopa during follow up.

Conclusion: Our data confirm the role of mitochondrial nuclear genes in the pathogenesis of mitochondrial parkinsonism and the importance of screening these genes when suspecting a parkinsonism associated with "mitochondrial red flags". Extrapyramidal features in mitochondrial parkinsonism appear to be similar to those of idiopathic parkinsonism with an overall positive response to current therapies.

Disclosure: Nothing to disclose.

EPO-101 | Mortality in tuberous sclerosis complex after the introduction of everolimus in the UK

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Background and Aims: Limited literature is available regarding causes of death of people with Tuberous Sclerosis Complex (TSC) since the introduction of everolimus therapy in 2016 in United Kingdom. The aim of this audit is to look for any change in the main causes of death of people with TSC

Methods: Patients who attended the Bath supra-regional TSC specialist clinic and died between 2016 and 2022 inclusive had their medical records reviewed to identify various disease-related factors and cause of death. Where cause of death was not available, information from the patient's general practitioner (GP) was used or their death certificate was sought from the General Registry Office. The cohort was then split into various subgroups to identify potential risk factors for earlier mortality.

Results: 369 patients attended this clinic from 2016 to 2022. Six deaths were definitely related to TSC, 5 possibly related and 8 unrelated. Primary causes of death included tumours in 7 (37%; one pancreatic neuroendocrine tumour), epilepsy in 3 (16%, including 1 probable SUDEP), aspiration pneumonia in 3 (11%), sepsis in 2 (11%), COVID in 1 (5%), hepatic AML in 1 (5%), SEGA in 1 (5%), and stroke in 1 (5%). Renal failure was a secondary cause in 2 (11%).

Conclusion: Death at the Bath TSC clinic was associated with learning disabilities and possibly larger AML size. Mortality related to SUDEP causes has become less prominent, while cancers appear to be more prevalent in this cohort. Everolimus appears to positively impact renal and LAM risk.

Disclosure: Nothing to disclose.

EPO-102 | Whole exome sequencing-based testing of adult epilepsy in the Polish population

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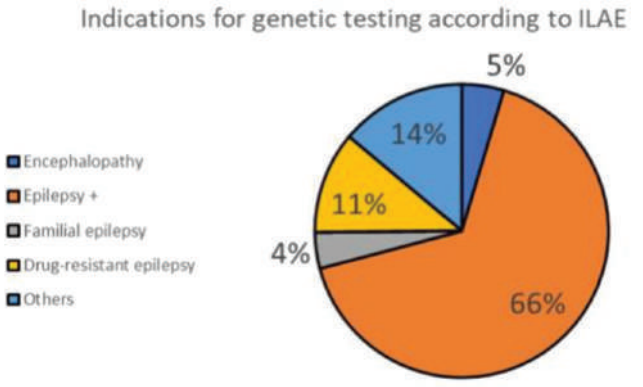
Background and Aims: Genetic testing in pediatric populations demonstrated clinical utility and provided a diagnostic yield of 18–40%, depending on the cohort tested. However, the diagnostic yield and data on the potential classification of adult epilepsies are limited.

Methods: This study aims to investigate the diagnostic yield, analyze genetic diagnoses and apply International League Against Epilepsy (ILAE) classification for pediatric epilepsies to adult patients with epilepsies in Poland. We recruited 151 patients from 42 clinical centers across Poland. The patients had a diagnosis of epilepsy/seizures, were older than 18 years old at the time of the genetic testing and did not have a genetic diagnosis. The median age of the patient was 28 years.

Results: We reached a diagnostic yield, when considering pathogenic/likely pathogenic variants according to ClinVar of 8.6% ($n = 13$) and of 17% ($n = 26$) when applying American College of Medical Genetics (ACMG) criteria. According to the indications for genetic testing according to ILAE, most adult patients were tested for epilepsy + ($n = 100$, 66%), 21 patients were tested for drug-resistant epilepsy (14%), 17 for encephalopathy (5%), and 6 patients were tested for familial epilepsy (4%).



Indications for genetic testing according to ILAE

Nr	Indications according to ILAE	Additional features	Molecular results	Classification ClinVar/ACMG
1	epilepsy +	mental disability, no speech, obstructed breathing, generalized weakness	Rett syndrome	CV-P
2	epilepsy +	cerebellar atrophy	Rett syndrome	CV-P
3	familial epilepsy		Rett syndrome	CV-P
4	familial epilepsy		Rett syndrome	CV-P
5	epilepsy +	abnormal muscle tone disorders, dysmorphic features, autism, NDD	AP4B1 p.Leu142Arg/p.Arg102Ter	ACMG
6	drug-resistant epilepsy	atypical autism, NDD	CHD4 c.439-2A>C	ACMG
7	drug-resistant epilepsy	autism, NDD	TSC2 p.Val126Phe	ACMG
8	epilepsy +	neuropathy, epilepsy, binocular cataract, spastic paraparesis	KIF1A p.Ser274Leu	CV-LP
9	epilepsy +	psychogenic epilepsy, muscular hypotonia	KMT2E p.Pro1505Ser	ACMG
10	epilepsy +	childhood autism, anxiety, auditory hypersensitivity	BBS1 c.817-1G>T; BBS10 p.Ala296Thr	ACMG
11	drug-resistant epilepsy	cortical dysplasia	CHRNA4 p.Met314Thr	ACMG
12	epilepsy +	cerebellar syndrome, myoclonus-dystonia	KCNC1 p.Arg320His	CV-P/LP
13	epilepsy +	NDD, high iron levels in the blood, congenital cataract	CYP27A1 p.Arg127Ipp/p.Arg127Trp	CV-P/LP
14	drug-resistant epilepsy	autism spectrum disorder, profound mental retardation, nystagmus, scoliosis, flat valgus feet, joint laxity, neuropsychiatric disorders	DYRK1A p.His545GlnfsTer18	ACMG
15	epilepsy +	hereditary epilepsies, dystonia, NDD, hypoglycaemia	MED12 c.6268-2A>G	ACMG
16	epilepsy +	epilepsy, dysmorphia (protruding ears, prominent lips), NDD	CHD2 p.Arg1074Trp	CV-LP
17	epilepsy +	atypical autism, NDD	NBEA p.Gly719ValfsTer4	ACMG
18	epilepsy +	severe mental retardation, dysmorphia, short stature, microcephaly	KDM3B p.Asp377GlyfsTer102	ACMG
19	epilepsy +	severe mental retardation, hypothyroidism, obesity, neuropsychiatric disorders	TSC1 p.Arg420GlyfsTer20	ACMG
20	epilepsy +	increased muscular tone in all extremities, severe mental retardation, aphasia, agenesis of the left kidney, microgyria	SOX9 p.Val462GlyfsTer56	CV-P/LP
21	epilepsy +	NDD, microcephaly, obesity	ANKRD11 p.Arg1388Ter	CV-P
22	epilepsy +	Cornelia de Lange syndrome, moderate mental retardation	ARID1B p.Pro617AlafsTer10	ACMG
23	epilepsy +	severe mental retardation, wheelchair bounded	NSD1 p.Lys1938Arg	ACMG
24	epilepsy +	mild NDD, cerebral palsy	ATP1A2 p.Pro775Leu	CV-LP
25	epilepsy +	cerebellar syndrome of unclear aetiology, tics, myotonias, flaccid paraparesis, cerebellar cortex atrophy	PCDH19 p.Trp748Ser/p.Ala143Val	ACMG
26	drug-resistant epilepsy	cerebral palsy, speech and language disorders, significant ID, spastic quadriparesis, swallowing disorders PEG-fed	TCF4 p.Ala323Val	CV-P

Summary of the molecular results and additional phenotypic features

Conclusion: There is a wide spectrum of diagnoses associated with epilepsy in adults. We applied the ILAE guidelines for childhood epilepsy to the adult population. Patients may have had a diagnosis related to childhood syndrome, but due to limited diagnostic possibilities it was not possible to diagnose them in childhood.

Disclosure: Nothing to disclose.

EPO-103 | Late-onset coats plus syndrome: Broadening the differential diagnosis of intracranial calcifications in adults

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Background and Aims: Coats plus syndrome (CPS) is a multisystemic disorder, with intracranial calcifications, cysts and leukoencephalopathy as characteristic neurological features. CPS typically presents in infancy or childhood and is caused by bi-allelic defects in CTC1 gene, involved in telomere maintenance and DNA replication.

Methods: A 46-year-old woman presented a 2-year history of behavioral changes and cognitive decline. Her medical history was unremarkable until 33 years of age when diagnosed with infertility. At 38, she developed retinal vasculopathy and progressive restrictive lung disease under consideration for lung transplantation. Her family history was irrelevant. Clinical examination revealed greying of the hair, atrophic skin with violaceous and brownish macules and low body mass index. Neurological examination highlighted attention and executive function deficits, left homonymous hemianopsia, left central facial palsy and hyperreflexia.

Results: Head MRI revealed a frontal white matter lesion involving U fibers, with peripheral gadolinium enhancement and vasogenic oedema, as well as multifocal calcifications in the subcortical and deep white matter. MR angiography was normal. CSF analysis showed hyperproteinorrachia, mirrored oligoclonal bands and elevated neopterins, excluding infection or neoplasia. To further clarify the radiological findings, exome sequencing was ordered and identified a homozygous variant NM_025099.6:c.2954_2956del in CTC1 gene. The patient died 9 months after presentation due to pneumonia.

Conclusion: Adult-onset CPS is very rarely reported. We presented a case associated with a homozygous in-frame deletion (p.(Cys985del)), which presented in adulthood with a milder phenotype. Clinicians should consider CPS in the differential diagnosis of intracranial calcifications and leukoencephalopathy in adults.

Disclosure: Nothing to disclose.

EPO-104 | Optimized testing strategy for molecular diagnosis of GAA-FGF14 (SCA27B) ataxia: French SCA27B ataxia study group

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Background and Aims: GAA expansions in FGF14 intron 1 are a common cause of autosomal dominant hereditary cerebellar ataxia (GAA-FGF14 ataxia; spinocerebellar ataxia 27B, SCA27B), particularly in Late Onset Cerebellar Ataxia (LOCA). SCA27B is classically characterized by a slowly progressive cerebellar syndrome with episodic onset in more than 2/3 of cases, over 40 years of age. Until now, molecular confirmation of FGF14 GAA expansions has mainly relied on long-read sequencing, a technology not yet routinely available in French genetics laboratories.

Methods: We developed and validated a three-step molecular diagnostic strategy: long-range fluorescent PCR (fLR-PCR) to determine allele sizes, bidirectional triplet-primed PCR (TP-PCR) to verify the presence and nature of the expansion and LR-PCR products gel electrophoresis and/or Sanger sequencing depending on the profile observed in TP-PCR. We compared this strategy to nanopore long-read sequencing on 22 Canadian SCA27B patients of French origin and then tested it on a national cohort of 560 patients with unresolved LOCA.

Results: We identified 107 patients (19.1%) carrying FGF14 expansions (GAA) ≥250 including 17/560 (3%) with expansions between 250 and 300 GAA (intermediate allele with incomplete penetrance). Further studies are needed to help in the interpretation of these intermediate alleles. We identified non-pathogenic non-GAA expansions and GAA-interruptions.

Conclusion: We confirm that SCA27B is a common cause of LOCA. Detailed phenotyping of patients appears essential particularly for the interpretation of intermediate alleles. This novel strategy reliably detected and sized FGF14 GAA expansions, and compared favorably to long-read sequencing.

Disclosure: None.

EPO-105 | Unveiling a stroke-like onset of Creutzfeldt-Jakob disease: A case report of V210I mutation

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Background and Aims: Genetic prion diseases (PrD) account for 10–15% of prion diseases and are caused by mutations in the prion protein gene (PRNP).

Methods: A 75-year-old man suddenly developed nominum aphasia ten days before admission. His medical history included hypertensive heart disease and atrial fibrillation. His brain computed tomography (CT) and angiography-CT were unremarkable. At neurological evaluation the patient executed simple orders, however, comprehension and production of complex speech were compromised. A first brain magnetic resonance imaging (MRI) excluded ischemic lesions and inflammatory processes. Meanwhile, he progressively and rapidly developed ataxia, cerebellar signs, spontaneous myoclonus and mutism. Analysis of cerebrospinal fluid (CSF) revealed increased levels of total tau (>2000 pg/ml). His electroencephalogram showed pseudo-periodic triphasic waves over the left frontotemporal regions. PrD was suspected, therefore the patient underwent a new brain MRI. Diffusion-weighted imaging exhibited diffuse cortical ribbons in the left frontal, insular and parietal cerebral cortex. After discharge, the patient died shortly after due to ab ingestis pneumonia.

Results: CSF RT-QuIC for prion protein returned positive. Sanger sequencing of the PRNP gene showed the heterozygous V210I genotype (c.628 G>A – p.Val210Ile) and the homozygous Met/Met genotype at codon 129. These findings were suggestive of genetic Creutzfeldt-Jakob disease (CJD).

Conclusion: An acute onset of symptoms in CJD is rare (2% of all cases) and so far has been associated exclusively with the V203I mutation. The sudden appearance of focal symptoms without corresponding brain lesions requires a thorough investigation to rule out other rare causes including CJD, especially in rapidly progressive clinical scenarios.

Disclosure: Nothing to disclose.

Epilepsy 1

EPO-106 | Heart rate variability in patients with Epilepsy

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Background and Aims: Several studies have reported alterations of heart rate variability (HRV) and decreased cardiac rhythm abnormality in patients with epilepsy. The purpose of this study is to investigate epilepsy and its impact on HRV.

Methods: We obtained HRV data from an ambulatory 24-hour rhythm holter monitorization recordings in 73 patients with epilepsy. We calculated HRV parameters in both time and frequency domains including low frequency (LF) power, high frequency power (HF), LF/HF ratio, square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), the standard deviation of all NN intervals (SDNN) and the standard deviation of the averages of NN intervals in all 5 min segments of the entire recording (SDANN). The HRV in epileptic patients was compared with 73 age- gender matched healthy controls.

Results: HRV analysis showed that epileptic patients presented lower values of HF than controls ($p=0.002$), also a lower values of LF (764.64 vs 801.3; $p=0.63$) with a significantly higher LF/HF ratio ($p<0.0001$). Time domain analyses also showed lower HRV and lower vagal activity in patients with epilepsy, as shown by lower SDNN (132.40 vs 136.24; $p=0.32$), lower SDANN (113.8 vs 123.11; $p=0.1$) and a significant lower RMSSD ($p=0.004$).

Conclusion: In conclusion, patients with epilepsy appear to have an altered autonomic control of the heart. The decrease in HRV parameters might be associated with the decrease in sympathetic tone. Further studies are warranted to explore these changes and their possible relevance for sudden death in epilepsy.

Disclosure: Nothing to disclose.

EPO-107 | Vagus Nerve Stimulation in paediatric drug-resistant epilepsy: Two decades experience in a Portuguese Tertiary Centre

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Background and Aims: Vagus Nerve Stimulation (VNS) is a therapeutic option in drug-resistant epilepsy. Real-world data on its application in children and long-term outcomes are crucial. We aimed to characterize an unicentric paediatric population undergoing VNS to evaluate its effectiveness/safety.

Methods: Clinical records of paediatric patients (<18 yo) implanted between 2000 and 2023 were reviewed. McHugh's classification (I-seizure frequency reduction 80–100%; II-50-79%; III-<50%; IV-magnet benefit only; V-no improvement) was applied at: a) first assessment after 1 year and stimulation >=1.5mA (T1) b) last assessment and stimulation >=1,5mA (T2).

Results: VNS was implanted in 56 paediatric patients; (51.8% were males. Median age and duration of epilepsy at implantation were 12 (IQR=6.8) and 9.2 (IQR=6.4) years. Ten patients had focal/multifocal, 20 generalized, and 26 combined focal/generalized epilepsies. Thirty were epileptic/developmental encephalopathies (16 with known mutations), 19 structural, 3 infectious, 2 immune, and 2 neurocutaneous syndromes. Median follow-up was 1.1 years (IQR=0.19) at T1 and 5.3 years (IQR=4.08) at T2. A reduction in seizure frequency was observed in 70.4% (T1) and 60% (T2) of patients, with 40.7% (T1) and 29.1% (T2) achieving ≥50% response. Among patients with falls, 48.5% had less events (T2). Cognitive-behavioural improvement was noticed in 50.9% of patients (T2). Mild complications occurred in 32.1%, most commonly dysphonia (61%) and cough (38.9%). VNS generator/battery was replaced in 15 patients, in 3 due to qualitative and/or cognitive-behavioural improvements. In 15 patients, lack of efficacy prevented its replacement.

Conclusion: Overall, VNS proved to be safe/effective, despite a less pronounced effect at T2. Notably, a significant qualitative and cognitive-behavioural benefit was observed.

Disclosure: Nothing to disclose.

EPO-108 | Time as a localizing sign: The challenge of identifying the origin of hyperkinetic seizures

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Background and Aims: Hyperkinetic seizures (HS), typically associated with the frontal lobe, are characterized by high amplitude, short duration, complex motor movements, although they may also originate from regions other than the frontal lobe. In our study, we aimed to differentiate HSs originating from the frontal and extra frontal lobes.

Methods: We retrospectively examined the data of 29 patients in whom HS was recorded with video-EEG. We reviewed the localization characteristics of HSs, onset time, duration of hyperkinetic movements, and ictal-postictal electrophysiological and semiological features. Two groups, early and late-onset HS, were created based on whether the onset of hyperkinetic semiology occurred in the first 10 seconds or later during the seizure.

Results: Seizure onset originated from the frontal region in 21 patients, and from the temporal and temporo-occipital region in 6 patients (Table 1). Clustering of hyperkinetic seizures (>3 seizures/day) was detected in 13 patients (44.8%), while >=1 seizure within 24 hours was observed in 22 patients. HS started in the early period in 21 patients and late period in 8. HSs originating from the frontal region started earlier than those originating from the temporal region (11.7 s, 23 s; $p=0.008$). Electrophysiological (12.0 s, 22.3 s; $p=0.013$) and clinical (11.9 s, 22. 7 s; $p=0.011$) seizure durations were shorter in frontal onset seizures (Table 2).

TABLE 1 Demographic and clinical data of the patients

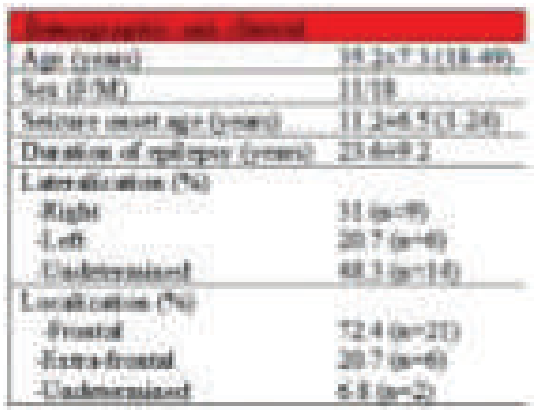
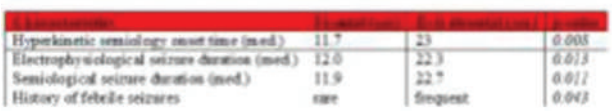


TABLE 2 Characteristics of seizures according to the region of onset



Conclusion: Our study indicates that the onset time and duration of hyperkinetic semiological findings are informative in terms of localization. Hyperkinetic semiology with earlier onset and shorter duration may suggest a frontal origin.

Disclosure: The authors declare no conflicts of interest. This study has been presented in the 39th National Clinical Neurophysiology EEG-EMG Congress, Turkey.

EPO-109 | The preliminary results of cortical thickness measurements in elderly patients with epilepsy and Alzheimer's dementia

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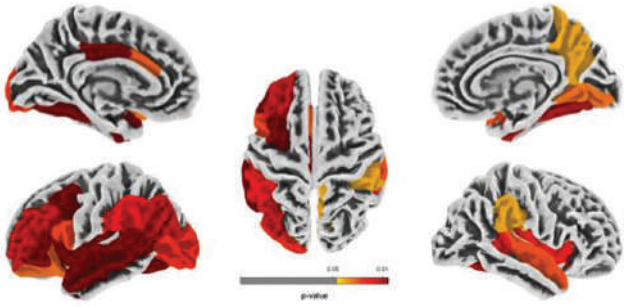
Background and Aims: Observational studies have suggested a bidirectional relationship between Alzheimer's dementia (AD) and epilepsy. However, whether a causal relationship exists and in which direction it operates is still a matter of debate. This study aims to assess the relationship between late-onset non-lesional epilepsy and AD by measuring cortical thickness in both patient groups.

Methods: Thirteen patients with epilepsy who experienced onset of seizures aged 50 and above, had a MOCA (Montreal Cognitive Assessment) score greater than 26, and exhibited normal findings in conventional neuroimaging, were included in the study. They were compared with 13 gender- and age-matched patients diagnosed with AD and 13 healthy controls. All subjects were scanned on 3T-MRI scanner. CAT12 software was employed to analyze T1-weighted images from each participant. Cortical thickness maps, smoothed with a 15 Gaussian kernel, were generated from the central surface classified according to anatomical cortical brain regions.

Results: No significant difference was detected in any brain region measured between the epilepsy and control groups. A significant decrease was detected in all brain regions in the dementia group compared to both groups (Figure).



Anatomical brain regions with cortical measurements between AD and Epilepsy

Conclusion: In the study conducted with the expectation of observing cortical changes in terms of the structural relationship between epilepsy and AD, the absence of any alterations may be attributed to the limited number of participants. It is aimed to continue the study by increasing the number of patients.
Disclosure: Nothing to disclose.

EPO-110 | Implementation of urgent eeg on-call in a tertiary hospital

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Background and Aims: Urgent video-EEG (uvEEG) is crucial for early diagnosis and treatment of seizure and non-convulsive status epilepticus (NCSE) but is not always available. We aimed to evaluate its yield after implementation in our center.
Methods: We retrospectively identified patients who underwent an uvEEG at a tertiary hospital from September 2021 to January 2023. We categorized uvEEG findings and evaluated antiseizure medication (ASM) escalation.
Results: A total of 498 uvEEG were collected and 245 performed on-call (weekdays 5p-10p and weekends 9a-10p). Most studies were requested from the intensive care units (ICU) (47.2%) compared to neurology (21.4%) or the emergency room (ER) (17%), and other services (14.5%). UvEEG revealed non-convulsive seizures (NCS)/NCSE in 10.2% patients, epileptiform patterns (Lateralized and generalized periodic discharges, focal and generalized epileptiform activity) in 15.9%, attenuation/burst-suppression patterns in 8.98%, slowing/rhythmic patterns in 43.7%, normal activity in 18.8% and other patterns in 2.40%. We observed an association between hospital settings (ICU, ER or neurology) and uvEEG findings ($p=0.0003$). The proportion of normal uvEEG in the ER (44.6%) and neurology (39.4%) was similar but significantly different to the ICU (4.3%) and other departments (11.7%) ($p<0.000$). Most of the uvEEG were requested between 12 and 24h after clinical onset. Neurology, ICU and ER applications were significantly higher after-hours in contrast to other departments ($p<0.000$). Modifications of ASM were present in 84% ($n=95$) of patients.
Conclusion: uvEEG guides initiation and modifications of ASM in complex patients with neurological focal deficits at different hospital settings. uvEEG is mandatory in patients with NCS/NCSE for appropriate care.
Disclosure: No disclosures.

EPO-111 | Perampanel as only add-on treatment in post-stroke epilepsy: Real-world data from multicenter, observational study

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Background and Aims: Post-stroke epilepsy (PSE) is one of the most common causes of acquired epilepsy, with an estimated occurrence of 4–6% in the stroke population. Currently there is limited evidence regarding the clinical profile of antiseizure medications (ASMs) in PSE. This study aims to evaluate the 12-months effectiveness and tolerability of adjunctive perampanel (PER) as only add-on drug in patients with PSE in a real-world setting
Methods: We performed a subgroup analysis of PSE patients included in a previous 12-month retrospective, longitudinal, multicentre observational study investigating use of PER as only add-on treatment. Effectiveness outcomes included responders' rate (≥50% reduction of frequency), seizure-freedom and retention rate at 3, 6 and 12 months. Safety and tolerability outcomes included incidence of adverse events (AEs) and rate of treatment discontinuation due to AEs.
Results: The sample included 56 people with PSE (median age 49 years; IQR: 18.9–67.1). The mean daily dose of PER at 12 months was 5.3 ± 2 mg. We found a one-year retention rate of 66.7%. Responders' rate was 83.9% at the 12-month visit, with 51.6% of patients being seizure-free. Poor tolerability represented the main reason for drug withdrawal (11/13, 84.6%). AEs were registered in 25 out of 54 (46.3%) patients. Only 5 serious AEs (without deaths) were noticed. Behavioural problems resulted the most frequent AE, reported by 14 subjects.
Conclusion: Adjunctive PER was efficacious and generally well tolerated in patients with PSE in a real-world setting and could represent a suitable therapeutic option in this specific category.
Disclosure: All authors report no disclosure.

EPO-112 | Final analysis of perampanel as the only adjunctive anti-seizure medication from the observational PERPRISE study

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Background and Aims: In Germany, prior to perampanel reintroduction in 2017, only limited data of its use as late-line therapy were available. PERPRISE (PERampanel in patients with PRImary or

SEcondarily generalised seizures; NCT04202159) was a 12-month, prospective, observational, non-interventional study in a real-world setting in Germany evaluating the effectiveness and safety of perampanel as an only add-on anti-seizure medication (ASM) or a substitute for one ASM during dual therapy.

Methods: Patients (>=18 years) with focal or idiopathic generalised epilepsy who had >=1 focal to bilateral tonic-clonic seizure (FBTCS) or generalised tonic-clonic seizure (GTCS) <=3 months prior to inclusion were eligible. The Full Analysis Set included patients who received >=1 dose of perampanel. The primary endpoint was retention rate at 12 months; secondary endpoints were retention rate at 6 months, seizure-freedom rate at 12 months and safety.

Results: The Full Analysis Set included 183 patients (add-on: 86 patients; substitution: 96 patients). At 12 months, retention rates were 66.7% in the overall population and 67.4% and 66.7% in the add-on and substitution groups, respectively (Figure 1). Seizure-freedom rate in the overall population was 42.3% for FBTCS+GTCS at 12 months (Figure 2). Treatment-emergent adverse events (TEAEs) occurred in 44.0% (*n*=80/182 [Table 1]) of patients; 6.0% of patients reported serious TEAEs and 16.5% of patients withdrew from the study due to TEAEs.

Figure 1: Retention rates of perampanel in the overall population and add-on and substitution groups at 6 and 12 months (Full Analysis Set)

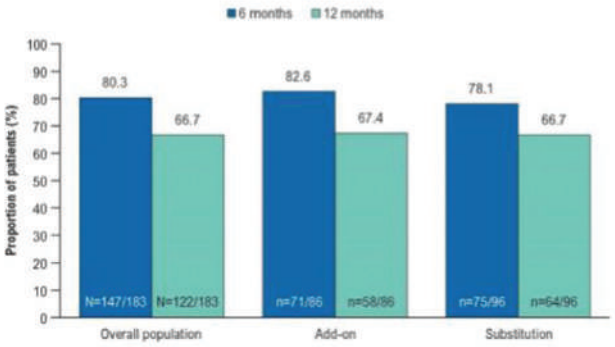
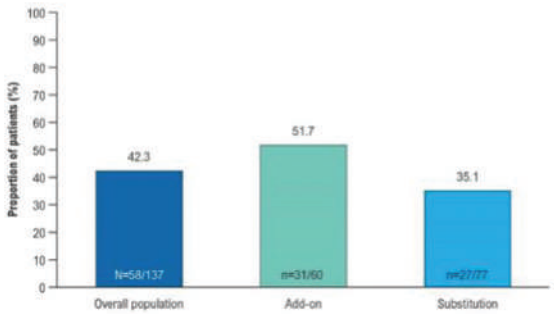


FIGURE 1

Figure 2: Seizure-freedom rates[a] of perampanel for patients with FBTCS and/or GTCS in the overall population and add-on and substitution groups at 12 months (Full Analysis Set)



[a]Percentages were calculated based on non-missing values. Seizure-freedom data were recorded for each month and patients who reported no generalised tonic-clonic seizures (FBTCS and GTCS) for all documented months were included in this analysis

FBTCS, focal to bilateral tonic-clonic seizure; GTCS, generalised tonic-clonic seizure

FIGURE 2

Table 1: Summary of TEAEs (Full Analysis Set)

	Overall population[a] (N=182)	Add-on (n=86)	Substitution (n=96)
Any TEAE, n (%)	80 (44.0)	43 (50.0)	37 (38.5)
Any serious TEAE, n (%)	11 (6.0)	4 (4.7)	7 (7.3)
Any severe TEAE, n (%)	7 (3.8)	3 (3.5)	4 (4.2)
Any TEAE with ADR, n (%)	59 (32.4)	29 (33.7)	30 (31.3)
Any TEAE leading to perampanel withdrawal, n (%)	30 (16.5)	14 (16.3)	16 (16.7)
Any serious TEAE leading to perampanel withdrawal, n (%)	4 (2.2)	1 (1.2)	3 (3.1)
Most common TEAEs (>=2% of patients overall), n (%)			
Dizziness	22 (12.1)	15 (17.4)	7 (7.3)
Fatigue	14 (7.7)	10 (11.6)	4 (4.2)
Nausea	10 (5.5)	7 (8.1)	3 (3.1)
Gait disturbance	8 (4.4)	4 (4.7)	4 (4.2)
Headache	8 (4.4)	6 (7.0)	2 (2.1)
Irritability	8 (4.4)	1 (1.2)	7 (7.3)
Aggression	5 (2.7)	3 (3.5)	2 (2.1)
Seizure	4 (2.2)	3 (3.5)	1 (1.0)

[a]Data were missing for one patient

ADR, adverse drug reaction; TEAE, treatment-emergent adverse event

Conclusion: This study showed that perampanel, as an only adjunctive therapy, had a favourable retention rate and was well tolerated in patients with FBTCS and/or GTCS during routine clinical care in Germany.

Disclosure: This study was funded by Eisai GmbH. Bernhard J Steinhoff has received speaker honoraria from Angelini, Arvelle Therapeutics, Desitin, Eisai GmbH, GW Pharmaceuticals, Tabuk Pharmaceuticals, Teva and UCB Pharma; and has served as a paid consultant for Angelini, Arvelle Therapeutics, B. Braun Melsungen, Eisai GmbH, GW Pharmaceuticals and UCB Pharma. Tobias Goldmann is an employee of Eisai GmbH. Yaroslav Winter has received honoraria for educational presentations and consultations from Angelini Pharma, Arvelle Therapeutics, Axsome, Bayer AG, BIAL, Bioprojet, Eisai, Idorsia Pharmaceuticals, JAZZ Pharmaceuticals, LivaNova, Novartis and UCB Pharma.

EPO-113 | GATORopathies: An observational study of patients with familial focal epilepsy

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Background and Aims: In the last few decades, increasing interest in the genetics underlying familial focal epilepsy syndromes has emerged. Mutations in mTOR pathway regulatory genes, including the GATOR1 complex (DEPDC5, NPRL3, NPRL2), have been linked to malformations of cortical development and epilepsy.

Methods: A unicentric, retrospective observational study of adult patients with epilepsy and GATOR1 variants diagnosed between 2019 and 2023.

Results: We identified six patients (4 males) from three families. Two families had heterozygous pathogenic variants in DEPDC5 (2 patients with c.2760dupC and 2 with c.4098del) and the third family in NPRL3 (c.1374del). 4/6 patients had a known family history of epilepsy. The median age at onset of epilepsy was 10 years (3–22). One patient experienced focal impaired awareness seizures, 1/6 focal to bilateral tonic-clonic (FBTC), and 4/6 focal and FBTC seizures, mostly nocturnal in all cases. Brain MRI did not reveal any abnormalities. Interictal focal epileptiform abnormalities were detected by electroencephalogram in 2/6. Epilepsy was drug-resistant in three patients, 2/3 with three anti-seizure medications, whereas the other three were seizure-free with one drug. In family C, proband's relative III-13 presumably died of sudden unexpected death in epilepsy (SUDEP). None of them had cognitive impairments or psychiatric comorbidities.

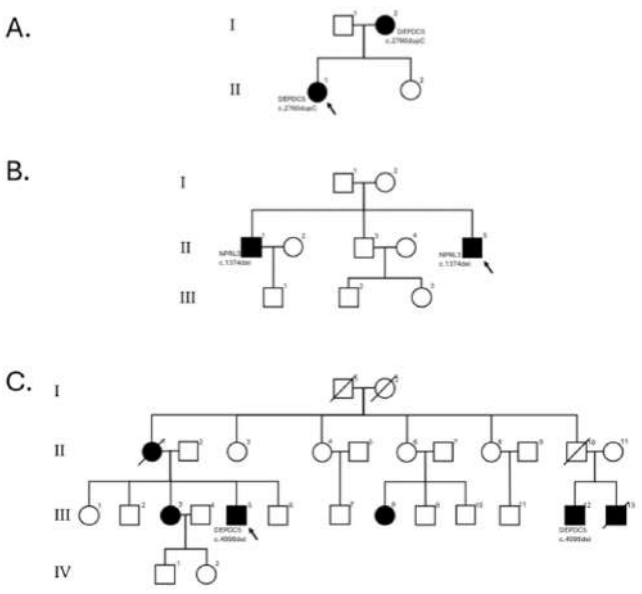

FIGURE 1 Pedigrees of the three families. Black squares/circles indicate male/female members with epilepsy in the family. Individuals with confirmed pathogenic variants in the GATOR complex are specify.

TABLE 1 Clinical and genetic characteristics of patients with GATOR1-related epilepsy included in the study. Abbreviations: F, female; M, male; N, normal

Table 1. Clinical and genetic features of the patients with GATOR1-related epilepsy

Patient	Variant	Age (onset)	Gender	Type of seizures	ASM (used)	Effective ASM	Drug resistant	EEG	MRI
Family A									
I-2	DEPDC5 c.2760dupC	9	F	Focal impaired awareness	VPA, CBZ, LTG	LTG	No	N	N
II-1	DEPDC5 c.2760dupC	11	F	Focal aware seizures Focal to bilateral tonic-clonic	LTG	LTG	No	Right parietal interictal epileptiform discharges	N
Family B									
II-1	NPRL3 c.1374del	22	M	Focal to bilateral tonic-clonic	CBZ	CBZ	No	N	N
II-5	NPRL3 c.1374del	13	M	Focal impaired awareness Focal to bilateral tonic-clonic	LEV, CBZ, ESL, CLB		Yes	Bifrontal (Right > Left) interictal epileptiform discharges	N
Family C									
III-5	DEPDC5 c.4098del	5	M	Focal impaired awareness Focal to bilateral tonic-clonic	LEV, CBZ, LCM		Yes	N	N
III-12	DEPDC5 c.4098del	3	M	Focal aware seizures Focal to bilateral tonic-clonic	LEV, CBZ, LCM		Yes	Generalized mild unspecific abnormalities	N

Conclusion: Pathogenic variants in the GATOR1 complex are associated with a broad spectrum of phenotypes, even in the same family, but typically cause familiar focal epilepsy with incomplete penetrance and nocturnal seizures. Drug-resistant epilepsy is frequent not only in our series but also in literature. Moreover, a higher risk of SUDEP has been reported.

Disclosure: Nothing to disclose.

EPO-114 | Abstract withdrawn

EPO-115 | The effect of epilepsy education on knowledge level, self-management, and stigma in individuals with epilepsy

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Background and Aims: This study aims to examine the impact of effective education for individuals with epilepsy on their knowledge level, self-management, and stigma.

Methods: A survey containing an 'Epilepsy Knowledge Form,' 'Epilepsy Self-Management Scale,' and 'Stigma Scale' was sent to all patients registered at our epilepsy outpatient clinic. Afterwards, patients were invited to an online live epilepsy lesson. Participants were re-tested after the training.

Results: Of the 265 patients who completed the pre-education survey, 69 (26%) attended the education. University graduates and individuals who use the internet as a source of information were more motivated to attend, while singles attended less. The average age of participants was 39.1 ± 9.2 (21–68) years; 42 (60.9%) were women, 65.2% were university graduates, and 60.9% were actively working. 44.9% had focal, 21.7% had generalized, and 33.3% had both focal and generalized seizures. 69.6% of the participants had seizure frequency of less than once a month. 50.7% were on monotherapy, and 94.2% regularly took their antiseizure medication. The most

common sources of information were doctors, the internet, other patients, television, and social media (100%, 65.2%, 27.5%, 20.3%, 17.4%, respectively). After the education, patients answered more knowledge questions correctly ($p=0.000$, before: 37.0 ± 6, after: 40.7 ± 6.1), awareness about the risks of swimming increased, and their motivation to carry health information cards, participate in support groups, and teach epilepsy to relatives increased. No change was observed in the stigma scale.

Conclusion: Education for individuals with epilepsy positively contributes to their awareness and self-management regarding their condition. Combating stigmatization requires broader societal involvement.

Disclosure: This study has been presented in 59th Turkish National Neurology Congress.

EPO-116 | Intraoperative recordings in bottom-of-the-sulcus focal cortical dysplasia with new highly flexible cortical strip

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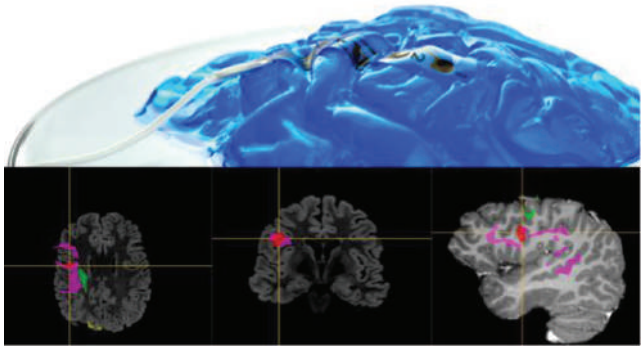
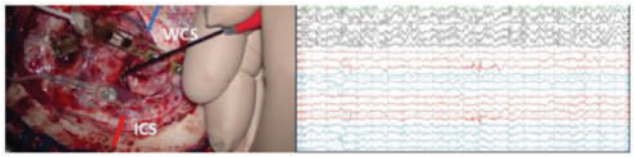
Background and Aims: the recording of epileptiform discharges from Bottom-Of-Sulcus focal cortical Dysplasia (BOSD) is often difficult during intraoperative electrocorticography (iECoG) due to the deep localization. We describe how the use of new generation electrodes with high flexibility easily adapting to cortical gyri and sulci can improve electrocortical recording.



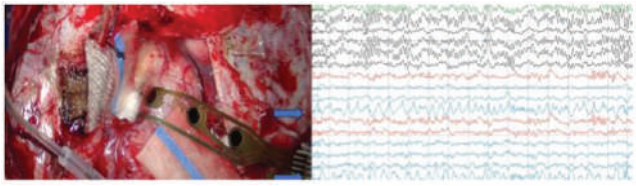
1) Example of the high flexibility of the strip 2) pre-surgical 3D reconstruction showing major tracts (BOSD in red)

Methods: a right-handed 20-years-old male with drug-resistant focal epilepsy due to a BOSD of the inferior frontal gyrus and daily focal aware seizures was evaluated for epilepsy surgery. Based on electroclinical and neuroimaging results a focal cortectomy guided by iECoG was proposed. iECoG recordings were performed with new generation cortical strips (Wise Cortical Strip; WCS®) and with standard cortical strips. Both bipolar and referential electrode montages were reviewed to identify epileptiform activity.

Results: iECoG, performed on the convexity of the frontal cortical surface recorded only sporadic spikes with both strip's types. Then, after a microsurgical trans-sulcal dissection, WCS was molded along the sulcal surface of the suspected BOSD based on 3D- imaging reconstruction, showing a continuous/subcontinuous 3–4 Hz rhythmic spikes activity from the deepest electrode. Registration after resection of the BOSD didn't show any epileptiform activity. Pathology showed dysmorphic neuron and gliosis. No surgical complications occurred. Patient is seizure free after 12 months.



Placement of the strip on the cortical convexity with related electocorticography (WCS in blue, ICS in red), No clear epileptic activities reordered



Placement of the strip at the bottom of the sulci, with electrocorticography showing continuous ictal activity from the deepest electrodes

Conclusion: This case report showed that new generation cortical electrodes with high flexibility features allowed to perform high-quality recordings from the bottom of the sulcus, overcoming a limit of classical iECoG that typically doesn't allow registration from the deepest of the cortical sulci.

Disclosure: Nothing to disclose.

EPO-117 | Tailored surgery guided by intraoperative electrocorticography (iEcoG) in temporal lobe encephalocele (TE)

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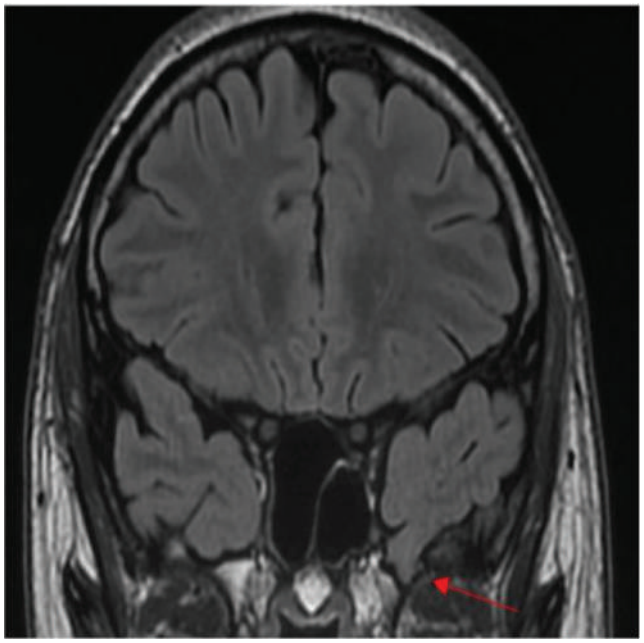
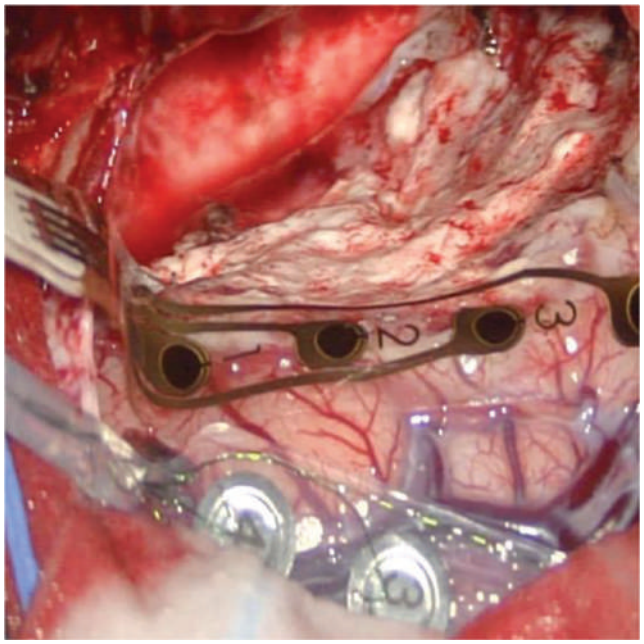
Background and Aims: TE can lead to medically refractory epilepsy, warranting surgical intervention. However, there is a lack of consensus on the appropriate surgical approach. This case series illustrates the potential effectiveness of iEcoG in guiding personalized lobectomy procedures for TE.

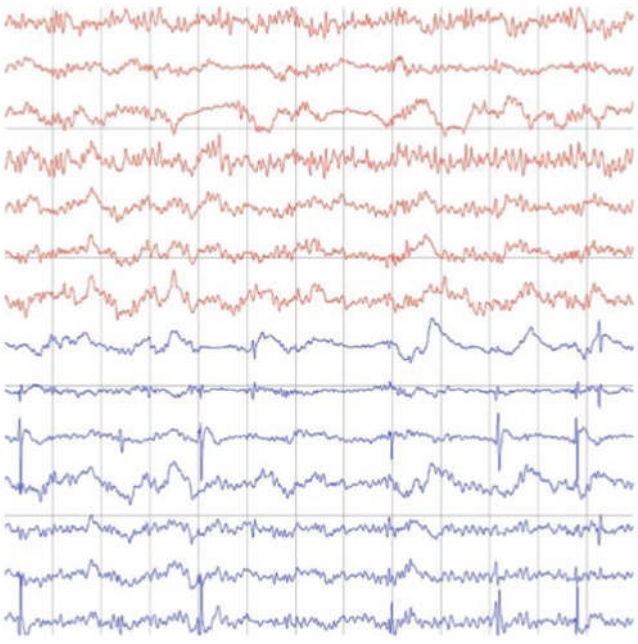


COR FLAIR brain MRI at the level of the temporal poles with finding of left temporal encephalocele (indicated by the red arrow)

Methods: patients underwent surgery following thorough anamnestic, neurophysiological, and neuroradiological assessments. iECoG were conducted on the cortical area pre- and post-resection, concluding with assessments on mesial temporal structures.
Results: Patient 1: 38-year-old male with left temporal pole encephalocele. iECoG show sporadic spikes on the neocortical temporal surface before surgical resection, while no epileptic activity was recorded on the amygdala and hippocampus. Therefore, the mesial structures were spared. Pathology: FCD-Ia. Patient 2: 20-year-old male with left mesial temporal pole encephalocele. iECoG revealed frequent irregular spiking on the neocortical temporal surface before surgical resection and persistent epileptic activity on the posterior temporal resection margin, so the surgical procedure was extended until the sylvian vein. No epileptic activity was seen on the hippocampus thus it was spared. Pathology: cortical dyslamination. Patient 3: 72-year-old female with extensive right temporopolar encephalocele. iECoG recorded sporadic epileptic activity in anterior section close to the borders of the encephalocele, sparing resection borders and temporomesial structures. Pathology: gliosis. All patients are in Engel class IA.



EcoG (patient 2) at the level of the encephalocele and neighboring cortex pre-resection



electrode strip placed on the posterior margin of the resection

Conclusion: These 3 cases show the usefulness of ECoG for a tailored surgical resection according to the irritative zone.
Disclosure: Nothing to disclose.

EPO-118 | Comparisons between traditional, brief, and ultra-brief anxiety and depression inventories in people with epilepsy

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Background and Aims: While fast (and accurate) large scale detection of anxiety/depression symptoms is desirable for people with epilepsy (PWE), traditional inventories are time-consuming and less practical. Here, we compared traditional questionnaires (Beck Anxiety Inventory [BAI] and Beck Depression Inventory-II [BDI-II]) with brief inventories (Generalized Anxiety Disorders-7 [GAD-7] and Neurological Disorders Depression Inventory for Epilepsy [NDDIE]) and ultra-brief inventories (GAD-2, GAD Single-item [GAD-SI], and NDDIE-2) for symptom's detection.
Methods: We evaluated 548 consecutive PWE (60% women; median-age 41 years) with different questionnaires for anxiety/depression. We considered as symptomatic the individuals scoring ≥14 points in both BAI/BDI-II, ≥7 in GAD7, ≥3 in GAD-2, ≥2 in GAD-SI, ≥13 in NDDIE, and ≥ 4 in NDDIE-2. We used SPSS for the Receiver Operator Characteristic (ROC) curve analysis (with area under-curve values [AUC]) and cross-accuracy analysis (with Kappa-Index [KI] values).
Results: We compared the BAI's performance with GAD-7 (AUC=0.88; $p=0.017$), GAD-2 (AUC=0.84; $p=0.019$), and GAD-SI (AUC=0.80; $p=0.022$ – Figure 1A). We also compared the GAD-7's performance with GAD-2 (AUC=0.94; $p=0.01$) and GAD-SI (AUC=0.85; $p=0.019$ – Figure 1B). Moreover, we obtained similar values comparing BDI-II with both NDDIE (AUC=0.87; $p<0.001$) and NDDIE-2 (AUC=0.84; $p<0.001$ – Figure 1C) and comparing NDDIE with NDDIE-2 (AUC=0.93; $p<0.001$ – Figure 1D). There was an overall moderate-to-substantial agreement in the cross-accuracy analysis: KI=0.57 (BAI and GAD-7), KI=0.49 (BAI and GAD-2), KI=0.5 (BAI and GAD-SI), KI=0.62 (BDI-II and NDDIE), and KI=0.43 (BDI-II and NDDIE-2).

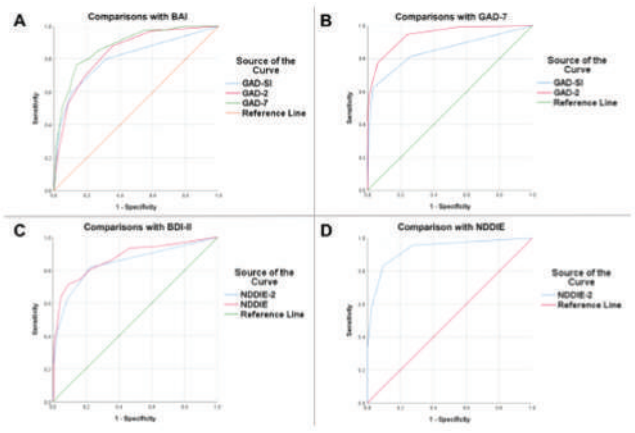

FIGURE 1 The ROC curve analysis showed high AUC in the comparisons between traditional, brief, and ultra-brief anxiety and depression inventories in people with epilepsy.

Conclusion: The shorter anxiety/depression inventories may be a fast and reliable alternative to traditional tests for PWE.
Disclosure: Nothing to disclose.

EPO-119 | A clinical case of targeted memantine treatment in a patient with GRIN2A mutation and epileptic encephalopathy

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Background and Aims: Epileptic encephalopathy with continuous spike and wave during sleep (CSWS) is a syndrome marked by progressive cognitive decline, epileptic seizures, specific EEG patterns, and a complex/polygenic inheritance. Given the elevated incidence of drug resistance, the development of more effective and targeted treatment approaches for patients is relevant.
Methods: In our study, we intentionally selected 88 patients diagnosed with epileptic encephalopathy with continuous spike and wave during sleep. All participants were tested with: neuropsychological, clinical, neurophysiological, neuroimaging, and genetic assessments, including whole exome sequencing (WES). Among these individuals, we identified one with a GRIN2A mutation showing a gain of function variant (GoF), for further targeted treatment with memantine with daily dose 0.5 mg/kg per day."
Results: At a memantine dosage of 0.5 mg/kg, with no adjustments to antiepileptic drug doses, we observed a notable 65% reduction in average seizure frequency. This decline manifested within several weeks of reaching the full memantine dose and persisted throughout the 3-month follow-up period. We also observed an improvement in interictal EEG recordings, with no epileptiform discharges during both wakefulness and sleep, contrasting with the EEG prior to memantine initiation. While there were slight changes in cognitive skills, overall improvement was noted.
Conclusion: This clinical case exemplifies the significant potential of targeted treatment for epilepsy. Further clinical research and continuous follow-up are necessary to gather additional insights and information.
Disclosure: Nothing to disclose.

EPO-120 | Calponin-3 in astrocytes accelerate astrocytic activation and adenosine metabolism affects epileptogenesis

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Background and Aims: Calponin-3—a member of the calponin family of actin-binding proteins, which is highly expressed in the mammalian brain—has been found increased in temporal lobe epilepsy (TLE)

patients and pilocarpine-induced epileptic rats. However, its role in the epileptogenesis is unclear.

Methods: Serum and brain tissues of epileptic patients and Kainic acid (KA) and pentattrazene (PTZ) induced epilepsy mouse model were used to detect the expression level and cellular localization of calponin-3. calponin-3 in the hippocampus of C57BL/6 mice was up-regulated, and calponin-3 in hippocampus of KA-induced epilepsy mice was down-regulated. The effect of calponin-3 expression change on the occurrence and development of epilepsy was observed in mice with specific knockout of calponin-3 in astrocytes.

Results: In epilepsy patients and KA-induced epilepsy models, calponin-3 was significantly up-regulated in serum and brain tissue. Meanwhile, the up-regulated calponin-3 expression was mainly in astrocytes. Behavioral and EEG findings showed that upregulation of calponin-3 increased the susceptibility to epilepsy, while down-regulation of calponin-3 in KA-induced mouse models had a protective effect on spontaneous seizures. Finally, it was found that the susceptibility to epilepsy was significantly reduced in transgenic GFAP-CNN3-KO mice. Mechanism, in vitro and in vivo confirmed that down-regulation of calponin-3 in astrocytes can suppress astrocyte activation and reduce adenosine metabolism.

Conclusion: Targeting calponin-3 in astrocytes, and reducing its expression will have a protective effect on epilepsy by regulating astrocyte activation and adenosine metabolism

Disclosure: Nothing to disclose.

Headache 1

EPO-121 | Plasma calcitonin gene-related peptide levels in idiopathic intracranial hypertension: An exploratory study

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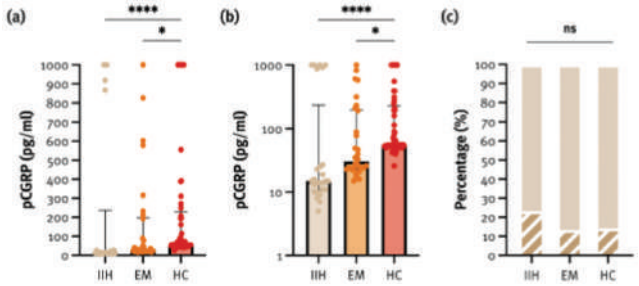
Background and Aims: Idiopathic intracranial hypertension (IIH) is a condition characterized by increased intracranial pressure often presenting with migraine-like headache. Calcitonin gene-related peptide (CGRP) plays an important pathophysiological role in primary headaches, whilst its role in IIH has not been established.

Methods: This longitudinal exploratory study included patients with definite IIH, episodic migraine (EM) in a headache-free interval and healthy controls (HC). Subjects were divided into those with: (1) log pCGRP Z scores ≤1.5 (termed as 'non-elevated'), and (2) log pCGRP Z scores >1.5 (termed as 'elevated').

Results: A total of 26 patients with IIH (mean age 33.2 years [SD 9.2], 88.5% female), 30 patients with EM (mean age 27.6 years [7.5], 66.7% female) and 57 HC (mean age 25.3 years [5.2], 56.1% female) were included. Median pCGRP levels in patients with IIH, EM and HC were 15 pg/ml (10.8–237), 30.5 pg/ml (23.2–197.4), and 56.3 pg/ml (53.4–228.2), respectively ($p < 0.001$). We found no differences between the prevalence of elevated pCGRP levels in patients with IIH, EM and HC (6 [23.1%], 4 [13.3%] and 8 [14.0%], respectively, $p = 0.523$). PwIIH with elevated pCGRP levels had more often a history of migraine (5/6 [83.3%] vs. 3/20 [15.0%], $p = 0.004$) and photo- and/or phonophobia as concomitant symptoms (6/6 [100.0%] vs. 7/20 [35.0%], $p = 0.015$). Elevated pCGRP levels were not associated with ophthalmological parameters.



pCGRP levels (pg/ml) in patients with IIH, EM in a headache-free interval, and HC; linear (a) and logarithmic (b) scale. Proportion of subjects with elevated pCGRP levels (log pCGRP Z score >1.5) in pwIIH, EM and HC (c).

Conclusion: PwIIH display similar prevalence of elevated pCGRP levels as pwEM. As elevated pCGRP levels are associated with headache presence and frequency, CGRP may play a role in the pathophysiology of headache in IIH.

Disclosure: Nothing to disclose.

EPO-122 | Brain resting state networks in episodic cluster headache: Cerebral connectivity analysis with HD-EEG

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Background and Aims: A convincing explanation for the switch between the active and remission phases of episodic cluster headache (eCH) is lacking. In this study, we aim to shed some light on these mechanisms by analyzing internodal connectivity patterns in the brains of eCH patients by means of high-density electroencephalography (HD-EEG).

Methods: Twenty-four eCH patients underwent HD-EEG recordings in two conditions: active phase (T0) and remission period (T1).

Nineteen sex and age matched controls underwent a single HD-EEG evaluation. Through these data we reconstructed the inter-networks and intra-network connectivity of six resting state networks: default mode network (DMN), dorsal attention network (DAN), ventral attention network (VAN), language attention network (LAN), somatomotor network (SMN), visual network (VN).

Results: At T1 there was a significant difference in alpha band connectivity between eCH patients and HCs in the intra-network connectivity of the DMN (eCH = 0.089 ± 0.007; HC = 0.115 ± 0.009; mean difference 0.026 ± 0.012; $p = 0.034$) and of the VN (eCH = 0.085 ± 0.007; HC = 0.109 ± 0.008: mean difference 0.025 ± 0.011; $p = 0.034$). Moreover, eCH patients and HCs showed a significant difference at T1 in alpha band inter-network connectivity between the DMN and the VN (eCH = 0.089 ± 0.007; HC = 0.114 ± 0.008; mean difference 0.025 ± 0.012; $p = 0.038$).

Conclusion: Our findings show how eCH patients have a reduced alpha band connectivity during the remission period within and between the DMN and the VN networks. These alterations may be associated to the shift between the two states of the disease and support the relevance of electrophysiological studies in providing insights into cluster headache physiopathology.

Disclosure: None.

EPO-123 | Evaluation of premonitory symptoms among patients with cluster headache

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Background and Aims: Cluster headache (CH) is a rare primary headache known for its unilateral very severe pain accompanied by cranial autonomic symptoms, which has a strong impact in patients' quality of life. Several studies have identified premonitory symptoms of migraine while few studies have evaluated the frequency and type of premonitory symptoms in patients with CH. This study aimed to assess the presence and type of premonitory symptoms in patients with CH.

Methods: A retrospective study was conducted to investigate the presence and type of premonitory symptoms in a cohort of patients with CH attended at a Headache Unit of a tertiary hospital specialized in CH treatment. Demographic data and premonitory symptoms in CH patients were evaluated as part of a service evaluation. The primary endpoint was the presence of premonitory symptoms in patients with CH. Secondary endpoints involved the description of the type of premonitory symptoms.

Results: A total of 164 patients, 121/165 (74%) males, 45.9 (SD: 13.8) years old, 66/164 (40%) chronic, from clinical CH cohort. Premonitory symptoms were present in 139/164 (85%) of CH patients. The most common general premonitory symptoms in CH patients were mood changes (44%), cognitive impairment (28%), neck stiffness (23%), fatigue (22%) and yawning (17%).

Conclusion: In summary, this study underscores the presence of recognisable spontaneous premonitory symptoms in CH that may have an impact in management of CH. Understanding the CH premonitory symptoms can aid in the development of more tailored treatment strategies for these patients.

Disclosure: AGM reports, over the last 36 months, speaker honoraria from TEVA and Altermedica, and reports no disclosures related with this work. PJG reports, over the last 36 months, grants from Celgene and Kallyope, and personal fees from Aeon Biopharma, Abbvie, Amgen, eNeura, CoolTech LLC, Dr Reddys, Eli-Lilly and Company, Epalex, Linpharma, Lundbeck, Man&Science, Novartis, Pfizer, Sanofi, Satsuma, Shiratronics, and Teva Pharmaceuticals, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer. DW, NK and HG report nothing to disclose.

EPO-124 | Neurophysiological and neuropsychological correlates of migraine with aura

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Background and Aims: Migraine with aura afflicts about 5% of the population and is frequently associated with psychological disturbances like depression and anxiety. Few studies in the literature have analyzed the functional connectivity of patients with this comparing it with that of healthy subjects. This study aims to fill this gap in the literature by comparing neurophysiological correlates of functional connectivity at resting state-EEG (rs-EEG) of subjects with migraine with aura and controls.

Methods: Migraine with aura subjects and controls were enrolled in a 1:1 ratio. The inclusion criteria were age between 18 and 50 and absence of other neurological, psychiatric, or system disorders in both groups of subjects. A 20-minute inter-ictal rsEEG was performed after subjecting them to a neuropsychological assessment including BAI and BDI II. Then EEG functional connectivity was evaluated by using coherence analysis.

Results: Comparisons in the beta frequency band showed hyperconnectivity in the right central-parietal regions in migraineurs. Furthermore, hyperconnectivity was found in the alpha band in the right occipital and parietal areas.

Conclusion: Migraineurs present a different resting state connectivity pattern in brain regions correlated with pain perception and elaboration (pain matrix), even in the inter-ictal phase. Our results

indicate that migraineurs share a neurophysiological "fingerprint" with other conditions associated with chronic or relapsing-remitting pain (e.g., fibromyalgia).

Disclosure: Nothing to disclose.

EPO-125 | Contemporary prospective understanding of migraine real-world evidence (CAPTURE): Baseline clinical characteristics

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Background and Aims: CAPTURE is a 2-year, international, prospective, longitudinal study that aims to enhance our understanding of disease burden and treatment patterns among people living with migraine, stratified by headache frequency.

Methods: Adults with >=1-year migraine diagnosis aged <50 years at onset who were taking >=1 medication indicated for migraine and had >=4 monthly headache days (MHDs) in the 3 months before screening were assigned to cohorts based on MHD frequency (cohort 1: 4-<8; cohort 2: 8-<15; cohort 3: >=15; Figure). Descriptive data for baseline demographics and clinical characteristics (migraine duration, MHDs, monthly migraine days [MMDs], monthly acute medication use days, migraine-related comorbidities) are presented. Changes from baseline in MHDs, MMDs, acute medication use days, and patient-reported outcomes across the study period and durations of current and subsequent migraine treatment use will be assessed.

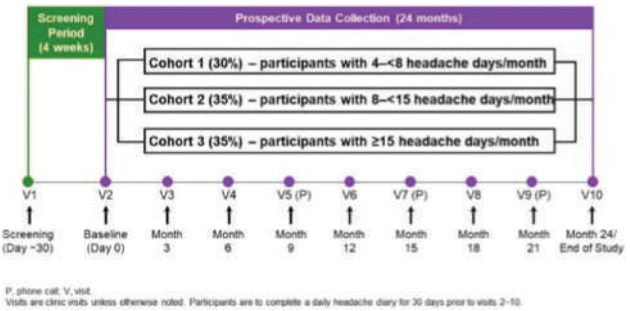

FIGURE CAPTURE Study Design

Results: As of December 2023, among the 239 participants (cohort 1: *n*=68; cohort 2: *n*=104; cohort 3: *n*=67), mean age was 40.8–42.6 years, >95% of participants were White, >78% were female, and >77% resided in Europe (Table 1). Mean duration of migraine since onset was similar among cohorts (23.0–23.8 years) (Table 2). Past use of preventive treatments was high (cohort 1, 81.8%; cohort 2, 81.4%; cohort 3, 92.3%). The most prevalent migraine-related comorbidity was hypertension (cohort 1: 4.4%; cohort 2: 7.7%; cohort 3: 9.0%).

TABLE 1 Baseline Demographic Characteristics

Characteristic	Cohort 1: 4 to <8 MHDs (n=68)	Cohort 2: 8 to <15 MHDs (n=104)	Cohort 3: ≥15 MHDs (n=67)
Age, mean (SD), y	42.3 (12.5)	42.6 (12.7)	40.8 (12.4)
Sex, n (%)[a]			
Female	52 (77.6)	87 (86.1)	57 (91.9)
Male	15 (22.4)	14 (13.9)	5 (8.1)
Missing	1	3	5
Race, n (%)[a]			
White	64 (95.5)	102 (100.0)	62 (96.9)
Black or African American	1 (1.5)	0	0
Asian	2 (3.0)	0	0
American Indian or Alaska Native	0	0	2 (3.1)
Missing	1	2	3
Region, n (%)[a]			
North America	15 (22.1)	23 (22.1)	14 (20.9)
Europe	53 (77.9)	80 (76.9)	53 (79.1)
South America	0	1 (1.0)	0

MHDs, monthly headache days; SD, standard deviation.
[a]Percentages calculated using nonmissing values.

TABLE 2 Baseline Migraine Disease Characteristics

Characteristic	Cohort 1: 4 to <8 MHDs (n=68)	Cohort 2: 8 to <15 MHDs (n=104)	Cohort 3: ≥15 MHDs (n=67)
MHDs, mean (SD)	6.1 (1.1)	10.7 (1.9)	20.5 (5.0)
MMDs, mean (SD)	4.4 (1.8)	7.6 (3.0)	15.6 (6.5)
Monthly acute medication use days, mean (SD)	5.3 (1.8)	8.9 (2.6)	13.6 (6.4)
Migraine disease duration, mean (SD), y	23.2 (14.0)	23.0 (13.7)	23.8 (12.6)
Past preventive migraine treatment use, n (%)	54 (81.8)	83 (81.4)	60 (92.3)
Migraine-related comorbidities, n (%)			
Hypertension	3 (4.4)	8 (7.7)	6 (9.0)
Asthma	2 (2.9)	8 (7.7)	4 (6.0)
Depression	2 (2.9)	5 (4.8)	2 (3.0)
Insomnia	3 (4.4)	3 (2.9)	1 (1.5)
Fibromyalgia	1 (1.5)	2 (1.9)	2 (3.0)
Obesity	1 (1.5)	0	2 (3.0)
Irritable bowel syndrome	1 (1.5)	0	1 (1.5)
Diabetes mellitus	1 (1.5)	0	1 (1.5)
Myocardial infarction	1 (1.5)	0	0
Neck pain	0	0	1 (1.5)

MHDs, monthly headache days; MMDs, monthly migraine days; SD, standard deviation.

Conclusion: CAPTURE aims to provide pivotal data on the longitudinal course of migraine and associated treatment patterns, stratified by headache frequency. This study promises to provide insights for developing tailored treatment approaches for people with migraine.

Disclosure: This study was supported by AbbVie.

EPO-126 | Female sexual dysfunction and distress in migraine: Results from a tertiary referral hospital

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Background and Aims: Female sexual dysfunction (FSD) is a persistent, underdiagnosed, and undertreated problem, associated with psychological suffering. Only a few studies have addressed the sexual distress caused by migraine. We aimed to determine if migraine is associated with sexual dysfunction/distress and what their risk factors.
Methods: Retrospective, cross-sectional study, including 71 premenopausal female patients with migraine, followed in a tertiary hospital (05/2023–12/2023), and 34 healthy age-matched-controls. Female sexual function index-6 (FSFI-6), FS distress scale-revised (FSDS-R), Hospital depression and anxiety (HADS), Migraine disability assessment (MIDAS), and Satisfaction Alertness Timing Efficiency Duration of sleep (SATED) scales were applied.
Results: Of the 71 female patients [median age: 40.0 (AQR = 11.00) years; married/stable relationship: 78.9%], only 9 (12.7%) were not under migraine preventive treatment; most (33, 62.3%) reported severe disability (MIDAS-IV). Migraine patients showed lower FSFI-6 scores [19.0 (9.0) vs controls with 24.0 (6.0), $p = 0.003$), with significantly lower levels of desire ($p = 0.011$), lubrification ($p = 0.002$), and satisfaction ($p = 0.013$), and higher sexual distress [11.2 (25.6) vs 3.2 (9.6), $p = 0.001$). They had also higher anxiety [10.0 (6.0) vs 5.0 (6.0), $p \leq 0.001$] and depression [7.0 (7.0) vs. 2.0 (3.0), $p \leq 0.001$] levels, and lower sleep health scores [18.0 (12.0) vs 23.5 (9.0), $p = 0.005$] compared to healthy controls. Anxiety, depression, and dysfunctional sleep were found to be significantly related to sexual dysfunction.
Conclusion: This work showed that migraine is associated with sexual dysfunction and distress, reflecting the necessity of an evaluation of sexual health in these patients, mainly in the ones with higher levels of anxiety, depression, or poor quality of sleep.
Disclosure: Nothing to disclose.

EPO-127 | Role of venous sinus stenosis in intracranial hypertension: Pathophysiology and response to medical treatment

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Background and Aims: Venous sinus stenosis (VSS) is described in intracranial hypertension (IH), but its role in its pathophysiology is not entirely established. We aimed to characterize VSS in intracranial hypertension and its possible influence in cerebrospinal fluid (CSF) opening pressure and clinical response to medical therapy.
Methods: We analyzed 21 patients admitted to the Neurology Ward of Hospital de São José in Lisbon, Portugal, between 2016 and 2023 with intracranial hypertension (19 with idiopathic IH). Using SPSS, we carried out a descriptive analysis of the variables and applied the Chi-squared, Shapiro-Wilk, Mann-Whitney, and Student's t tests.
Results: We identified VSS in 19% of the patients ($n = 4$), half in the transverse sinus and half in the transverse-sigmoid transition. The median CSF opening pressure was 32.67(9.5)cm H_2O and it was lower in the VSS group, suggesting a negative impact of the stenosis on this measure ($p = 0.017$). We found a correlation between the presence of VSS and poor clinical response to medical therapy ($p = 0.018$). There were no statistically significant differences in the CSF opening pressure or response to medical therapy between the group with transverse sinus stenosis and the group with transverse-sigmoid transition stenosis.
Conclusion: The presence of VSS seems to correlate with a less favorable clinical response to medical therapy in IH. We couldn't establish a correlation between VSS and the pathophysiology of IH. The role of VSS should be further explored to clarify its pathophysiology and the therapeutic potential of venous sinus stenting.
Disclosure: Nothing to disclose.

EPO-128 | Contemporary prospective understanding of migraine real-world evidence (CAPTURE): Baseline migraine treatment patterns

C. Tassorelli[1]; M. Matharu[2]; J. Ailani[3]; M. Lanteri-Minet[4]; E. Tucker[5]; J. Lam[5]; Y. Liu[6]; H. Ha[5]; L. Delahaye[7]; P. Pozo-Rosich[8]
[1]*University of Pavia and C. Mondino Foundation, Pavia, Italy;* [2]*Queen Square Institute of Neurology, London, England, UK;* [3]*MedStar, Georgetown University Hospital, Washington, DC, USA;* [4]*Pain Department and FHU InovPain, CHU Nice and Côte Azur University, Nice, France and INSERM U1107 Migraine and Trigeminal Pain, Auvergne University, Clermont-Ferrand, France;* [5]*AbbVie, Toronto, ON, Canada;* [6]*AbbVie, North Chicago, IL, USA;* [7]*AbbVie, Rungis, France;* [8]*Headache Unit, Neurology Department, Vall d'Hebron University Hospital and Headache and Neurological Pain Research Group, Vall d'Hebron Institute of Research, Universitat Autònoma de Barcelona, Barcelona, Spain*

Background and Aims: CAPTURE is a 2-year, international, prospective, longitudinal study that aims to elevate understanding of burden of illness, disease course, and treatment patterns among people living with migraine, stratified by headache frequency.
Methods: Adults with migraine diagnosed for >=1 year, aged <50 years at onset, and taking >=1 medication indicated for migraine with >=4 monthly headache days (MHDs) in the 3 months before screening were assigned to cohorts based on MHD frequency (cohort 1: 4-<8; cohort 2: 8-<15; cohort 3: >=15; Figure). Descriptive data for baseline characteristics, including current/prior migraine medications, are presented. Endpoints include change from baseline in MHDs, monthly migraine days, monthly acute medication

use days, and patient-reported outcomes across the study period. Durations of current and subsequent migraine treatment use and migraine-related healthcare resource utilisation will also be assessed.

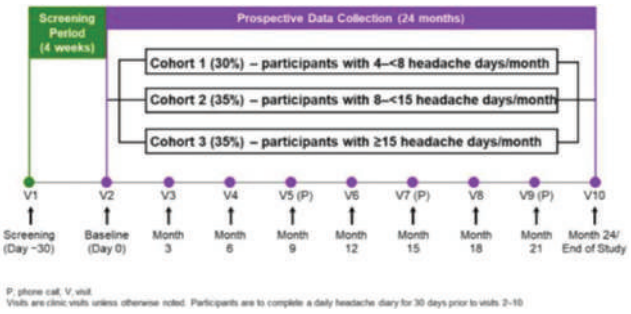

FIGURE CAPTURE Study Design

Results: This analysis set (December 2023) included 239 participants (cohort 1: $n = 68$; cohort 2: $n = 104$; cohort 3: $n = 67$; mean age 40.8–42.6 years); more than 78% were female (Table 1). In cohorts 1, 2, and 3, current use of acute migraine medication only was reported for 5.9%, 2.9%, and 0% of participants; preventive medication only for 19.1%, 27.9%, and 32.8%; and both acute and preventive medication for 27.9%, 20.2%, and 26.9%, respectively (Table 2). Most common current acute medications were triptans and propionic acid derivatives; most common current preventive medications were topiramate, amitriptyline and calcitonin gene–related peptide receptor monoclonal antibodies.

TABLE 1 Baseline Demographic Characteristics

Characteristic	Cohort 1: 4 to <8 MHDs (n=68)	Cohort 2: 8 to <15 MHDs (n=104)	Cohort 3: ≥15 MHDs (n=67)
Age, mean (SD), y	42.3 (12.5)	42.6 (12.7)	40.8 (12.4)
Sex, n (%)[a]			
Female	52 (77.6)	87 (86.1)	57 (91.9)
Male	15 (22.4)	14 (13.9)	5 (8.1)
Missing	1	3	5
Race, n (%)[a]			
White	64 (95.5)	102 (100.0)	62 (96.9)
Black or African American	1 (1.5)	0	0
Asian	2 (3.0)	0	0
American Indian or Alaska Native	0	0	2 (3.1)
Missing	1	2	3
Region, n (%)[a]			
North America	15 (22.1)	23 (22.1)	14 (20.9)
Europe	53 (77.9)	80 (76.9)	53 (79.1)
South America	0	1 (1.0)	0

MHDs, monthly headache days; SD, standard deviation.
[a]Percentages calculated using nonmissing values.

TABLE 2 Baseline Medication Use

Characteristic, n (%)	Cohort 1: 4 to <8 MHDs (n=68)	Cohort 2: 8 to <15 MHDs (n=104)	Cohort 3: ≥15 MHDs (n=67)
Prior migraine medications, ≥10%[a]			
Prior acute medications			
Triptans	33 (48.5)	45 (43.3)	27 (40.3)
Propionic acid derivatives[b]	22 (32.4)	24 (23.1)	14 (20.9)
Paracetamol/Paracetamol combinations[c]	7 (10.3)	7 (6.7)	8 (11.9)
Prior preventive medications			
Topiramate	22 (32.4)	30 (28.8)	18 (26.9)
CGRP receptor antagonists/mAbs[d]	18 (26.5)	22 (21.2)	18 (26.9)
Amitriptyline	15 (22.1)	23 (22.1)	16 (23.9)
Flunarizine	10 (14.7)	15 (14.4)	4 (6.0)
Propranolol	10 (14.7)	10 (9.6)	11 (16.4)
OnabotulinumtoxinA	10 (14.7)	19 (18.3)	19 (28.4)
Current migraine medications, ≥10%[e]			
Acute only	4 (5.9)	3 (2.9)	0
Preventive only	13 (19.1)	29 (27.9)	22 (32.8)
Acute and preventive	19 (27.9)	21 (20.2)	18 (26.9)
Current acute medications			
Triptans	20 (29.4)	28 (26.9)	23 (34.3)
Propionic acid derivatives[b]	14 (20.6)	8 (7.7)	11 (16.4)
Current preventive medications			
Topiramate	18 (26.5)	22 (21.2)	16 (23.9)
Amitriptyline/Amitriptyline combination[f]	15 (22.1)	24 (23.1)	14 (20.9)
CGRP mAbs[d]	15 (22.1)	16 (15.4)	20 (29.9)
Beta blockers[g]	9 (13.2)	10 (9.6)	5 (7.5)
Flunarizine	9 (13.2)	10 (9.6)	2 (3.0)
OnabotulinumtoxinA	8 (11.8)	15 (14.4)	13 (19.4)

CGRP, calcitonin gene–related peptide; mAb, monoclonal antibody; MHDs, monthly headache days.
[a]Defined as any medication taken prior to the date of the baseline visit. Participants are counted once in each row regardless of the number of medications they may have taken. Medications that are potentially migraine-related and were taken by >=10% of participants are shown.
[b]Dexketoprofen, ibuprofen, ketoprofen, and naproxen.
[c]Paracetamol (±caffeine) and acetylsalicylic acid (+caffeine/paracetamol).
[d]mAbs: Eptinezumab, erenumab, fremanezumab, or galcanezumab; CGRP receptor antagonists: atogepant, rimegepant, or ubrogepant.
[e]Medication indicated for migraine at the time of consent. Participants are counted once in each row regardless of the number of medications they may have taken.
[f]Amitriptyline ±chlordiazepoxide or ±perphenazine.
[g]Tenolol, bisoprolol, metoprolol, and propranolol.

Conclusion: The CAPTURE study will build a large, longitudinal database on migraine treatment patterns in the contemporary era and associated disease trajectories.

Disclosure: This study was supported by AbbVie.

EPO-129 | **Prophylactic polytherapy for chronic migraine: Evaluating the addition of atogepant to onabotulinumtoxinA**

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Background and Aims: OnabotulinumA (BotoxA) may reduce migraine burden only partially in patients with chronic migraine (CM). We sought to determine whether adding atogepant 60 mg daily to ongoing treatment with BotoxA might be synergistic.

Methods: We prescribed atogepant 60 mg daily to a clinic population of CM patients who had been receiving BotoxA for at least one year and whose response had remained stable for the last 2

consecutive 12-week intervals between treatments. We assessed mean monthly migraine days (MMMDs), mean monthly headache days (MMHDs), mean monthly days of functionally incapacitating headache (FIHDs), mean monthly days of symptomatic medication use (MMDSMU), migraine burden index (MBI) and MIDAS scores for the 3 months preceding initiation of treatment with atogepant and again 12 weeks following initiation of treatment with atogepant. A patient was considered to be a positive responder to polytherapy if he/she reported a 50% or greater reduction in MMMDs relative to their pre-atogepant status (primary endpoint).

Results: Of 211 patients, 132 (63%) achieved the primary treatment endpoint of a 50% or greater reduction in MMMDs experienced over the 12 week treatment period relative to their pre-atogepant status. MMHDs declined by 6.6 days, mean FIHDs by 2.7 days, MMDSMU by 5.4 days, MIDAS by 21.6 and MBI score by 14.6.

Conclusion: Adding atogepant 60 mg to the prophylactic regimen of CM patients receiving BotoxA resulted in apparent synergism in almost two-thirds.

Disclosure: Dr. Rothrock has served as an consultant to/promotional speaker for AbbVie. His parent institution has received funding from AbbVie for research he has conducted.

EPO-130 | Management of migraine without aura in adolescents: The efficacy of flunarizine in a Turkish Cohort

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Background and Aims: Flunarizine is a specific calcium antagonist and is frequently used in adults for the prophylactic treatment of migraine. The use of flunarizine may lead to somnolence and weight gain, depression, and rarely extrapyramidal symptoms in adults. However, studies detecting the efficacy and safety of flunarizine use in adolescents are limited. In the current study, the effectiveness of flunarizine for the management of chronic migraine without aura in Turkish adolescents was evaluated.

Methods: Forty-six patients with migraine without aura, aged 12–18 years, receiving flunarizine 5mg per day were included. In this retrospective study, the medical records of the cases were examined. Changes in the Numeric Pain Rating Scale (NPRS) and MIDAS scores were compared to assess the efficacy of the treatment in 3 months.

Results: The mean age was 14.37 ± 1.83 years. There was a significant improvement in the NPRS and MIDAS scores of the patients at the end of 3 months ($p < 0.05$). Side effects were detected in 23.9% of the patients, and these symptoms were sedation in 8.7% of the patients, mood swings in 4.3%, and vomiting %4.3 of them. None of the patients discontinued the treatment due to side effects.

Conclusion: Although the advancement of migraine research and treatment is inevitable, our findings support that flunarizine should still be considered in mind as an effective and tolerable treatment option in adolescent migraineurs

Disclosure: Nothing to disclose.

EPO-131 | Acute medication overuse in people with migraine from the 2022 European National Health & Wellness Survey

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Background and Aims: Acute medication overuse (AMO) is a cycle of high-frequency analgesic use, such as triptans and non-steroidal anti-inflammatory drugs (NSAIDs) that may result in medication overuse headache (MOH). There is limited understanding of the frequency of analgesic use of both prescription and over-the-counter analgesics among people with migraine (PwM) in Europe.

Methods: Using the 2022 5-country European National Health and Wellness Survey (NHWS, Cerner Enviza), patients diagnosed with migraine receiving $>=1$ acute medication were described. AMO criteria were: 1) $>=10$ cumulative days per month with use of triptans, combination analgesics, ergotamines, or opioids; or 2) $>=15$ days of nonopioid analgesic, acetaminophen, or NSAID use. AMO was assessed separately among analgesics for migraine only and those used for migraine plus other pain conditions.

Results: Among over 16.7 million PwM represented by the survey, 21.2% reported AMO of migraine-specific medications, and 36.9% had AMO after including medications used for other conditions. Over half (51.4%) met the first AMO criterion with a cumulative mean [SD] of 21.0 [14.1] days, and 61.5% met the second criterion with 28.3 [15.9] cumulative days. PwM with AMO versus without AMO reported higher use of prescribed triptans (38.4% vs. 29.9%), NSAIDs (66.4% vs. 51.4%), and opioids (33.6% vs. 12.5%). Compared to individuals without AMO, those with AMO experienced worse quality of life, higher migraine disability scores, decreased productivity, and increased use of healthcare resources.

Characteristics	AMO 3,554 (21.2%)		w/o AMO 13,220 (78.8%)	
	N	%	N	%
AMO criterion 1: ≥ 10 days/month for ergot derivatives, triptans, opioids, combination analgesics	1828	51.4%	-	-
Total days of MO criterion 1 analgesic use (mean)	21.0	14.1	-	-
AMO criterion 2: ≥ 15 days/month for nonopioid analgesics, acetaminophen, and NSAIDs	2185	61.5%	-	-
Total days of MO criterion 2 analgesic use (mean)	28.3	15.9	-	-
Use of Rx acute agents	3114	98.9%	7400	81.0%
Rx acute agent type				
Triptans	1208	38.4%	2732	29.9%
NSAIDs	2089	66.4%	4697	51.4%
Opioids	1058	33.6%	1144	12.5%
Ergotamines	110	3.5%	181	2.0%
Gepant (acute treatment)	21	0.7%	12	0.1%
Combination analgesics	48	1.5%	102	1.1%
Other	39	1.3%	86	1.0%
Use of OTC acute agents	1330	72.2%	4777	63.6%
OTC acute agent type				
Triptans	73	3.95%	264	3.5%
NSAIDs	773	41.9%	2903	38.6%
Acetaminophen	622	33.8%	1776	23.6%
Acetaminophen/opioid combination analgesics	117	6.4%	310	4.1%
Combination analgesics	171	9.3%	474	6.3%
Other	55	3.0%	42	0.6%
Quality of life, productivity, and healthcare resource utilization				
Mean Mental health composite T score	33.1	10.9	36.4	10.6
Mean Physical health composite T score	36.3	10.8	40.4	10.2
Global health composite T score	32.4	11.3	36.5	10.8
Work productivity loss among employed	47.6	29.6	40.5	31.1
Visited ER in past six months	1243	35.0%	3187	24.1%
Hospitalized in past six months	731	20.6%	1816	13.7%

Characteristics of patients with and without AMO of migraine medications

Conclusion: AMO is common in over 20% of PwM and related to poorer quality of life. Treatments not associated with MOH are needed in this population.

Disclosure: GC has received honoraria for participation in clinical trials and contribution to advisory boards or presentations from TEVA, Biohaven, Eli Lilly, Abbvie, and Pfizer. He serves as an Associate Editor for Cephalalgia, BMC Neurology – Pain section, Frontiers in Neurology – Neurotechnology section, Frontiers in Human Neuroscience – Brain Imaging and Stimulation section, and on the Advisory Board of The Journal of Headache and Pain. AG reports financial support for ad boards, consulting and speaker honoraria from: Grünenthal, Mundipharma, Abbvie/Allergan, Lilly, Teva, Amgen, Novartis, Hormosan, Stada, Lundbeck, Pfizer, Hexal, Esanumperfood, Medscape, streamed up, Ärztekammer Nordrhein, Ärztekammer Westfalen Lippe, DGS, Regionalbeauftragte der DMKG. ML, AJ, JC, KHB, JY, LA, and JB are employees of Pfizer.

EPO-132 | Combining monoclonal antibodies and onabotulinumtoxina against highly resistant and invalidated migraine patients

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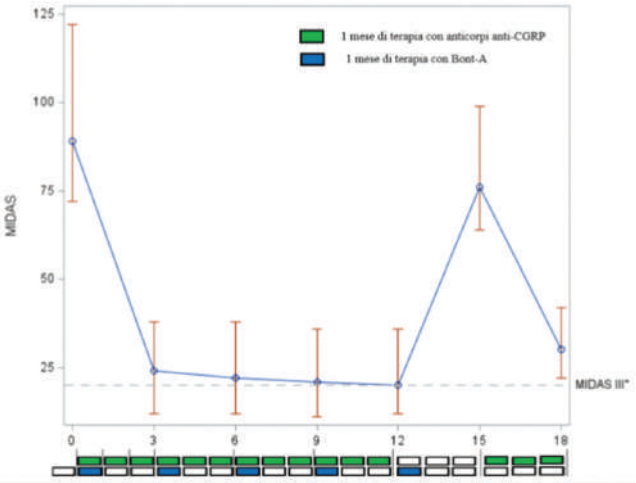
Background and Aims: Onabotulinumtoxin A (BonTA) and monoclonal antibodies (mAbs) are approved migraine treatment targeting CGRP cascade. However, monotherapy does not always yield satisfactory benefits, which raises the question of whether dual therapy with BonTA and mAbs hold promise in patients with treatment-resistant chronic migraine (CM).

Methods: We retrospectively analyzed 75 subjects diagnosed with highly disabling (MIDAS >30) and resistant CM treated with BonTA that were considered responders, but had a decrease in effect or the effect was non-sufficient after one year. Therefore, they started a dual therapy with BonTA and mAbs for 1 year. CGRP-mAbs were stopped for 3 months continuing only BonTA, subsequently a monotherapy with CGRP-mAbs was performed for 3 months. We evaluated the MIDAS, HIT6, VAS, PGIC and drug intake for all patients in the different timepoints.

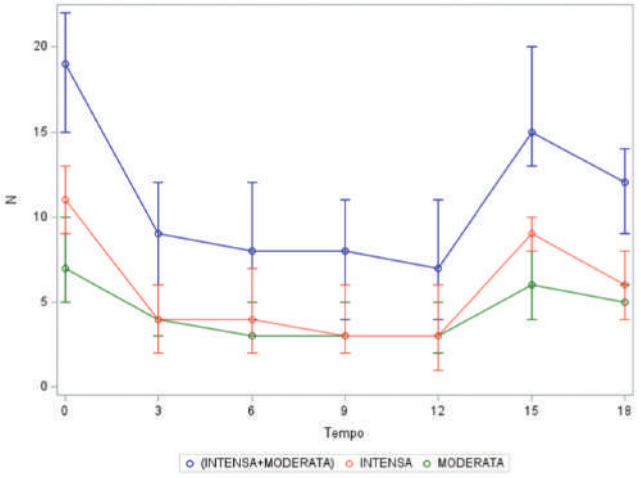
Results: 73/75 patients completed the treatment regimen, 2 dropped out for ineffectiveness. No adverse events were reported. Analysis showed a marked decrease in the MIDAS, HIT6, VAS, PGIC scores and analgesic drug intake from visit T0 to visit T3, while on dual therapy; subsequently the scores remained stable up to T12. When patients were on BonTA alone or mAbs alone, there was a worsening of evaluated scores.



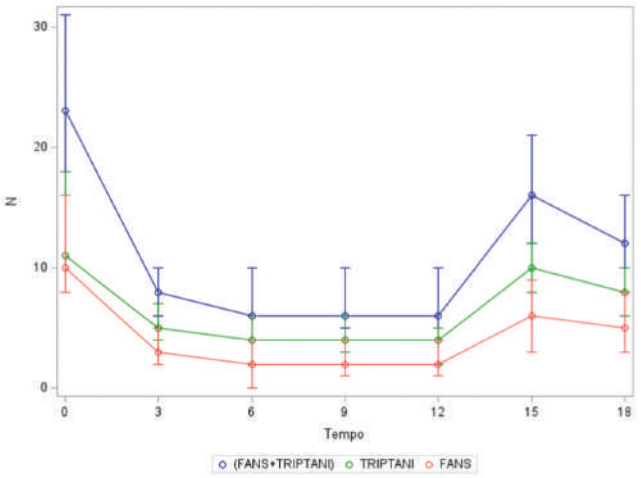
MIDAS reduction during different times of therapies. In green antiCGRP mAbs, in blue BonTA injections

Conclusion: Our work suggests a possible synergistic effect of these two different therapies in modulating CGRP cascade, determining a greater control of migraine attacks in a population of patients suffering from highly resistant CM. This result without any increase of side effects.

Disclosure: Eleonora Colombo, Daniela Ungaro, Martina Sodano, Gianluca Demirtzidis and Stefano Messina report no disclosure. Alberto Doretti received compensation for consulting services from Abbvie, Teva, Eli Lilly, Lundbeck, Novartis, Neopharmed Gentili, Zambon. Vincenzo Silani received compensation for consulting services and/or speaking activities from AveXis, Cytokinetics, Italfarmaco, LiquidWeb, Srl and Novartis Pharma AG. He receives or



Numbers of days with headache during different times of therapies. Blue line VAS intense+ moderate, in red Intense in green moderate



Numbers of drugs taken during different times of therapies. In blue NSAID+triptans, in green triptans, in red NSAID

he has received research support from the Italian Ministry of Health, AriSla, and E-Rare Joint Translational Call. He is on the Editorial Board of Amyotrophic Lateral Sclerosis and Frontotemproal Degeneration, European Neurology, American Journal of Neurodegenerative Disease and Frontiers in Neurology. Nicola Ticozzi received compensation for consulting services from Italfarmaco, Biogen, Amylyx Pharmaceutical and Zambon Biotech SA. He received research funding from the Italian Ministry of Health and AriSLA. He is associate editor of Frontiers in Aging Neuroscience.

EPO-133 | Slow responders instead of late responders: Assessing the time to response to anti-CGRP/R monoclonal antibodies

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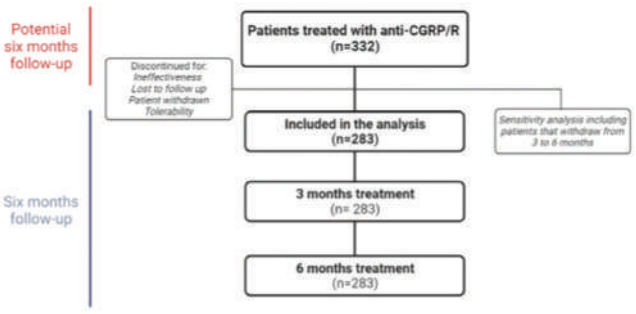
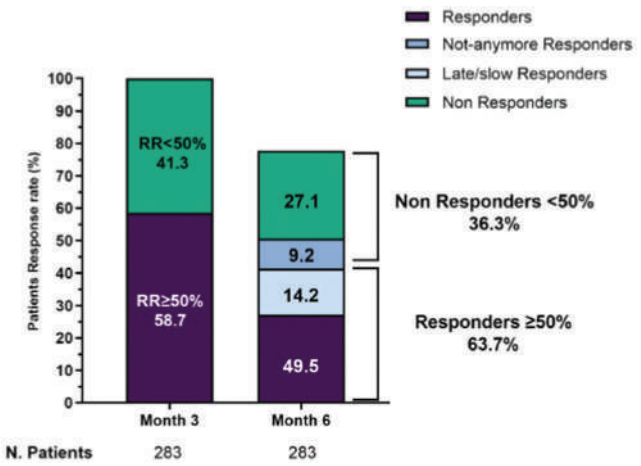
Background and Aims: To evaluated whether late responders to anti-CGRP mAbs (achieving response between 3 and 6 months) are actually slow responders, namely patients who already achieve a clinically meaningful response at 3 months and improve over time.
Methods: We performed a prospective analysis on outpatients that started treatment, with a potential 6-month follow-up. Based on studies on late responders, response was defined as a ≥50% reduction in MHDs at 3 and 6 months. The response rate was then evaluated using different intervals (0–9; 10–19; 20–29; 30–49; ≥50%) to assess responses at three months. The primary outcomes were the number of potential late responders and to evaluate how many patients defined as late responders have a response ≥30% at three months (slow responders).
Results: We include 332 patients and among them 283 (85.2%) continue treatment for six months. Responders were 63.6% (180/283) at six months. In particular, 40 (14.1%) patients not responders at three months achieve response status at six months, 140 (49.5%) persisted in response, 77 (27.2%) continued to be not responders and 26 (9.2%) lost the responder status. However, among the 40 patients defined as late responders, 21 (47.5%) already achieved a response ≥30% at three months with 14 (35.0%) of them with a 40–49% response.



Flowchart of patients' selection



Responder rate variation from 3 to 6 months of treatment

Table 1. Patients demographic and clinical features at baselines.

	Cohort (n=283)
Demographics	
Age [years], mean ± SD	47.8±13.3
Sex female, n (%)	229 (80.9)
Migraine features	
Chronic migraine, n (%)	252 (89.0)
Medication overuse, n (%)[i]	215 (76.0)
Aura, n (%)	21 (7.5)
Migraine duration [years], mean ± SD	32.5±14.4
Chronicization duration [years], mean ± SD	17.5±14.9
Monoclonal antibody	
Erenumab, n (%)	118 (41.7)
Galcanezumab, n (%)	121 (42.8)
Fremanezumab, n (%)	44 (15.5)
Baseline features	
Monthly headache days, mean (SD)	23.8 (6.0)
Days with at least one analgesic use, mean (SD)	20.5 (8.5)
Analgesics number, median (IQR)	34.2 (28.5)
MIDAS score, mean ± SD	91.4±61.1
HIT-6 score, mean ± SD	68.0±6.2

IQR, interquartile range; SD, standard deviation. Percentages are expressed on column total.
[i]Only patients with chronic migraine.

Patients' demographic and clinical features at baseline

Conclusion: The majority of patients designed as late responders are instead slow responders, starting a meaningful response to anti-CGRP at three months and improving over time. Nevertheless, to maximize response, we recommend evaluating the treatment after a minimum of three to six months.

Disclosure: P.G.: received personal fees from Allergan, Eli Lilly, Novartis, Amgen, TEVA; Grants from Amgen, TEVA, Eli-Lilly, Allergan, Chiesi; Scientific Advisory Board, Endosome Therapeutics; Founding scientist of FloNext srl, Spinoff of the University of Florence. F.D.C. received personal fees from TEVA, Eli Lilly, Novartis, Abbvie. L.F.I. received personal fees from TEVA, Eli Lilly, Pfizer, Abbvie, Lundbeck. Other authors have no conflicting interests.

EPO-134 | POTS and autoimmune conditions as predictors of vestibular migraine

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Background and Aims: The vestibular migraine phenotype (VM) presents with vertigo/dizziness as a prominent non-headache symptom. Autoimmune conditions, such as rheumatoid arthritis or psoriasis, are potentially comorbid and may have a genotypic association with migraine. Cranial autonomic symptoms in migraine has been described and could be a protective mechanism in patients with severe symptoms. Dysautonomic symptoms could correlate with chronification of headache in patients with POTS. Our aim was to search for potential comorbidities that could predict a "dizzy" phenotype.

Methods: Cross-sectional study and clinical evaluation of migraine patients on the headache, neuro-otology and general neurology clinics at King's College Hospital and Charing Cross Hospital in London; February 2020 to July 2023. Predictors: sex, the presence of Postural Orthostatic Tachycardia syndrome (POTS), hypermobility, inflammatory/autoimmune and cutaneous conditions such as urticaria. Dependent variable: migraine type. SPSS 28 and generalised linear model with negative binomial-logit function were used.

Results: Age and biological sex were similar among migraine types. Of 525 cases; 185 had a diagnosis of vestibular migraine and 340 chronic migraine. Significant predictors of vestibular migraine: POTS ($B=1.08$, $p=0.045$) and autoimmune conditions ($B=0.53$, $p=0.01$). The rest of the predictors were not significant.

Conclusion: Dysautonomic conditions, such as POTS and the presence of autoimmune disorders, could predispose to a vestibular phenotype of migraine. Patients with the vestibular migraine phenotype may present a more dysfunctional autonomic nervous system with not only cranial, but also systemic symptoms.

Disclosure: Nothing to disclose.

EPO-135 | Is transcranial direct current stimulation effective as add-on therapy to monoclonal antibodies anti-CGRP in migraine?

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Background and Aims: Transcranial direct current stimulation (tDCS) is a non-invasive central neuromodulation technique with potential effectiveness in migraine, while monoclonal antibodies acting on the calcitonin gene-related peptide pathway (CGRP-MAbs) act peripherally. We aimed to assess whether tDCS, as a synergic add-on, can enhance migraine prevention or affect cortical excitability.

Methods: TACTIC (NCT05161871) is a randomized, double-blind, multicenter, sham-controlled trial including patients with migraine on CGRP-MAbs treatment, with residual monthly migraine days (MMD) ≥8. After 5-day of tDCS bilateral occipital-cathodal and frontal-anodal stimulation (20-minutes sham/active sessions) we followed-up patients for 28 days. We recorded 64-channel EEG at day 1 (pre-stimulation) and day 5. We analyzed change in MMDs, clinical scales, and EEG spectral changes in the delta (2–4 Hz), theta (5–7 Hz), alpha (8–12 Hz) and beta-bands (13–30 Hz) through two-way mixed-design ANOVAs with Session (baseline vs. follow-up), as within-subjects factor, and Treatment (Sham vs. Active) as between-subject factor.

Results: We included 29 patients (median age = 48.0 [Interquartile-Range 38–56], 92.0% female), 15 active session and 14 sham. We found no significant interaction between Session and Treatment. However, explorative post-hoc t-test showed that only in the active group tDCS led to a decrease in MMDs (mean difference = 4.00, standard error (SE) = 1.52, $p = 0.014$). Moreover, a noteworthy enhancement was observed in the HIT6 scale for both active ($p = 0.005$) and sham ($p = 0.003$) groups. tDCS decreased the occipital alpha-power and the frontal delta-power only in the active stimulation group (both $p < 0.050$).

Conclusion: Centrally acting tDCS, as add-on therapy to peripherally acting CGRP-MAbs, has a significant preventive benefit on migraine associated with changed basal cortical activity on stimulated areas.

Disclosure: Nothing to disclose.

Movement disorders 1

EPO-136 | Plasma pTAU levels can discriminate HC, PD, PDD, DLB and AD patients

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Background and Aims: plasma biomarkers are a promising field of research in neurodegenerative diseases, both oriented to diagnostic and therapeutic implications. Many patients with PD dementia or DLB have an AD-pathology overlap. In this study, we seek to explore the usefulness of plasma biomarkers in distinguishing between healthy controls, PD, DLB, PDD, and AD patients.

Methods: plasma PTau181, PTau231, Aβ1-40, Aβ1-42, GFAP and NfL concentrations were measured by Single molecule array (Simoa) technology in healthy controls (HC) and consecutive PD and AD patients who underwent an extensive motor and non-motor assessment. We established a cut-off in pTau181 and pTau231 levels based on their average values in patients with AD pathology. We compared clinical and demographic variables between normal and abnormal pTAU groups.

Results: One hundred fifty-three PD patients, thirty-two PDD, forty-two DLB, sixteen AD and ninety-five age matched HC entered the analyses. The percentage of patients with abnormal pTAU levels increases from HCs to PDs but especially in patients with DLB and PDD. When considering only alpha-synucleinopathies, the group with higher PTau231 showed lower MMSE scores at baseline.

Conclusion: The present findings confirm the potential utility of plasma AD biomarkers to differentiate healthy controls from PD patients and more importantly to separate PD cognitive unimpaired patients from patients with DLB or PDD.

Disclosure: Andrea Pilotto served in the advisory board of Z-cube (technology division of Zambon pharmaceuticals); he received honoraria from Z-cube s.r.l., Biomarin, Zambon, Nutricia and Chiesi pharmaceuticals. He received research support from Vitaflo Germany and Zambon Italy. Henrik Zetterberg has served at scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, Alzinova, ALZPath, Annexon, Apellis, Artery Therapeutics, AZTherapies, CogRx, Denali, Eisai, Nervgen, Novo Nordisk, Optoceutics, Passage Bio, Pinteon Therapeutics, Prothena, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures in symposia sponsored by Cellectricon, Fujirebio, Alzecure, Biogen, and Roche, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program (outside submitted work). Alessandro Padovani is consultant and served on the scientific advisory board of GE Healthcare, Eli-Lilly and Actelion Ltd Pharmaceuticals, received speaker honoraria from Nutricia, PIAM, Lansgstone Technology, GE Healthcare, Lilly, UCB Pharma and Chiesi Pharmaceuticals. He is founded by Grant of Ministry of University (MURST).

EPO-137 | Longitudinal impact of vascular risk factors on progression and disability in Parkinson's disease

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Background and Aims: Vascular risk factors are common in the elder population in Western countries. Parkinson's disease incidence is increasing in the last years, along with population aging. Aim of the study was to address the impact of single and multiple vascular risk factors on cognitive and motor progression in patients with PD.
Methods: Consecutive Parkinson's disease patients underwent a comprehensive motor and non motor evaluation including baseline motor and non motor performances. A longitudinal motor and cognitive evaluation was performed with an average of 5 years of follow-up for each patient. The impact of vascular risk factors on motor and cognitive progression was implemented by linear, COX regression and repeated measures analyses adjusting for the effect of age, motor severity and disease duration.
Results: forty-hundred eighty six patient (62.1 % male) entered the study. 52–1% of patients had hypertension, while 21.2% had hypercholesterolemia, 17.3% had diabetes, and 27.2% had cardiac diseases. There was no correlation between vascular risk factors and neither cognitive nor motor impairment at baseline. Patients with diabetes and hypertension showed higher LEDD at follow up; patients with hypercholesterolemia had a higher incidence of falls, while patients with diabetes had a higher incidence of walking impairment at follow-up.
Conclusion: vascular risk factors impact on disease progression and disability in PD. More studies are warranted to evaluate the causality and best management strategies to reduce the impact of vascular risk factors on PD progression and disability.
Disclosure: Nothing to disclose.

EPO-138 | The midbrain-pons ratio as a marker for the vestibular stimulation effectiveness in the postural instability treatment

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Background and Aims: Axial symptoms associated with Parkinson's disease (PD), such as freezing of gait (FOG) and postural instability (PI) are frequently refractory to therapy. Due to the vestibular system deficiency participates in postural imbalance and gait disorders, vestibular galvanic stimulation (GVS) could become an effective neuromodulatory treatment for these symptoms. However, the effectiveness of GVS may vary depending on the neurodegeneration severity in brainstem locomotor centers, and midbrain-pons ratio (MPR) may provide valuable information about change in these regions. Objective: To assess the GVS effectiveness on cVEMP parameters, FOG and PI severity depending on the MPR.
Methods: Participants included 34 PD and 30 age-matched controls. Additionally to MRI-based measurements, we assessed the cVEMP, FOG-Q, TUG test and evaluated the PI severity before and after 12 GVS sessions.
Results: PD patients had longer of VEMP components latencies than controls, indicating slower vestibulospinal conduction. Nevertheless, there were no differences between groups in MRI measurements (table). GVS improved test scores and reduced N23 latency independent of MRI findings in PD patients. While the PI improvement depended on the MPR, and GVS was effective in PD patients with MPR >0.64 (figure).

TABLE Comparative assessment of the PD patients group and the control group

Parameters	PD patients group n = 34	Control group n = 30
	Median (IQR)	
Age, years	63 (57 – 68)	60 (55 – 70)
H & Y stage	2,5 (2–3)	-
Disease duration (years)	7 (6 – 13)	-
UPDRS (part III)	38 (28 - 49)	-
Midbrain (mm)	11,3 (10,9 – 11,5)	11,2 (10,7 – 11,6)
Pons (mm)	17,6 (17,1 – 18,5)	17,5 (16,9 – 18,4)
Midbrain to pons ratio	0,64 (0,61 – 0,66)	0,65 (0,64 – 0,66)
FOG-Q		
Before intervention	14 (7–19)	-
After intervention	9 (5 – 14) Δ	-
Changes	5 (2 – 7)	-
Timed Up and Go Test (TUG) (seconds)		
Before intervention	16 (14– 19)*	8 (7 – 9)
After intervention	13 (11 – 15) Δ	-
Changes	3 (2 – 4)	-
Postural instability (from 0 to 4, where 0 is the norm; 4 - cannot stand without help)		
Before intervention	2 (1 – 3)	-
After intervention	1 (0 – 2)	-
Changes	0 (0 – 1)	-
Cervical Vestibular Evoked Myogenic Potential (cVEMP) P13 latency / N23 latency (msec)		
Before intervention	13,25 (12,4 – 14,3)* / 24,8 (23,6 – 25,9)*	11,7 (10,8 – 22,1) / 22,5 (22,05 – 22,9)
After intervention	13,1 (12,1 -14) / 23,7 (23 – 24,2) Δ	-
Changes	0,15 (0,1 – 0,4) / 1,1 (0,6 – 1,7)	-

* - p ≤ 0,05 - Significant differences between PD patients and control group (Mann-Whitney test)
Δ - p < 0.05 - Significant difference when comparing results before and after GVS in the Wilcoxon Matched Pairs Test

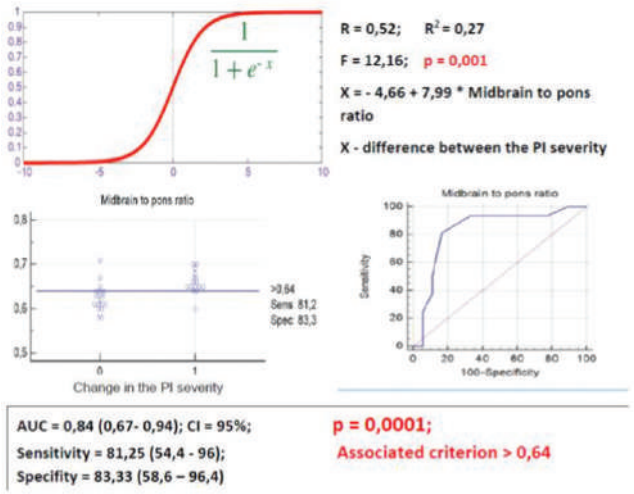

FIGURE Results of multiple regression and ROC analysis

Conclusion: GVS, acting on vestibular afferents, modifies the conflict between sensory systems and thereby reduces the severity of gait disorders. But the ability of GVS to reduce PI in PD probably depends more on morphometric features of the brainstem. Due to its high sensitivity and specificity, the MPR can be considered as a prognostic marker of the GVS effectiveness in the PI treatment.
Disclosure: Nothing to disclose.

EPO-139 | Amantadine improves executive and memory skills in patients with Parkinson's disease: A randomized controlled trial

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Background and Aims: Amantadine improves motor symptoms in patients with Parkinson disease (PD) as monotherapy or adjuvant therapy. However, data on cognitive functions are lacking. This Single blind randomized controlled study over 12 months investigated the effect of amantadine on PD cognition.
Methods: Mild cognitive impaired 35 PD patients (mean HY: 2), with amantadine 200 mg/day (100 mg twice a day) orally as monotherapy (Group A) and 30 PD patients without amantadine (only levodopa treatment Group B) were randomly enrolled. The data collected for each patient included: (1) verbal learning and memory (Hopkins Verbal Learning Test-Revised immediate total recall across trials and delayed recall trial), (2) auditory working memory (Letter-Number Sequencing subtest from the Wechsler Adult Intelligence Scale – III), (3) processing speed (Digit Symbol subtest from the Wechsler Adult Intelligence Scale-Revised), (4) visuospatial working memory/switching (Trail Making Test, Part B), (5) semantic verbal fluency (animals), (6) phonemic verbal fluency (letters F-A-S or C-F-L), (7) visuospatial functioning (Benton Judgment of Line Orientation), 8)Depression (Geriatric Depression scale).
Results: The cognitive function improved progressively in 3-, 6 and 12-month treatment interval as shown by significant improvement on verbal short term ($p < 0.001$) and auditory working memory ($p < 0.001$) and visual working memory ($p < 0.001$) in Group A compared to Group B. Even after controlling for depression, disease duration, there are persistent differences in the above cognitive tests between the two groups over the time
Conclusion: Amantadine alone significantly improved memory and visual-spatial skills in PD patients.
Disclosure: Nothing to disclose.

EPO-140 | Determination of clinical profile of patients with Parkinson's disease at 2-year follow up with deep brain stimulation

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Background and Aims: Despite the beneficial effect of deep brain stimulation (DBS) on motor and non-motor symptoms, the selection of Parkinson's disease (PD) patients is challenging. This study aims to develop a random forest (RF)-based PD model to determine the postoperative clinical profile at 2 years follow-up with DBS using motor and non- motor symptoms.
Methods: 130 PD subjects (76 male, 54 female; age at baseline: 56.24 ± 4.23) were evaluated in years 0 and 2 by the Unified Parkinson's Disease Rating Scale part III (UPDRS- III). Hours of "Off" and dyskinesia time (UPDRS-IV), the Montreal Cognitive Assessment (MoCA), Geriatric Depression Scale (GDS), the Non-Motor Symptoms Scale (NMSS), Hoehn/Yahr(HY) and PD questionnaire- 39(PD39). RF analysis, with 10000 trees, was used to combine both non-motor and motor variables to determine motor outcome (UPDRS-III year 2: 22.55 ± 12.22).
Results: The proper combination of motor and non-motor measures significantly improved ($p < 0.001$) the prediction of outcome, reducing the RMSE (root-mean-square-error) of predicting UPDRS-III from 4.686567 to 4.04672 which signifies that the model was optimized quite well. Based on the "IncNodePurity", the factors of UPDRS-III (year 2) were, in descending order of magnitude, UPDRSIII (year 0), disease duration (year 2), GDS (year 0), NMSS (year 2), Time Dyskinesia (year 0), PDQ39 (year 2) after the implementation of DBS.

Conclusion: In the new era of neuromodulation, these results are promising for accurate patient selection for DBS by artificial intelligence models.
Disclosure: Nothing to disclose.

EPO-141 | Phenotype's evolution of cervical dystonia (CD) in patients treated with Botulinum toxin

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Background and Aims: Cervical dystonia (CD) phenotypes may change over the years. Objective of the study is to evaluate how such phenotypes change in CD treated with botulinum toxin (BoNT). Finally, we aim to identify the time within those changes may occur, the most predisposed CD phenotypes and predisposing factors.
Methods: We divided idiopathic CD patients into two groups – switch YES/NO, collecting general clinical and demographic variables. We added to general clinical variables the duration of BoNT treatment, Tsui total scores and subscores – assessed at T0 – before BoNT start – and at T1 – switch time in the YES group or last visit in the NO group. The risk of switch was assessed by Kaplan Meyer curves and Cox regression analysis. Finally, Multivariate linear regressions were employed to assess if Tsui severity correlated with the switch.
Results: Among 100 patients (60 women) aged 47.9 years (SD 15.3) at CD onset, 37 experienced a phenotype switch, mostly in the first five years of BoNT treatment, YES and NO groups were comparable. Multivariate Cox Regression revealed the presence of laterocollis or rotatocollis at T0 as predictors of switch (respectively $p=0.01$, HR = 3.5; $p=0.03$, HR = 1.5). Multivariate linear regressions revealed that high Tsui subscores for the tilt and low Tsui total scores were risk factors for the switch (respectively $p=0.002$, OR = 6; $p=0.03$, OR = 0.8).
Conclusion: Latero and Rotatocollis are the CD phenotypes most predisposed to switch. Dystonias with a low degree of severity improve after treatment with botulinum toxin, changing to a different and even simpler phenotype.
Disclosure: Nothing to disclose.

EPO-142 | The long-term response to botulinum toxin injections in patients with blepharospasm undergoing upper eyelid surgery

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Background and Aims: BACKGROUND Upper eyelid surgery (UES) is a therapeutical strategy used for those patients affected by blepharospasm (BSP) who either do not respond or experience a gradual decrease in responsiveness to botulinum toxin (BoNT) injections. Nevertheless, most of them need to restart with BoNT despite the intervention. AIM To evaluate the long-term post-surgical response to BoNT in patients with BSP and to identify predictive factors associated to treatment outcome.
Methods: We collected data of 60 BS patients, divided into two groups – blepharoplasty YES (8) and NO (52), collecting demographic – age, sex – and clinical data –disease duration, duration of the treatment with BoNT. Respective responses to injections – evaluated through the differences of both Jancovic Rating Scale and the Blepharospasm Disability Index pre and post BoNT (delta JRS and delta BSDI) just before their periodic three-month injection and after 1 month from it – were compared. Finally, clinical and demographics variables were included in multivariate regression and correlation analyses to assess their impact on the long-term response to injections.
Results: Patients who underwent UES had significantly lower delta at both scales, showing a poorer outcome after BoNT treatment. No variable was found to be associated with the response.
Conclusion: Our data seem to suggest that surgery does not improve response to BoNT injections on the long run. As such, UES could be considered as an efficacious treatment in BSP just if evaluated soon after its performing. Long-term BSP management seems still difficult to be performed adequately and new therapeutical approaches are still needed.
Disclosure: The authors have nothing to disclose.

EPO-143 | Assessment of the deep brain stimulation efficiency for the tremor correction in Parkinson's disease: STN vs Vim

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Background and Aims: Correcting severe tremor, one of the disabling symptoms in Parkinson's disease (PD), is the most difficult tasks for neurologists. If there is no effect from drug correction of severe tremor, neurosurgical treatment is used, including deep brain stimulation (DBS) of the ventralis intermedius thalamic nucleus (Vim) or subthalamic nucleus (STN). To evaluate the efficiency of DBS Vim vs STN for the tremor correction in PD patients.
Methods: We examined 72 (59–II stage, 13–III stage of H&Y.) PD patients during DBS. The main characteristics of patients are presented in the table (Fig. 1). In patients with DBS Vim, the primary symptom was disabling tremor. The tremor index (TI) consists of

UPDRS scores 16, 20, 21. To assess the changes of drug therapy used LEDD.

Indicators	DBS STN	DBS Vim
Amount, patients	63	9
M/F	36/27	5/4
Age, years	57,0 (95% CI 54,0;59,0)	59,0 (95% CI 50,8;62,0)
PD duration, years	10,3 (95% CI 9,3;11,2)	8,4 (95% CI 5,8;11,1)
LEDD, before	1175,0 (95% CI 1000,0;1250,0)	750,0 (95% CI 656,2;987,5)
III part UPDRS, off med, before	41,0 (95% CI 34,0; 54,0)	46,0 (95% CI 33,5;58,0)
TI (16,20,21 UPDRS), off med, before	6,5 (95% CI 3,5; 12,5)	14,0 (95% CI 11,5;16,0)

FIGURE 1 Description PD patients before DBS

Results: The postoperative follow-up period was up to 2 years. The score by III UPDRS in the off-med decreased in patients with DBS STN ANOVA $\chi^2 = 12.44$, $p < .00001$ and DBS Vim ANOVA $\chi^2 = 11.58$, $p = .00011$(Fig 2). The TI in the off-med period decreased in patients with DBS STN ANOVA $\chi^2 = 14.68$, $p < .00001$ and DBS Vim ANOVA $\chi^2 = 4.51$, $p = .014$ (Fig 3). The LEDD score in DBS STN was decreased ANOVA $\chi^2 = 9.22$, $p < .000001$, but not under DBS Vim ANOVA $\chi^2 = 1.92$, $p = .15$.

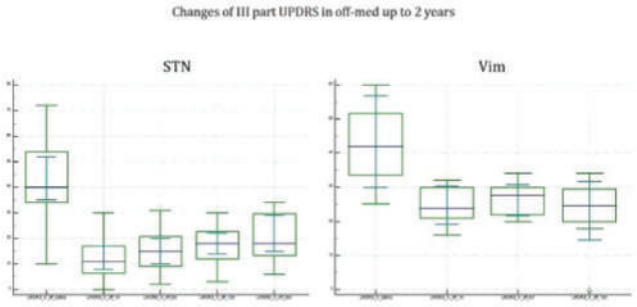

FIGURE 2 Changes of III part UPDRS in off-med DBS STN vs DBS Vim up to 2 years

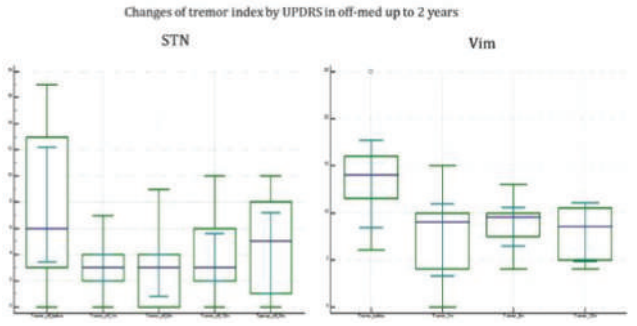

FIGURE 3 Changes of tremor index by UPDRS in off-med DBS STN vs DBS Vim up to 2 years

Conclusion: The results indicate an improvement of tremor both by DBS STN and DBS Vim. To correct hypokinesia and rigidity during DBS Vim, patients should take levodopa at the correct dose.
Disclosure: Nothing to disclose.

EPO-144 | Pain and related factors in patients with Parkinson's disease

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Background and Aims: Pain is a common non-motor symptom in Parkinson's disease (PD). We aimed to investigate pain frequency and pain-related factors in PD.
Methods: We interviewed PD patients from our movement disorders unit to assess pain presence, categorising it into four types: musculoskeletal pain (MP), radicular or neuropathic pain (RNP), dystonia-related pain (DRP), and central parkinsonian pain (CPP). We investigated demographic differences, General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), EQ-5D-3L, MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Hoehn and Yahr scale (H&Y) scores, PD duration, PD drugs, and insomnia. Comparisons were made between patients with and without pain, and among those with different pain types.
Results: Ninety-three patients (34 female, 59 male; median age: 66 years, IQR: 17) were included. Seventy-five had pain (23 MP, 18 RNP, 12 DRP, 5 CPP, and 17 had a combination). No associations were found between pain and age, gender, GAD-7, PHQ-9, MDS-UPDRS, H&Y scores, PD duration, PD drugs, and insomnia. However, EQ-5D-3L scores were higher in patients with pain ($p = 0.019$). Among different pain types, no relationships were identified regarding age, PHQ-9, MDS-UPDRS and H&Y scores, PD drugs, and insomnia. RNP correlated with longer PD duration ($p = 0.01$), MP with shorter PD duration ($p = 0.04$). MP was less common in males ($p = 0.016$), and anxiety was more prevalent in CPP patients ($p = 0.008$).
Conclusion: Pain impairs PD patients' quality of life, and longer PD duration correlates with increased RNP. Anxiety correlates with CPP, suggesting a potential link between anxiety-control networks and CPP. Further studies are needed to support this hypothesis.
Disclosure: Nothing to disclose.

EPO-145 | Neurology survey on referral practices and perception of functional neurosurgery solutions in essential tremor in Europe

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Background and Aims: Functional neurosurgery for treatment of essential tremor (ET) has evolved in recent years. Magnetic resonance–guided focused ultrasound (MRgFUS) was introduced as an alternative neurosurgery modality. We investigated changes in referral patterns and familiarity with functional neurosurgery among European neurologists.

Methods: An anonymised web survey was conducted between 16-01-23 and 24-02-23. Relevant privacy legislation on personal data protection (GDPR 2016/679) and professional guidelines were followed. General neurologists (GN) and movement disorder neurologists (MDN) were interviewed about the ET pathway and their experience and perception of functional neurosurgery.

Results: The survey was answered by 224 neurologists (68 MDN, 156 GN). Patients came to the neurologist's attention mainly via their general practitioner (GP) and the patient's own initiative (up to 33% in Italy). Disease was mainly severe in those referred to the neurologist (approximately 55%) (Figure 1). Most were managed directly by the neurologist, without referral to another neurologist or centre (<18%); when the neurologist referred the patient to another centre, disease was generally severe (approximately 70%) (Figure 2). Most neurologists were familiar with deep brain stimulation (DBS [96.4%]), radiofrequency (RF [72.8%]), and gamma-knife thalamotomy (GKT [79.3%]). Fewer were familiar with MRgFUS (67.5%) (Figure 3).

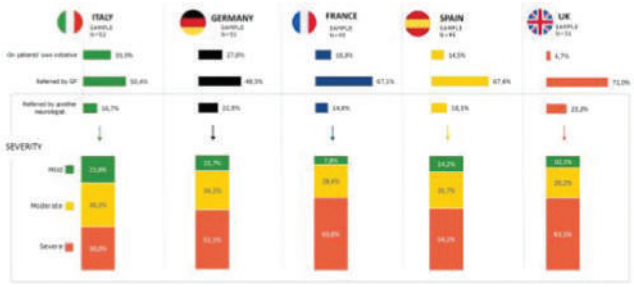

FIGURE 1 Origin and severity of essential tremor patients referred to general and movement disorder neurologists in Europe (Italy, Germany, France, Spain, and the UK). The sample number of neurologists per country is reported.

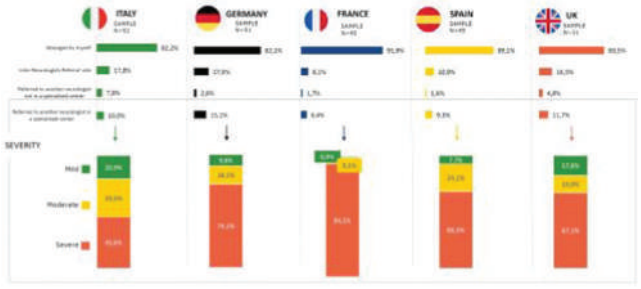

FIGURE 2 Distribution and management of essential tremor patients by and between neurologists in Europe (Italy, Germany, France, Spain, and the UK). The sample number of neurologists per country is reported.

FIGURE 3 Reported level of knowledge of non-pharmacological therapies among both general and movement disorder neurologists. The sample number of neurologists is reported. Familiarity is defined as the overlap between the 3 highest levels of knowledge.

Conclusion: Referral of ET patients remains variable and is mainly via the GP or the patient's own initiative. The most common profile is severe disease. Despite recent inclusion in national/international guidelines, MRgFUS remains the least familiar option for neurologists, followed by RF, GKT, and DBS. Further study is necessary to explain the low referral rate (<18%).

Disclosure: The authors are all employees of Insightec. To carry out the survey, support was provided by Stethos Srl, Italy, Milan. Writing assistance was provided by Content Ed Net, Madrid, Spain. The responses were used for market research purposes.

EPO-146 | General and movement disorder neurologists survey on prescription and perception of MRgFUS in Europe

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Background and Aims: Magnetic resonance–guided focused ultrasound (MRgFUS) emerged in the 2010s and is now a recommended neurosurgery alternative for essential tremor (ET). The increased presence of MRgFUS means that perception and potential application in ET may have changed. We investigated changes in perception of MRgFUS among European neurologists.

Methods: An anonymised web survey was conducted between 16-01-23 and 24-02-23. Relevant data privacy legislation and guidelines were followed. Both general neurologists (GN) and movement disorder neurologists (MDN) were asked about the positioning of MRgFUS, barriers to adoption, and medical education.

Results: The survey was completed by 68 MDN and 156 GN. Approximately two-thirds of patients had severe ET. Quality of life was poor, and many patients had not responded to previous therapy (Figure 1). Most neurologists (>70%) were satisfied with the effects of MRgFUS on patient management. The main conditions for extending referral were access to protocols and referral criteria. (Figure 2). Most felt that MRgFUS could be extended to a wider range of patients by enhancing communication with neurologists, creating access channels between MRgFUS centres and other centres, and offering staged-bilateral treatment. The recommended educational content to extend use of MRgFUS includes clinical efficacy data, safety-tolerability data, and side effects, as well as explanation of the technique/procedure (Figure 3).

FIGURE 1 Severity and main characteristics of essential tremor patients prescribed MRgFUS by neurologists in Europe (Italy, Germany, France, Spain, and the UK). The sample number of neurologists per country is reported.

FIGURE 2 A) Level of satisfaction for post-MRgFUS patient management among general and movement disorder neurologists. B) Conditions for extension of MRgFUS to more patients.

FIGURE 3 A) Channels of communication for extension of MRgFUS to more patients. B) Content to be included in communications on MRgFUS. The sample number of neurologists is reported. Outcomes are reported for general and movement disorder neurologists.

Conclusion: In Europe, MRgFUS is prescribed mainly in severe ET. Satisfaction was high. More widespread adoption depends on better access to centres, well-defined referral criteria, and the possibility of staged-bilateral treatment. Further education on MRgFUS is necessary.

Disclosure: The authors are all employees of Insightec. To carry out the survey, support was provided by Stethos Srl, Italy, Milan. Writing assistance was provided by Content Ed Net, Madrid, Spain. The responses were used for market research purposes.

EPO-147 | Use of the MNCD classification/staging in advanced Parkinson's disease patients treated with a device-aided therapy

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Background and Aims: Staging Parkinson´s disease (PD) with a novel simple classification called MNCD, based on 4 axes (Motor; Non-motor; Cognition; Dependency) and 5 stages, correlated with disease severity and patients´ quality of life and caregivers´ strain and burden (1,2). Our aim was to apply the MNCD classification in patients treated with levodopa-entacapone-carbidopa intestinal gel (LECIG) infusion.

Methods: A multicenter observational retrospective study of the first patients to start LECIG in Spain was performed (LECIPARK). The MNCD total score (from 0 to 12) and MNCD stages (from 1 to 5) were collected by the neurologist at V0 (before starting LECIG) and V2 (follow-up visit). Wilcoxon's signed rank and Marginal Homogeneity tests were applied to compare changes from V0 to V2.

Results: Forty-five PD patients (55.3% males; 69.6 ± 10 years old) with a mean disease duration of 13.9 ± 6.4 years were included. The mean treatment duration (V2) was 132.2 ± 81.3 days (range, 10–302). At V0, patients were classified as in stage 2 (31.9%), 3 (44.7%) or 4 (23.4%). The frequency of patients in stage 4 decreased to 10.6% at V2 ($p = 0.007$) (Figure 1A). The MNCD total score decreased from 6.6 ± 1.8 at V0 to 5.4 ± 2.1 at V2 ($p < 0.0001$). From V0 to V2, motor and non-motor symptoms burden decreased and autonomy for activities of daily-living improved (Figure 1B and 2).

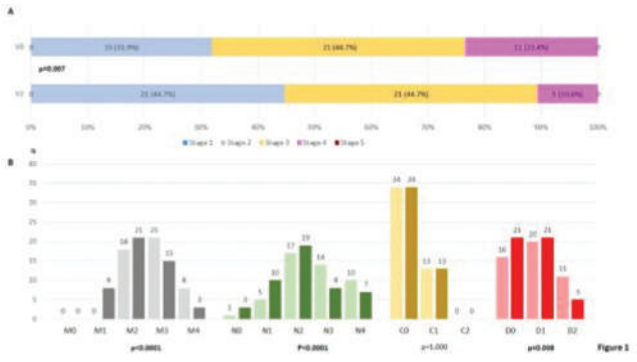

FIGURE 1 A. Frequency of different MNCD stages (from 1 to 5) at V0 (V0; pre-LECIG) compared to at V2 (follow-up visit; 132.2 ± 81.3 days after starting LECIG) ($p = 0.007$). B. Number of patients with each score of the MNCD classification (M, N, C and D) at

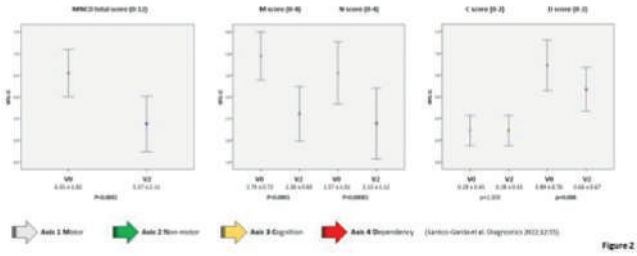

FIGURE 2 Change from the baseline (V0; pre-LECIG) to the follow-up visit (V2) in the MNCD total score (from 0 to 12), M and N scores (from 0 to 4), and C and D scores (from 0 to 2). Wilcoxon's signed rank tests was applied. The bars represent mean ± stan

Conclusion: The MNCD classification could be useful to classify advanced PD patients and to monitor the response to a device-aided therapy.

Disclosure: The authors report no conflict of interest.

EPO-148 | Exploring the distinct effect of onset age and caudate denervation on cognitive deficits in early PD

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Background and Aims: Older age at onset and baseline caudate dopaminergic denervation are recognized risk factors for cognitive impairment in Parkinson's disease (PD), posing challenges in identifying their relative contribution to cognitive outcomes. The objective of this study was to assess the distinct contribution of age at onset and baseline caudate dopaminergic binding to the early cognitive deficits in PD patients.

Methods: We examined the relationship between baseline dopaminergic striatal dysfunction (measured using [123I]FP-CIT SPECT, age at disease onset and neuropsychological performance in 126 drug-naive PD patients, utilizing putaminal and caudate binding values of 77 healthy controls (HC) for a comparative exploration of age-dependent loss of DAT availability. Additionally, we investigated whether age at onset and caudate DAT binding could independently predict cognitive changes over a median of 7-year follow-up.

Results: [123I]FP-CIT-SPECT binding values had a significant negative correlation with age in both PD and HC, but in PD, aging was linked with a steeper slope for the caudate than the putamen. Older age at onset and lower caudate uptake were associated with worse global cognitive function and performance in specific neuropsychological tests at baseline and demonstrated to be significant independent predictors of cognitive dysfunction at follow-up.

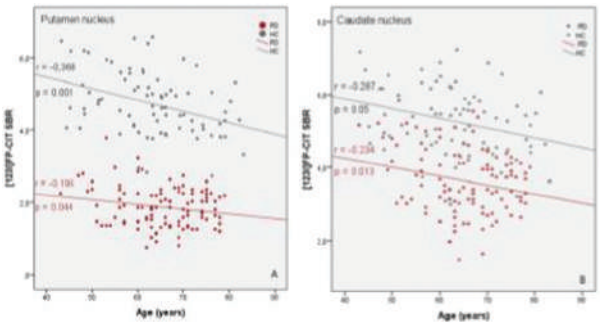

FIGURE 1 Effects of age: comparison of [123I]FP-CIT binding values between PD and HC in the putamen (A) and caudate (B)

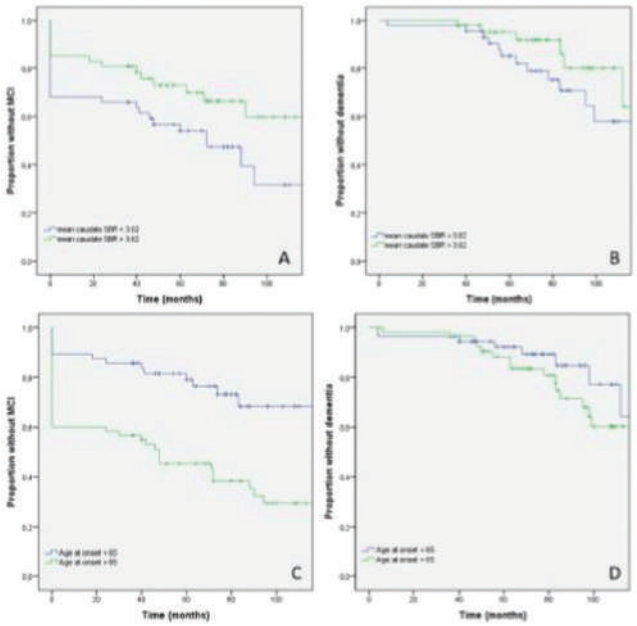

FIGURE 2 The survival curve determined using the Kaplan-Meier for cognitive decline in our patient cohort according to baseline [123I]FP-CIT SPECT binding values (A and B) and age at the onset of PD (C and D)

Conclusion: Our findings confirm a differential age effect on [123I] FP-CIT binding in the striatal subregions of denovo PD patients. Notably, we found less age-related attrition of dopaminergic binding in the putamen than in the caudate, reflecting likely the superimposition of putaminal compensatory mechanisms and an increased predisposition of old onset PD patients to develop cognitive disturbances.

Disclosure: The authors declare that there are no financial disclosures to report concerning the research related to this abstract.

EPO-149 | Vestibular and saccadic abnormalities in Parkinson's disease patients: Possible marker of neurodegenerative burdern?

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Background and Aims: Vestibular dysfunction has been suggested as possible non-motor symptom in Parkinson's disease (PD), however so far data are still lacking in literature. Moreover, saccadic eye movements have been studied in PD with mixed results. The aim of our study is to assess vestibulo-ocular reflex gain and voluntary saccade eye movements in PD patients exploring possible correlation between vestibular and saccadic variables and demographic and clinical features. Secondary aim is to compare these variables in GBA1-PD and non-mutated PD (NM-PD) subgroups.

Methods: A consecutive cohort of GBA1-PD patients has been paired for age, sex, disease duration, Hoehn & Yahr stage, and Charlson Comorbidity Index with a cohort of consecutive NM-PD. Patients underwent clinical neurological assessment (MDS-UPDRS total scores and subscores, the Montreal Cognitive Assessment scale (MoCA)), the video head impulse test (vHIT) and saccadic instrumental assessment.

Results: 40 PD patients were included in this study: 20 GBA1-PD and 20 NM-PD. Bilateral saccadic latency directly correlated with age ($p < .05$), disease duration ($p < .001$) and PIGD subscore ($p < .001$), while it negatively correlated with MoCA score ($p < .05$). The bilateral vHIT gain of the lateral semicircular canal directly correlated with disease duration ($p < .05$), while the gain of the posterior semicircular canal negatively correlated with rigidity subscore ($p < .05$). No differences were found in vestibular and saccadic variables between GBA1-PD and NM-PD.

Conclusion: Our results highlight that vestibular and saccadic abnormalities may be associated with specific clinical features in PD. Particularly, saccadic latency could represent a marker of neurodegenerative burden, correlating with age, disease duration and axial and cognitive impairment.

Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

EPO-150 | Atypical presentations of Huntington disease-like 2 in South African individuals

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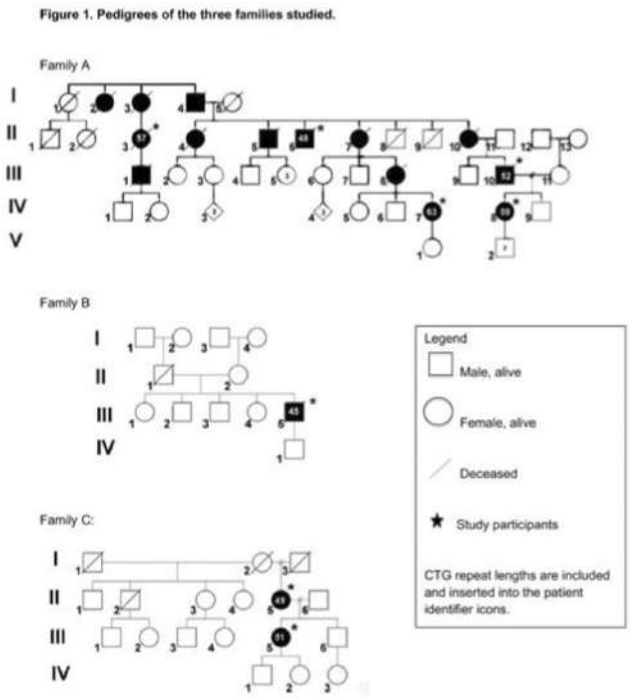
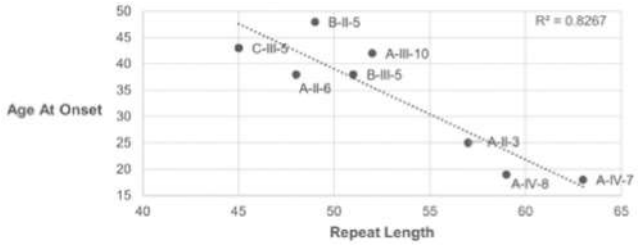
Background and Aims: Huntington's Disease Like 2 (HDL2) is a neurodegenerative disorder, described as being similar to HD with respect to phenotypic, radiologic and pathologic features. HDL2 only affects individuals of African ancestry. Affected individuals have 40–59 triplet repeats. We describe the phenotypic variability of HDL2 in a group of mixed ancestry individuals from South Africa.

Methods: Eight patients were assessed with the Unified HD Rating Scale (UHDRS), Montreal Cognitive Assessment (MoCA) tool, MR brain imaging, and analysis of repeat size.

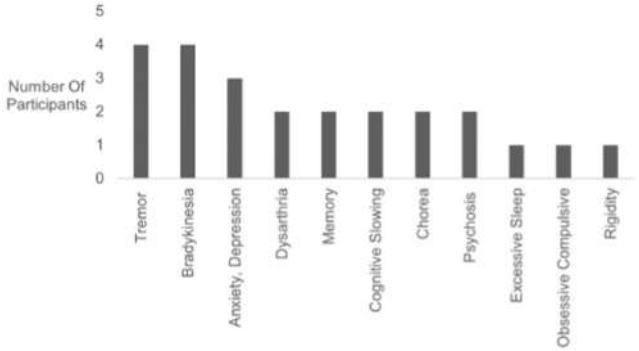


Pedigrees of the three families studied.

Results: Cognitive domains were more severely affected than motor domains. Neuropsychiatric symptoms were common in all, evident as behavioural change, memory impairment, depression, anxiety, and/or hallucinations. MoCA scores reflected impairments across all domains, although orientation and memory were less severely affected. UHDRS motor scores were notable for bradykinesia. Tremor and dystonia were also prominent motor symptoms; only one patient had marked chorea. Repeat lengths ranged from 45 to 63 and were inversely related to age at onset (AAO). We report two unique cases of juvenile onset HDL2, noting that an AAO younger than 20 years has not been previously documented.



Age at onset and corresponding repeat length



Symptoms at presentation

Conclusion: It is important for clinicians to be aware that individuals with HDL2 may present with severe and rapidly progressive cognitive and behavioural impairments, with variable degree of motor deficit and even absent chorea. The atypical HDL2 phenotype in this South African group of mixed ancestry is likely related to large repeat sizes and may represent a forme fruste of the Westphal variant seen in Huntington disease.

Disclosure: Nothing to disclose.

Movement disorders 2

EPO-151 | EEG microstate abnormalities in prodromal Lewy body diseases

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Background and Aims: Described EEG patterns may serve as diagnostic and prognostic biomarkers for prodromal dementia with Lewy bodies (DLB). While spectral frequency analysis is used to evaluate EEG patterns, EEG microstates (MS) provide temporal and spatial characteristics. We aimed at elucidating early changes in network dynamics across spectrum of healthy controls (HC), prodromal DLB and at-risk population using both EEG patterns and MS assessment.

Methods: 120 cognitive and dopaminergic medication-naïve subjects with or without core and supportive clinical features of prodromal DLB +- presence of mild cognitive impairment underwent a 5-minute recording of high-density resting state scalp EEG. Participants were sorted based on their EEG patterns into groups: pattern 1 (normal EEG), pattern 2 (early DLB) and pattern 5 (advanced DLB). EEG microstates were analyzed using k-means approach and temporal parameters were calculated.

Results: Results revealed higher mean duration ($p < 0.001$ and $p = 0.005$) and higher time coverage (TC) ($p = 0.004$ and $p = 0.004$) of the MS C, and lower TC ($p = 0.003$ and $p < 0.001$) and segment density ($p < 0.001$ and $p < 0.001$) of MS A in EEG pattern 1 compared to pattern 2 and 5, respectively. No significant differences between pattern 2 and 5.

Conclusion: MS A involves temporal cortices and represents sensory (auditory, visual) and arousal networks while MS C anterior cingulate and insular cortices representing salience network. Our results support early engagement of anterior insular cortices in prodromal DLB which reflects deficits in executive, autonomic, visual and affective/behavioral functions while abnormally enhanced involvement of the sensory/arousal network is related to cognitive fluctuations, and/or illusions/hallucinations in early DLB.

Disclosure: No disclosure.

EPO-152 | Functional Neurological Disorders (FND): Experience at a tertiary hospital in Madrid

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Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

Background and Aims: Diagnosing functional neurological disorders (FND) might be daunting. Although the prevalence of overlapping structural neurological pathology in FNDs has been previously stated, the relationship between both is yet to be fully understood. Our aim was to describe all diagnoses reached at our FND-Unit and analyze its characteristics.

Methods: Prospective observational study of all patients referred to an FND-Unit, May-2022 to December-2023.

Results: 154 patients (72.7% female, median age 41 years) were included. 89.0% were diagnosed with FND, 11,0% received alternative diagnoses (non-FND). The most prevalent reason for referral were syncopes (22.1%) and gait abnormalities (20.1%). Amongst the alternative diagnoses, the most common clinical presentation was sensory disturbances (64.7%).The most prevalent alternative diagnosis was restless legs syndrome (RLS) (44.4%), followed by peripheral neuropathy (33.3%). 3.7% of FND confirmed cases presented an overlapping RLS (FND/RLS). The resulting prevalence of RLS was 8.4%. 46.2% of RLS patients presented exclusively sensory symptoms, and most of them (87.5%) were non-FND/RLS ($p = 0.047$). Within the FND/RLS group, median age was significantly lower (30.0 versus 49.5 years, $p = 0.021$) and median time to diagnosis after symptom onset was longer (60 versus 10 months, $p = 0.08$). No other differences were found.

Conclusion: The possibility of diagnostic errors at a FND-Unit is relevant. The most frequent misdiagnosis was RLS, which also commonly overlapped with FND. Age, solely sensory symptoms, and time to diagnosis might help distinguish FND/RLS from non-FND/RLS.

Disclosure: Nothing to disclose.

EPO-153 | Novel CACNA1A mutation associated with cerebellar ataxia and mild cognitive impairment in a Czech family; a case report

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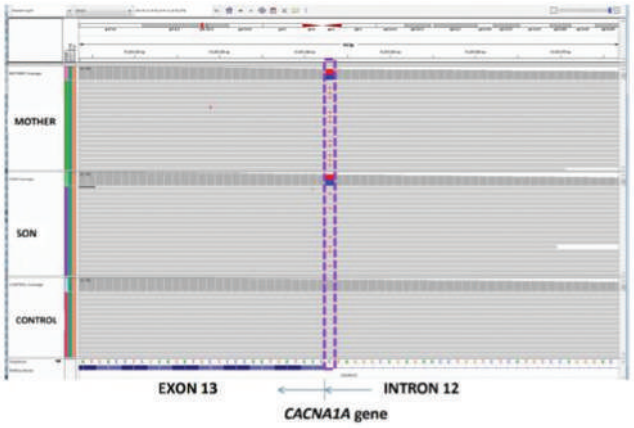
Background and Aims: Spinocerebellar ataxias (SCA) are a group of heterogenous neurodegenerative hereditary disorders characterized by progressive loss of balance and coordination, as well as other distinguishing symptoms that vary with the particular type and the involved genetic defect. Pathogenic variants in CACNA1A gene have been implicated in autosomal dominant hereditary spinocerebellar ataxia 6, episodic ataxia type 2, familiar hemiplegic migraine, and infantile epileptic encephalopathy 42.

Methods: Index case, 43-year-old patient, presented with progressive cerebellar ataxic gait clinically manifesting at age 41, horizontal nystagmus and mild cognitive impairment. Noteworthy from his history; he suffered epileptic seizures from ages 3–16, and his biological mother developed similar gait disorder since age 44. Her examination showed cerebellar ataxic gait, horizontal nystagmus with saccadic intrusions, ataxic dysarthria, intentional tremor and mild cognitive impairment. Both patients had global cerebellar atrophy on MRI. Patients initially tested negative for most common SCAs (SCA1-3 and SCA6-7). Subsequently, CACNA1A gene was analysed using new generation sequencing and bioinformatic analysis.

Results: In both patients, molecular genetic examination confirmed the presence of the heterozygous variant c.1672-1G>A in CACNA1A (NM 000068.3). In Sophia DDM, as well as Varsome and Franklin predictions, the variant is assessed as likely pathogenic (applied ACMG criteria PVS1, PM2). The mutation probably causes aberrant splicing by disrupting splicing acceptor site. To our knowledge, this variant is not yet recorded in literature and dbSNP, gnomAD and HGMD databases.

Conclusion: Based on our results, we propose that the above-mentioned variant in CACNA1A is likely to be associated with cerebellar ataxia, nystagmus and mild cognitive impairment.



Read alignments visualized with IGV (Integrative Genomics Viewer) shows the novel heterozygous germline variant c.1672-1G>A in the CACNA1A gene (NM 000068.3) (chr19-13308529 C>T) in the patient and her son and a comparison with a control sample.

Disclosure: Supported by MH CZ–DRO (FNOI, 00098892).

EPO-154 | Serum biomarkers of neurodegeneration in mitochondrial membrane protein-associated neurodegeneration (MPAN)

M. Skowrońska[1]; A. Cudna[1]; A. Antos[1]; M. Rydzewski[1]; J. Janikiewicz[2]; A. Dobosz[2]; A. Wydrych[2]; B. Pakuła[2]; P. Jakubek[2]; M. Lebiedzińska-Arciszewska[2]; M. Cwyl[3]; M. Popielarz[3]; A. Dobrzyń[2]; M. Więskowski[2]; I. Kurkowska-Jastrzębska[1]
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Background and Aims: Neurodegeneration with iron accumulation (NBIA) associated with the mitochondrial protein C19orf12 – MPAN, is one of the hereditary diseases characterized by the accumulation of iron in the brain. There is currently no cure for MPAN, and the primary focus is on discovering the role of the C19orf12 protein, which may aid in the search for effective treatment. In this study, we aim to identify biomarkers that can serve as indicators of disease progression and treatment effectiveness.
Methods: Twenty-five patients with genetically confirmed MPAN had biomarkers of inflammation and neurodamage tested, and results were compared to those of an age- and sex-matched control group of healthy volunteers. Venous blood was collected in the fasting state in the morning, and serum was then frozen at −80°C for storage until testing. MMP-9, S100B, ICAM-1, E- and P-selectins, and total α-synuclein were measured using a sandwich-type ELISA following the manufacturer's instructions. Serum NfL, GFAP, Tau protein, and UHC-L1 were measured using SIMOA Quanterix methods.
Results: Our findings reveal that MPAN patients exhibited higher serum levels for all biomarkers, except BDNF. MMP-9, E- and P-selectins were increased 1.4–2 times above the control level. S100B was 10 times higher in MPAN patients, indicating potential blood-brain barrier damage. Alpha-synuclein was elevated 25 times, corresponding to an accumulation of this protein in the brain. NfL, GFAP, and UCH-L1 were higher by 8, 2, and 5 times, respectively.
Conclusion: Our results suggest that S100B, alpha-synuclein, NfL, and UHC-L1 might be useful as biomarkers in MPAN
Disclosure: Nothing to disclose.

EPO-155 | Gait and postural responsiveness to subthalamic stimulation and levodopa: A prospective clinical-instrumental study

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Background and Aims: This study delves into the dynamic interplay of balance and mobility, specifically probing their nuanced response to subthalamic stimulation.
Methods: We investigated alterations in the spatiotemporal dynamics of gait and posture in a prospective cohort of individuals with Parkinson's disease, examined both before and six months post subthalamic deep brain stimulation (STN-DBS) surgery. The standardized motor protocol included Timed-Up and Go, 18m walk test, quiet standing monitored by wearable inertial sensors.
Results: Twenty-eight patients were evaluated in 2 preoperative and 4 postoperative conditions comprising OFF/ON medication and stimulation states. Standardized response mean values were computed to assess the responsiveness of sensor-based motor parameters to treatments. Significant improvements in spatiotemporal gait parameters, including speed, cadence and stride length were observed following STN-DBS surgery. The effect of stimulation on postural parameters was less evident.
Conclusion: Our study revealed that stimulation and levodopa had similar effects on gait parameters, with stimulation proving more effective in enhancing gait speed and stride length.
Disclosure: Nothing to disclose.

EPO-156 | Mortality analysis in a Portuguese cohort of hereditary cerebellar ataxias

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Background and Aims: Hereditary cerebellar ataxias (HCA) are a heterogeneous group of diseases, associated with high morbidity and mortality. We aimed at analysing survival rate, causes, and place of death in a cohort of patients with HCA.
Methods: Prospective study of an HCA cohort, from the North of Portugal.
Results: Out of 252 patients with HCA, 38(15.1%) deceased, and 25(9.9%) lost to follow-up. Among those deceased, 20(52.6%) were male; 31(81.6%) had autosomal recessive (AR) HCA [16(42.1%) CANVAS; 4(10.5%) AOA4; 3(7.9%) HSP-MAG; 3(7.9%) FRDA; 1(2.6%) AOA1; 1(2.6%) HSP/ATX-PGN; 1(2.6%) ATX-PNPT1; 2(5.3%) undiagnosed]; and 7(18.4%) autosomal dominant (AD) HCA [5(13.2%) MJD/SCA3; 2(5.3%) undiagnosed]. Median age at death was 71.0 [IQR: 54.0–76.5] years. Overall survival was 35.6(±15.1) years after first symptoms, ranging from 19 (ATX-PNPT1) to 62 years (AOA1). AR-HCA patients lived with the disease for 39.4 (±13.8) years and AD-HCA patients for 20.0(±9.1) years ($p < 0.05$). Individuals with disease-causing variants survived for 42.5(±14.2) years, while those with disease causing repeats lived for 33.1(±11.8) years ($p < 0.05$). Causes of death were identified in 21 patients: 19(90.1%) infection, 1(4.8%) neoplasia, or 1(4.8%) stroke. Death occurred at the hospital in 13(34.2%), home in 8(21.1%), or nursing-home in 3(7.9%) [14(36.8%) unknown].
Conclusion: Life expectancy of HCA was lower than in general Portuguese population (71.0 vs. 81.5). Patients with AD-HCA or with disease-causing repeats had the lowest life expectancy. Survival rate, causes and places of death were similar to Huntington's disease. Knowledge on end-stage needs is crucial for patients and relatives advance-directive strategies and improving quality of life.
Disclosure: Nothing to disclose.

EPO-157 | The efficacy of Safinamide as an add-on treatment in improving the quality of life and the pain in Parkinson's disease

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Background and Aims: Safinamide was found to improve on-time without troublesome dyskinesia and reduce wearing off. Furthermore, we aimed to investigate its efficacy in enhancing patients' quality of life and reducing pain.
Methods: This study is a prospective interventional study in Parkinson's disease patients who are receiving levodopa, and experience motor fluctuations with > = 1.5 hours of "off" time throughout the day. If there were no tolerability issues within 4 weeks, the initial dosage of 50 mg/day was increased to 100 mg/day, and the patients continued with the 100 mg/day dosage for 18 weeks. The efficacy outcome was measured by the change from baseline to week 18 in the questionnaire examination of the quality of life (PDQ-39) and the pain (KPPS).
Results: In this study, we evaluated 196 patients using PDQ-39 and KPPS. The mean disease duration of them is 6.6 years, and the mean daily levodopa dose is 502.4 mg/day at baseline. At week 18, a significant improvement in the total PDQ-39 score was observed compared to baseline ($p < 0.001$). Moreover, each domain (Mobility,

Activities of daily living and Stigma) in PDQ-39 demonstrated a significant improvement from baseline. The assessment of pain using KPPS also showed a significant decrease at week 18 compared to baseline ($p=0.013$). Particularly, Safinamide significantly reduced Fluctuation–related Pain ($p=0.002$).

TABLE 1 PDQ-39 change after 18 weeks compared to baseline

Category	Baseline score (mean±SD)	Change [Week 18 - Baseline] (mean±SD)	P value
	N= 196	N= 196	
Total score	24.9±15.9	-2.7±10.3	<0.001*(WS)
Mobility	30.5±25.4	-4.4±18.7	<0.001*(WS)
Activities of daily living	26.4±23.3	-5.4±18.2	<0.001*(WS)
Emotional well-being	28.4±24.5	1.1±21.0	0.932(WS)
Stigma	30.7±27.9	-6.3±23.2	<0.001*(WS)
Social support	15.9±16.0	-1.5±13.9	0.131(WS)
Cognitions	23.6±21.0	-1.9±17.1	0.322(WS)
Communication	17.3±21.3	-1.9±13.2	0.061(WS)
Bodily discomfort	26.6±22.5	-1.1±20.9	0.605(WS)

(WS) Wilcoxon signed rank test
*: p-value < 0.05

TABLE 2 KPPS change after 18 weeks compared to baseline

Category	Baseline score (mean±SD)	Change [Week 18 - Baseline] (mean±SD)	P value
	N= 196	N= 196	
Total score	10.6±14.4	-1.5±11.3	0.013*(WS)
Musculoskeletal Pain	2.2±2.7	0.3±3.0	0.432(WS)
Chronic Pain	1.3±2.9	-0.3±2.7	0.126(WS)
Fluctuation-related Pain	2.6±6.0	-1.1±5.4	0.002*(WS)
Nocturnal Pain	2.0±3.7	-0.1±3.2	0.356(WS)
Oro-facial Pain	0.4±1.7	-0.1±2.1	0.312(WS)
Discolouration; Edema/swelling	0.7±2.6	-0.2±2.5	0.394(WS)
Radicular Pain	1.2±2.4	0.1±2.5	0.516(WS)

(WS) Wilcoxon signed rank test
*: p-value < 0.05

Conclusion: Safinamide at a dosage of 100mg/day demonstrated significant improvements in PDQ-39 scores and significant reductions in KPPS. These findings indicate that Safinamide contributes to enhancing patients' quality of life and reducing the pain, particularly pain associated with motor fluctuations

Disclosure: This Study sponsored by Eisai Korea Inc., Seoul, Republic of Korea.

EPO-158 | The DashPD-Consortium: Importance of addressing bone health and anticholinergics to achieve holistic care in Parkinson's

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Background and Aims: A dashboard incorporating clinical "prompts" of the often ignored "five vitals" of Parkinson's disease (PD) (Chaudhuri et al., 2022, Qamar et al., 2023) has been published based on expert opinion and patient preferences. In an ongoing international multicentre observation survey (DashPD) we collected data on awareness and documentation of bone health and anticholinergic (ACh)-index (risk factor for dementia and cardiovascular events) in PD in clinics.

Methods: This initial analysis refers to data from the ongoing DashPD Consortium as well as the UK-arm of the 'Nonmotor International Longitudinal Study' (NILS, UKCRN.10084). A questionnaire asking "yes", "no", or "not applicable" format was used. Focus was on bone health, falls, and documentation of the Ach-index.

Results: Data were collected between July 2022 to December 2022 ($N=906$ PD). Results show bone health assessment in only 21%, while only 9% had bone density scans, and vitamin D and calcium levels were recorded in 25%. Despite frailty assessment performed in 61% there was no documentation of any fall prevention strategies. ACh-index was measured in only 6% and no specific advice on dangers of ACh use was documented.

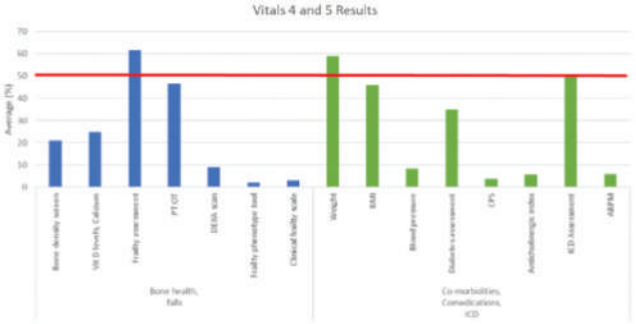

FIGURE 1 An extract of just vitals 4 and 5, from the multi-centre international observational survey analysis for the application of the Dashboard of Vitals in Neurology outpatient clinics.

Conclusion: This initial analysis of the DashPD-Consortium data, shows a glaring lack of awareness and documentation of bone health and Ach use related data which is likely to compromise patient health because of increased risk of fractures and negative effects of Ach use in PD.
Disclosure: Nothing to disclose.

EPO-159 | DysPKG project: Blinded clinical interrater reliability in assessing dyskinesia using the Parkinson's KinetiGraph (PKG)

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Background and Aims: In Parkinson's disease (PD), dyskinesia is levodopa-induced uncontrollable movements, which differ in phenomenology. We aim to visually recognise and characterise dyskinesia from reports using the validated Parkinson's KinetiGraph (PKG) and perform an interrater reliability analysis between independent clinicians to validate recognition of patterns of dyskinesia.
Methods: PKG reports with dyskinesia were identified from the UK-PKG database and two independent clinicians rated the dyskinesias (pattern and severity). Each clinician was given ninety-six patient PKG reports with the dyskinesia and bradykinesia graph. Raters were blinded to the patient's clinical assessment, medication, and history.
Results: PKG reports was assessed for daytime and night-time dyskinesia, with each further analysed for severity and characteristics of dyskinesia (figure 1). Cohen's K was performed to determine interrater reliability between two clinical raters in relation to presence of dyskinesia, severity of dyskinesia, and characteristic of dyskinesia. There was significant substantial agreement between the two clinicians' judgement for the presence, severity, and characterisation of dyskinesia at night-time (table 1). There was a significant substantial agreement for presence of daytime dyskinesia [k = 0.669 $p < 0.001$] and a significant moderate agreement for the severity of daytime dyskinesia [k = 0.555 $p < 0.001$]. However, there was only a fair agreement regarding the characterisation of daytime dyskinesia [k = 0.336 $p < 0.001$].

TABLE 1 Summary of Cohen Kappa (K) interrater agreement of PKG dyskinesia reports

	Cases (%)[1]	*K*[2]	95% CI[3]	p-value[4]	Strength of agreement[5]
Daytime Dyskinesia					
Presence	92.71	0.699	0.491 to 0.907	<.001	Good
Severity	70.83	0.555	0.416 to 0.694	<.001	Moderate
Characterisation	54.17	0.366	0.235 to 0.497	<.001	Fair
Night-time Dyskinesia					
Presence	94.79	0.753	0.547 to 0.959	<.001	Good
Severity	94.79	0.771	0.585 to 0.957	<.001	Good
Characterisation	92.71	0.66	0.446 to 0.874	<.001	Good

[1] Number of agreed cases between the raters from all reports analysed,
[2] Cohen's Kappa (*K*) measure of agreement,
[3] 95% confidence interval as calculated from the 65% CI of the Kappa standard error,
[4] Statistical significances, as defined as p<0.05,
[5] *K* interpretation of strength of agreement as suggested by Altman (1999) and adapted from Landis & Koch (1977).

TABLE 2 Level of agreement between raters about severity of dyskinesia

Daytime Dyskinesia severity	%	DKS range
Very mild	67.09	0.1-6.5
Mild	21.52	0.7-8
Moderate	6.33	6.2-12.5
Severe	5.06	6.5-123.3
Night-time Dyskinesia severity	**%**	**DKS range**
Very mild	66.67	1.7-8
Mild	0	0
Moderate	0	0
Severe	33.33	6.5-123.3

DKS: *dyskinesia score as defined by the PKG*

Conclusion: This is the first attempt to use visual interpretation of the PKG to grade dyskinesia. The results show there to be a role for the PKG, even if interpreted visually, in identifying and characterising dyskinesia. PKG analysis could therefore aid correct recognition and personalised therapies for dyskinesias in PD.
Disclosure: Nothing to disclose.

EPO-160 | Differences in prevalence of orthostatic hypotension between Parkinson's disease subtypes

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Background and Aims: Parkinson's disease (PD) is a clinically highly heterogeneous neurodegenerative disorder characterized by a wide range of motor and non-motor manifestations. The tremor-dominant (TD), mixed (M), and akinetic-rigid (AR) subtypes constitute one of the most commonly used classification systems. Orthostatic hypotension (OH), a common non-motor feature of PD, is linked to adverse outcomes and is evaluated with the modified Schellong test.
Methods: To investigate if patients with different motor subtypes also exhibit variations OH, we conducted a retrospective analysis

using data of inpatients admitted to our clinic, diagnosed with PD, based on the clinical diagnostic criteria of the Movement Disorders Society. The modified Schellong test was performed according to standard protocol.

Results: Of 1,809 patients included in the study, 1,121 were classified into AR-, 624 with M-, and 64 with TD-subtype. Interestingly, we found that patients with the AR-subtype exhibited significantly worse results in the modified Schellong test compared to patients with the M-subtype. Patients with the M-type were younger, had significantly worse motor function measured with the Unified PD Rating Scale part III but did not differ significantly in duration of disease or Hoehn and Yahr stage.

Conclusion: Our findings indicate differences in orthostatic regulation among PD motor subtypes (AR vs. M) and support the notion that PD patients with the AR motor phenotype may have distinct pathophysiological abnormalities, i.e., a prominent affection of noradrenergic pathways and a body-first pathogenesis. Further studies are needed to confirm these results, as they hold significant implications for personalized treatment and prognostic counseling in PD.

Disclosure: PO is an advisor for Stada. JK is an advisor and speaker for Desitin. CFA is an advisor for Zambon. WJ is an advisor and speaker for Abbvie, Bial, Desitin, Stada, UCB, and Zambon, The authors declare that they have no competing interests.

EPO-161 | Unmasking secondary parkinsonism: A case report of parkinsonism related to dural fistula

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Background and Aims: The most common cause for secondary parkinsonism is drug intake, but any disruption to the nigrostriatal dopaminergic pathway, such as a vascular insult or tumor, can prompt secondary parkinsonism. These secondary forms should always be considered in the differential diagnosis, as they often require specific therapeutic management, which may, in some cases, even lead to clinical reversal.

Methods: We present a case of a patient initially diagnosed with parkinsonism, later found to have a dural fistula, and experiencing clinical remission after undergoing fistula treatment.

Results: Presenting a 69-year-old woman who developed a progressive postural tremor, with a re-emerging and resting component. This tremor notably exhibited asymmetric predominance on the left side of the upper limbs, accompanied by bradykinesia, rigid-akinetic features, reduced arm swing, fragmented turning, and recurrent falls. The patient had no prodromal signs of synucleinopathy. DAT-SCAN revealed minimal asymmetry in the right putamen. Magnetic Resonance Imaging (MRI) revealed a dural fistula dependent on branches of the external carotids with drainage into the superficial and deep venous system. Angiography confirmed the diagnosis, and treatment led to a clear, progressive resolution of parkinsonian symptoms. We provide a comparative video of the neurological examination pre and post dural fistula embolization.

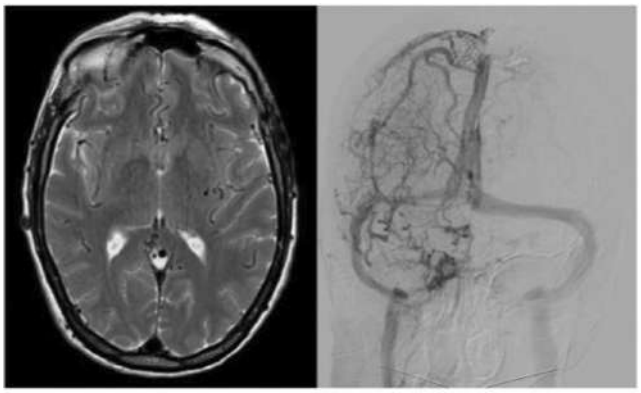

FIGURE 1 Cranial MRI with regurgitation of cerebral vessels and angiography revealing the dural fistula.

Conclusion: This case describes an uncommon cause of secondary parkinsonism- dural fistula, with limited instances reported in the literature. We suggest venous stasis as a potential trigger for dopaminergic pathway dysfunction, reflected in DAT-SCAN abnormalities. Emphasizing the need to rule out reversible conditions, as timely treatment offers symptom resolution.

Disclosure: No disclosure.

EPO-162 | Adult-onset PKAN with long disease duration: A case report and literature review

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Background and Aims: Pantothenate Kinase-Associated Neurodegeneration (PKAN), related to PANK2 gene mutation, is characterized by rapidly progressive movement disorders and cognitive impairment. While clinical presentation is typically in childhood, adult-onset forms have been described by milder clinical manifestations and slower disease progression[2], although data on the long-term outcome are scarce.

Methods: Case report and literature review.

Results: A 30 year-old man presented with slowly progressive speech disturbances and frequent falls. Over years, he had a gradual decline of intellectual functions, behavioral changes, orolingual dystonia with tongue protrusion, and spasticity leading to walking impairment. One brother and one sister had similar clinical manifestations with a slowly progressive course. At the age of 60, brain MRI revealed pathognomonic changes in the basal ganglia due to

iron accumulation. Genetic testing showed a homozygous c.965A>G mutation in the PANK2 gene. At 68 years of age, the patient's clinical and radiological manifestations remained stable, without further deterioration compared to the time of the diagnosis. Twenty-six additional cases of adult-onset PKAN with long-term follow-up available (all due to PANK2 gene mutation) were identified in the literature, for a total of 27 cases. The median age at symptoms onset was 30 (range, 20–67) and 9 (33.3%) were female. At last available follow-up, a median of 12 (range, 2–54) years from onset and 12 (44.4%) patients were alive.

Conclusion: The disease course in patients with adult-onset PKAN seems characterized by early development of symptoms followed by and a subsequent phase of clinical-MRI stability of years.

Disclosure: No disclosures.

EPO-163 | Phenotypic spectrum of GCH-1 pathogenic variants: A case series

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Background and Aims: Pathogenic variants in GCH1 are associated with dopa-responsive dystonia, and more rarely with Parkinsonism and spastic paraparesis (SP).

Methods: Analysis of clinical and genetic profile of patients with GCH1 pathogenic variants.

Results: Six female patients, from two families, were identified. Onset occurred in childhood, at 6.8 (±1.09) years. Presenting symptoms included foot dystonia ($n=5$, from the same family) and SP ($n=1$). Only dystonic patients had clinical deterioration throughout the day. There was progressive worsening over the years, into generalized dystonia, and marked SP. Clinical diagnosis, when observed at our center, was achieved 31.4 (±6.98) years after onset. Five, with dystonia, were treated with 200mg sustained-released levodopa/carbidopa and one, with SP, with 400mg immediate-release levodopa/carbidopa. All had major clinical improvement: dystonia resolution; improvement in spasticity and disappearance of Babinski and Trommer-Hoffman signs. With 24.0 (±16.4) years of follow-up, all retained clinical benefit. Dystonic patients were studied through single-gene testing of GCH1 [c.410T>A (p. (Met137Lys)], and SP with multigene panel for hereditary SP [c.541+1G>T (r.(spl))]. CSF analysis ($n=1$) disclosed reduced 5-HIAA level, increased HVA/5-HIAA ratio, 3-OMD, 5-OHTrp, reduced Pterins.

Conclusion: In our case-series the majority had a typical phenotype, of dopa-responsive dystonia, but an atypical presentation was also observed. Clinical diagnosis and treatment were only established three decades after onset, but still a dramatic response was observed. With this work we wish to contribute into the characterization of a treatable movement disorder.

Disclosure: All authors declare that they have no conflicts of interest related to the manuscript.

EPO-164 | A tablet based on artificial intelligence system to differentiate between Essential Tremor and Parkinson's disease

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Background and Aims: Patients with Essential Tremor were initially considered to have isolated tremor, but additional motor and non-motor features have been increasingly recognized. The term "Essential Tremor Plus" have started to be described in recent years with overlapping features that can make it difficult to differentiate between Essential Tremor (ET) and Parkinson's disease (PD). This study aims to evaluate on discriminatory features among ET and PD patients using handwriting analysis based on machine learning model.

Methods: We included a total of 90 participants: 30 ET, 30 PD and 30 age-gender matched controls. All participants were asked to perform five different handwriting tasks on a digitizer tablet recording various signals which are x-position, y-position and pressure. The tasks included drawing repetitive ellipses, spiral, repetitive digits and Latin character 'l' continuously eight times. Movement time, velocity and the size of writing were analyzed to characterise handwriting patterns and to compare between ET and PD patients.

Results: The results from this study showed that PD patients perform movements significantly slower than ET ($p=0.01$). Median time per repetition, median velocity and median acceleration of the 'l' task differed significantly between ET and PD ($p<0.05$). PD patients also produced smaller handwriting than ET as represented by smaller average width and height of the repetitive 'l' task compared to ET group ($p=0.035$).

Conclusion: We present a novel machine learning model that can serve as a complementary and promising support tool for the clinical diagnosis of ET and to differentiate between PD and ET.

Disclosure: Nothing to disclose.

EPO-165 | Differential diagnosis model in parkinsonian syndromes from calibrated diffusion tensor imaging

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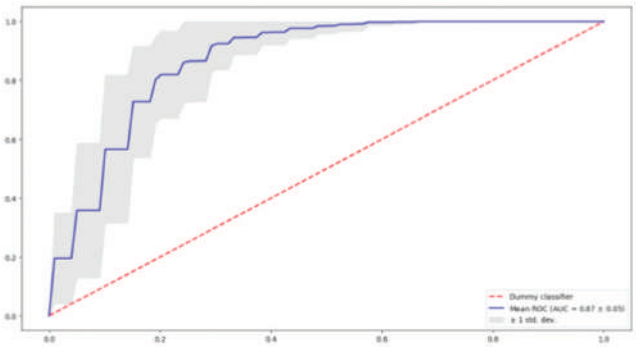
Background and Aims: Parkinson's disease (PD) poses a diagnostic challenge due to overlapping clinical features with other neurodegenerative disorders, such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). This study aimed at evaluating the ability of diffusion tensor imaging (DTI) biomarkers provided by brainTale-care, a CE-marked solution, to differentiate PD from MSA and PSP and deriving reliable differential diagnosis tool.
Methods: A total of 189 subjects presenting with parkinsonian symptoms (92 patients with PD, 45 with MSA and 42 with PSP) collected from three different clinical studies were included in the study. DTI data were processed by brainTale-care v3.0 (www.braintale.eu) to provide calibrated regional fractional anisotropy, radial, axial and mean diffusivity parameters. A classification model was implemented by using a support vector classifier and cross-validation procedure. Classification performances were assessed through receiver operating characteristics (ROC) analysis.
Results: The classification model between PD patients and MSA and PSP patients, achieved a mean area under the ROC curve of 0.87 ± 0.05, a mean specificity of 0.74 ± 0.10, and a mean sensitivity of 0.90 ± 0.07 (Figure 1).



Cross-validated receiver operating characteristic curve for the classification model PD versus MSA/PSP

Conclusion: This study shows that calibrated DTI biomarkers can be used to develop a classification model that efficiently differentiates patients with idiopathic PD and patients with MSA and PSP, two frequent parkinsonian syndromes. The easy access of diffusion tensor markers in clinical settings with brainTale-care platform paves the way for the use of MRI-assisted differential diagnostics in clinical settings as well as for drug development.
Disclosure: MG, VP, and JBM are BrainTale's employees. VP is cofounders of BrainTale.

MS and related disorders 1

EPO-166 | BeeWellwithMS Podcast: A pioneering platform for brain health advocacy in multiple sclerosis

A. Straukiene; F. Moxon; S. Hughes
Torbay and South Devon NHS Foundation Trust

Background and Aims: In response to the escalating need for comprehensive brain health education among people with Multiple Sclerosis (MS), this study examines the effectiveness of the "BeeWellwithMS" podcast www.beewellwithms.com, an innovative platform for disseminating brain health knowledge. As an EAN-certified brain health advocate, our objective was to leverage this medium to enhance understanding and self-management of MS.

Methods: We analyzed listener engagement and feedback from the podcast, which covers diverse MS-related topics, including brain health, emotional well-being, and lifestyle modifications. The podcast's evolution since its inception in 2020 was studied, with a focus on its expansion post-2024 following the integration of EAN-endorsed brain health advocacy strategies.
Results: Since incorporating EAN-certified brain health content, the podcast witnessed exponential growth in global listenership, with a significant increase in engagement from the MS community. Qualitative analysis of listener feedback highlighted an improved understanding of brain health issues and a more proactive approach to managing MS.

Downloads in the 25 countries, geolocation

Conclusion: The "BeeWellwithMS" podcast, underpinned by EAN's brain health initiatives, has proven to be a vital tool in educating and empowering the MS community. As an EAN brain health advocate, this platform signifies a novel approach to patient education, demonstrating significant potential in enhancing the quality of life for individuals living with MS.

Disclosure: No commercial support was received for this study. The podcast functions as an independent educational platform, with content driven by the latest research and patient needs in the MS community.

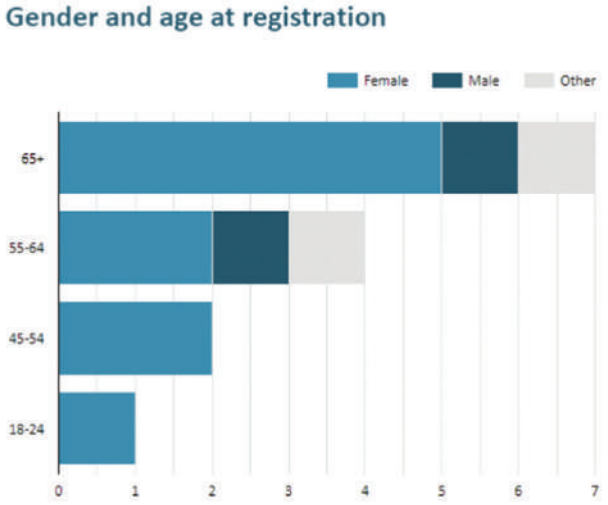
EPO-167 | Digital engagement in MS care: The impact of coordination on patient platform utilization

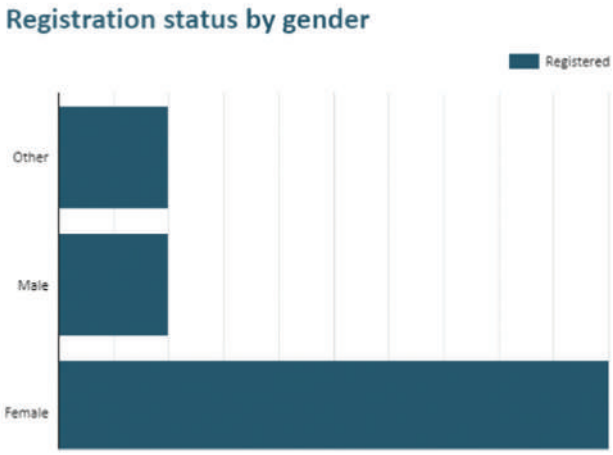
A. Straukiene; S. Hughes; F. Moxon
Torbay and South Devon NHS Foundation trust

Background and Aims: Innovative digital tools are reshaping MS care, aiming to enhance patient education and self-management. This study assesses the influence of dedicated coordination on user engagement with the MS Patients Know Best (MS PKB) platform.

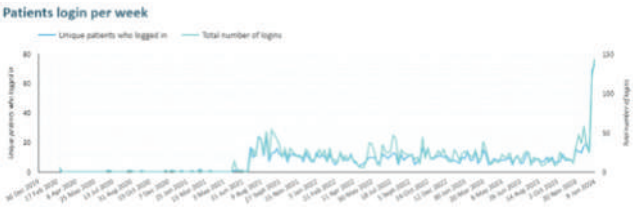
Methods: User engagement was analysed using the MS PKB dashboard, tracking weekly logins and registrations since its inception in 2016. In 2021, a dedicated coordinator role was introduced, providing personalized support and facilitating patient familiarity with the platform. Additionally, patient surveys and qualitative feedback assessments were conducted to measure user satisfaction and platform efficacy.

Results: Comparing 2016 to 2021, a substantial increase in engagement was observed. In 2016, user activity was minimal, with only 10 registered users. The appointment of a dedicated coordinator in July 2021 corresponded with an exponential increase in weekly logins to 130, a 225% rise from the preceding week, and total user registrations reached 100. A second peak in January 2024 demonstrated a further rise to 150 weekly logins. Qualitative feedback from patients showed high satisfaction, with the majority appreciating the platform's ease of use and the clarity of health information presented.

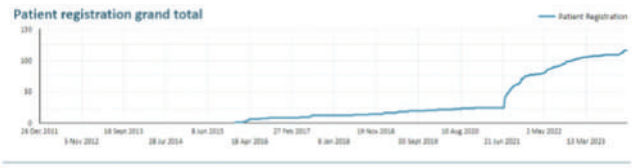




MS PKB demographics



MS PKB log in weekly



Total subscription of MS PKB

Conclusion: The implementation of a dedicated coordinator significantly boosted engagement with the MS PKB platform, as evidenced by increased logins and positive patient feedback. This suggests that

personalized guidance is crucial for maximizing the benefits of digital health tools in chronic disease management.

Disclosure: There are no financial conflicts of interest to declare. Data were sourced from hospital records within NHS guidelines.

EPO-168 | Thymic hyperplasia after autologous hematopoietic stem cell transplantation in multiple sclerosis: A case series

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Background and Aims: Reactivation of thymopoiesis in adult patients with autoimmune disorders treated with autologous haematopoietic stem cell transplantation (AHSCT) is supported by immunological studies. Thymic hyperplasia after AHSCT was previously reported in patients with systemic sclerosis, but, to our knowledge, it has not been described in multiple sclerosis (MS).

Methods: Monocentric case series of patients previously treated with AHSCT (BEAM/ATG regimen) for aggressive MS who performed a chest CT scan for clinical purposes. Chest CT exams before and after AHSCT were reviewed by a thoracic radiologist: thymic hyperplasia was defined as a rounded mass in the thymic loggia with density around 40HU and thickness >1.3cm.

Results: Fifteen MS patients were included (Table 1). The median time interval between AHSCT and CT scan was 2 (1–15) months. Thymic hyperplasia was detected in 3/15 (20%) patients in a scan taken 1 to 3 months after AHSCT; all these patients were females, and aged 30 to 40 years. Four further patients showed a thymic rebound, with increased thickness and soft-tissue lobulation. The time interval between AHSCT and CT was shorter in patients with thymic hyperplasia (median 1, range 1–2) vs those without (median 3; range 1–18); no differences in clinical-demographic characteristics were observed. All the patients were free from new focal inflammatory activity over median 36 months of follow-up (5–84).

TABLE 1 Clinical-demographic characteristics of the patients included.

	median	(range)
Age, years	40	(26 – 50)
Disease duration at AHSCT, years	16	(5 – 23)
Number of previous disease modifying treatments	3	(2 – 6)
EDSS at AHSCT	5.0	(1.5 – 6.5)
Time AHSCT – chest CT, months	2	(1 – 18)
	n	(%)
Sex, female	13	(87%)
MS form, relapsing-remitting	7	(47%)

Conclusion: Thymic hyperplasia was observed in 20% of MS patients recently treated with AHSCT. Our results suggest that AHSCT may promote thymic reactivation in MS patients, further supporting de-novo thymopoiesis as a cornerstone of immunoreconstitution after AHSCT.

Disclosure: Nothing to disclose.

EPO-169 | Treatment with anti-CD20 monoclonal antibodies after alemtuzumab in patients with relapsing-remitting multiple sclerosis

A. Llanes Ferrer[1]; D. Pérez Gil[1]; M. Espiño Martínez[2]; E. Rodríguez Martín[2]; A. Rodero Romero[2]; J. Fernández Velasco[2]; B. Martínez García[1]; P. Garay Albízuri[1]; R. Sainz Amo[1]; F. Rodríguez Jorge[1]; S. Sainz de la Maza[1]; E. Monreal Laguillo[1]; J. Masjuan[1]; M. Villar[2]; L. Costa Frossard[1]; J. Chico García[1]

[1]Neurology Department, Hospital Ramón y Cajal, Madrid, Spain; [2]Immunology Department, Hospital Ramón y Cajal, Madrid, Spain

Background and Aims: The aim of this study is to describe our experience using anti-CD20 monoclonal antibodies after alemtuzumab treatment failure in patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: Retrospective study including patients with high activity RRMS that received anti-CD20 monoclonal antibodies after alemtuzumab. Clinical and paraclinical data were reviewed, including lipid-specific oligoclonal IgM bands (LS-OCMB), plasmablasts over total peripheral blood mononucleated cells (PB/PBMC) before alemtuzumab first administration, B-lymphocytes over total lymphocytes (BL) before anti-CD20 initiation, and light chain neurofilaments in serum (sNfL), at baseline, 6 month and 1 year follow-up with anti-CD20 treatment. BL threshold was stablished at 15%, PB/PBMC at 0.1%, and sNfL at 10pg/ml.

Results: Twelve patients were included [75% women, 35.78 (26.7–41.3) years-old]. Patients received a median of 2 (2–3) cycles of alemtuzumab. An anti-CD20 was initiated because of severe disease exacerbation (relapses and/or new lesions on MRI). Nine patients received ocrelizumab, 2 ofatumumab, and 1 rituximab. At baseline, 3/11 (27.3%) had a median of 7 (1–14) gadolinium-enhancing lesions. All patients who underwent lumbar puncture (10/12) had LS-OCMB, 6/7 had PB/PBMC >0.1%, and 6/12 had baseline BL>15% (data of high B-cell activity). sNfL were elevated in 4/10 and normalized after 6 months of anti-CD20 therapies. Eight completed 1 year follow-up. Of them, 3 patients had new non-enhancing lesions, one with a relapse. None experienced confirmed disability progression. Five (62.5%) achieved NEDA3. Three patients developed hypogammaglobulinemia with no serious infections.

Conclusion: In our series, anti-CD20 monoclonal antibodies were a safe and effective alternative for RRMS patients with uncontrolled disease after alemtuzumab.

Disclosure: The authors report no relevant conflict of interest regarding the current study. JLCG has received honorary for speaking

engagements or consulting services from Biogen, Bayer, Bial, Bristol-Myers, Johnson&Johnson and Sanofi-Genzyme. RSA has received honorary for speaking engagements from Johnson&Johnson. EM received research grants, travel support or honoraria for speaking engagements from Biogen, Merck, Novartis, Roche, Almirall, Janssen, Bristol-Myers Squibb, and Sanofi-Genzyme. FRJ has received honorary for speaking engagements or consulting services from Bial, Biogen, Johnson&Johnson and Sanofi-Genzyme. SSM received payment for lecturing or travel expenses from Merck-Serono, Biogen, Sanofi-Genzyme, Roche, Janssen, and Novartis. LMV received research grants, travel support or honoraria for speaking engagements from Biogen, Merck, Novartis, Roche, Sanofi- Genzyme, Celgene and Bristol-Myers Squib. LCF received speaker fees, travel support, and/or served on advisory boards by Biogen, Sanofi, Merck, Bayer, Novartis, Roche, Teva, Celgene, Ipsen, Biopas, Almirall. The remaining authors have no conflicts of interest to declare.

EPO-170 | Neutropenia following ocrelizumab exposure in patients with multiple sclerosis: A single-center retrospective study

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Background and Aims: Aim of this study is to describe the occurrence of neutropenia, defined as a reduction of the absolute neutrophil count below 1.5×10^3/uL, during treatment with ocrelizumab in patients with multiple sclerosis (pwMS), as a single-center experience.

Methods: We retrospectively analyzed blood test including white blood cells count in particular neutrophils, lymphocytes and their subpopulation in consecutive pwMS at 1st, 3rd and 6th month after ocrelizumab infusions. Clinical and paraclinical variables were collected.

Results: Seventy-four pwMS were enrolled. 88% was affected by a relapsing-remitting form; 20% was treatment-naïve and 40.5% switched from a first line therapy. Among our cohort, eight patients (10.8%) developed neutropenia. In three cases neutropenia was severe, down to $0.08\times10^3/\mu$L. In six patients, neutropenia was registered one month after the infusion, whereas in two cases after 5 and 6 months, respectively. None of them developed any infection during neutropenia. In two cases G-CSF were administered after hematological evaluation. No MS relapses were reported during the treatment period.

Conclusion: Neutropenia after ocrelizumab treatment occurred in more than 10% of cases and it was usually observed within the first month after administration. In our cohort, all patients were asymptomatic and did not report viral or bacterial infections. Despite the quite frequent occurrence of neutropenia, our data confirm the safety of the medication under study, confirming previous data from literature.

Disclosure: L. Rossi has received funding for travel from Novartis. A. Dinoto has received funding for clinical trials from Roche and UCB, funding for travel from Horizon and research grants from Autoimmune Encephalitis Alliance and Encephalitis Internationals. S. Baldini has received funding research activity from Novartis. A. Bosco has received funding for travel and/or speaker honoraria from Sanofi, Roche, MBS, Teva and Biogen. Other authors have nothing to disclose.

EPO-171 | Early on-treatment NfL levels are associated with MRI changes up to 4 years in dimethyl-fumarate treated RRMS patients

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Background and Aims: Dimethyl fumarate (DMF) is widely used in the treatment of relapsing MS and has shown a significant reduction in neurofilament light chain (NfL) levels in CSF and blood. Understanding the relationship between NfL and MRI biomarkers may help improve management of DMF-treated patients.

Methods: The study included 42 treatment naïve newly diagnosed RRMS patients from the TREMEND phase IV trial (EudraCT 2014-000254-11). Plasma NfL and GFAP levels were measured using Simoa at baseline, month 6, 12 and 24. MRI data from baseline and up to year 4 since DMF initiation were included in the analysis. Annualized percent brain volume change (aPBVC) and lesion volume changes were determined with icobrain. Association between biomarkers was assessed with a generalized-linear-model with age as a covariate.

Results: Associations between plasma biomarkers and atrophy and lesion changes are respectively shown in Figures 1 and 2. From these, a few results seem to indicate a predictive value of plasma biomarkers in terms of brain atrophy and lesion changes. More specifically, NfL at 12 months was associated with brain atrophy measured with MRI available between year 1 and 4. Additionally, NfL at 6 months was associated with new and enlarging lesion volume at 2 and 3 years.

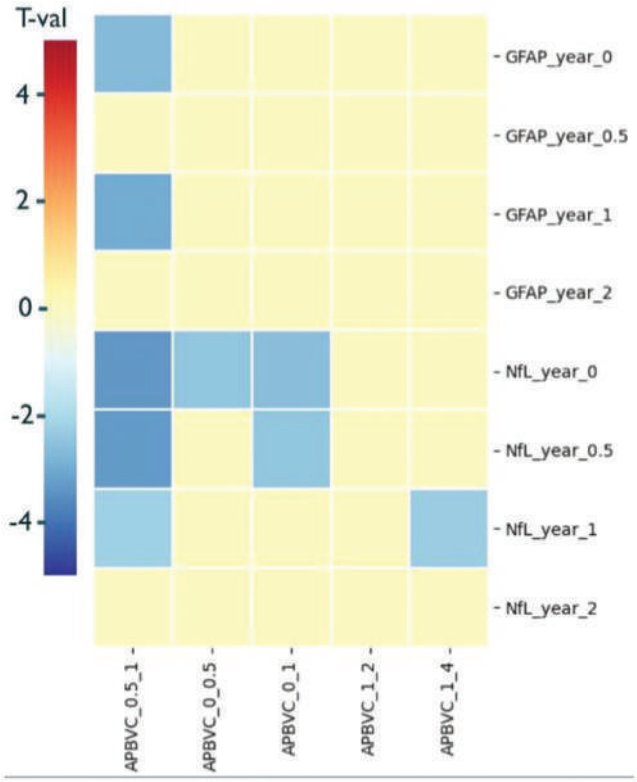

FIGURE 1 Associations between aPBVC measured in different intervals and plasma biomarkers collected at baseline, 6, 12 and 24 months. Only values with $p < 0.05$ shown.

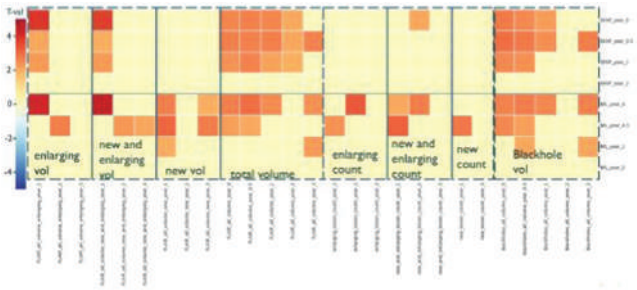

FIGURE 2 Associations between lesion volumes and plasma biomarkers collected at baseline, 6, 12 and 24 months. Only values with $p < 0.05$ shown.

Conclusion: In DMF-treated patients, higher plasma-NfL levels measured between 6 and 12 months are associated with subsequent lesion activity and brain atrophy, suggesting that NfL could be used additionally to MRI in the management of MS.

Disclosure: TS received travel grants from Biogen, Merck, Novartis and Roche, and research grants from Biogen, and served on advisory boards for Biogen, Merck and Novartis. NB and AR are employees of and hold stock/stock options in icometrix. JPM and JBL are employees of and hold stock/stock options in Biogen. ZI has received speakers' honoraria and/or research grants from Biogen, Roche, Sanofi, Novartis, Merck, Alexion, Bristol Myers Squibb, Lundbeckfonden, and Jascha Fonden, has been member of advisory boards at Alexion, Biogen, Sanofi, Merck, Roche, Novartis, has been member of the adjudication relapse committee in phase 3 trials, and has been principal investigator in studies sponsored by Biogen, Merck, Roche and Sanofi.

EPO-172 | Lesion parenchymal fraction as empirical support for the topographical model in MS

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Background and Aims: The topographical model of MS postulates that a combination of parenchymal tissue atrophy and lesion topography contribute to a patient's disability trajectory. We previously showed that the lesion parenchymal fraction (LPF = lesion load/parenchymal volume ratio) is a useful MRI correlate of MS clinical symptoms (Fig.1). Here we validate the differential impact between cerebral, infratentorial and cervical LPF for explaining disability.

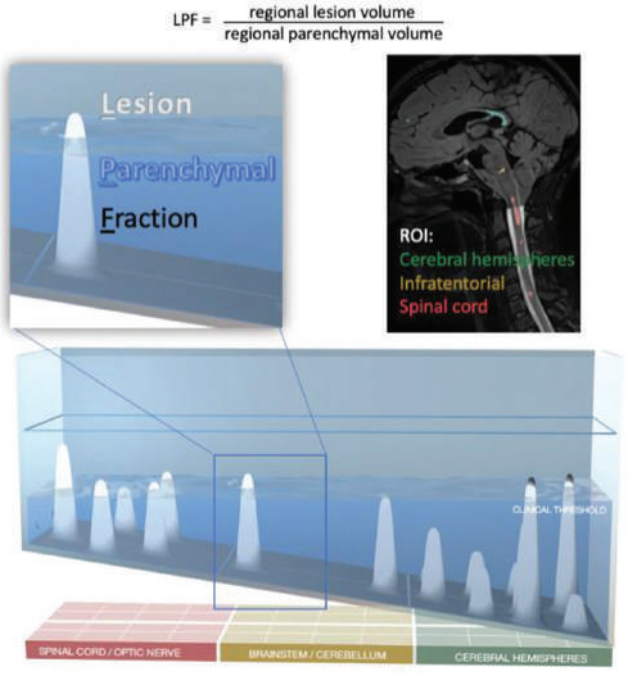

FIGURE 1 In the topographical model, the functional reserve is a water basin. Lesions (peaks) can cause clinical symptoms when crossing its surface. Lesion Parenchymal Fraction combines peaks (lesion volume) and water (parenchymal volume) in a single variable.

Methods: 78 MS patients with RRMS and SPMS were included (Table 1). Icobrain was used to measure T2-FLAIR lesions and parenchymal volumes on brain MRI, and adapted to measure T2 lesion volumes and mean upper cervical cord area. Per patient in the sample, the measurements were transformed into percentiles with respect to the remaining sample. A linear model for decoding EDSS with compartmental LPFs as factors was compared to models including lesion and/or parenchymal tissue measurements considered separately. Pearson correlation and root-mean-squared error (RMSE) between estimated and true EDSS were computed.

Results: Models with lesion or parenchymal measurements alone ranked last. In contrast, the LPF-model had the lowest error (RMSE = 1.638) and high correlation ($r = 0.275$). Setting the cerebral LPF coefficient to 1 in the LPF model, the ratio of the LPF coefficients was 2.5 for infratentorial and 3.8 for cervical. An individual case is depicted using LPF in Fig.2.

TABLE 1 Patient demographics

N	78
Gender - F	64
Age at onset (years, mean ± SD [min – max])	32.2±10.0 [15.0 - 59.0]
Clinical follow-up time (years, mean ± SD [min – max])	8.2±2.6 [3.6 - 17.1]
Number of brain MRI (mean ± SD [min – max])	5.1±3.1 [1.0 - 13.0]
brain MRI follow-up time (years, mean ± SD [min – max])	3.9±2.6 [0.0 - 8.8]
Number of spinal cord MRI (mean ± SD [min – max])	5.1±3.1 [1.0 - 13.0]
Spinal cord MRI follow-up time (years, mean ± SD [min – max])	3.9±2.6 [0.0 - 8.8]
Symptoms at Onset - Supratentorial - True N	11
Symptoms at Onset - Optic Pathways - True N	25
Symptoms at Onset - Brainstem-Cerebellum - True N	14
Symptoms at Onset - Spinal Cord - True N	32

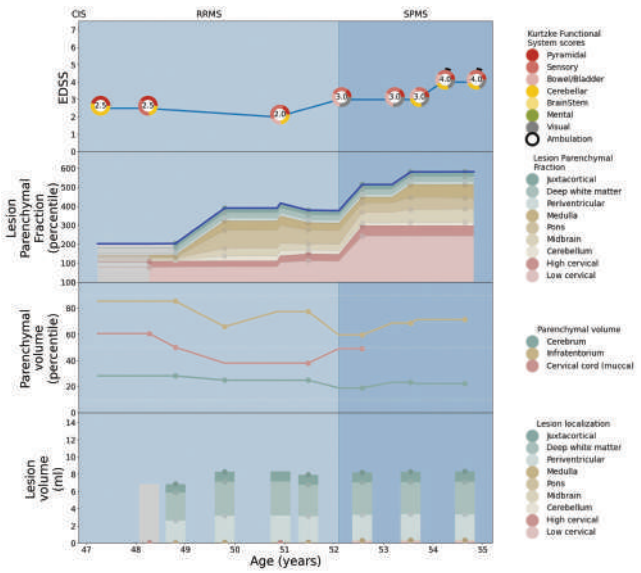

FIGURE 2 From bottom to top: Visualisation of lesion volume (bottom panel), parenchymal volume, the linear combination of local LPFs, resembling the longitudinal EDSS (top panel)

Conclusion: The results are in line with the topographical model describing proportional reserves for the spinal cord, infratentorium and cerebrum. LPF-based modelling helps explain disability by combining lesions and their topographical location with parenchymal reserve.

Disclosure: SCK: Dr. Krieger reports consulting or advisory work with Biogen, EMD Serono, Genentech, Novartis, Octave, Genzyme/Sanofi, and TG Therapeutics; non-promotional speaking with Biogen, EMD Serono, Novartis, and Genentech; and Grant and research support from Novartis, Biogen, BMS, and Sanofi. TB: Dr. Billiet is an employee of icometrix CM: Dr. Maes is an employee of icometrix TVP: Dr. Phan is an employee of icometrix NPdB: Dr. de Barros is an employee of icometrix WVH: Dr. Van Hecke is an employee of icometrix AR: Dr. Ribbens is an employee of icometrix TW: None KK: None LL: None JG: Dr. Garber reports research support from Biogen, and advisory work with Merck and Novartis. MHB: Dr. Barnett reports research grants from Genzyme-Sanofi, Novartis, Biogen, Merck and BMS; and is a Research Consultant for RxMx and Research Director for the Sydney Neuroimaging Analysis Centre.

EPO-173 | Identifying neuropsychological multiple sclerosis phenotypes using latent profile analysis

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Background and Aims: Multiple sclerosis (MS) patients may present with a high variability in cognitive and psychological (i.e. depression and fatigue) impairment. However, clinic-demographic features underpinning such variability are still lacking. Hence, phenotypic classification base on clinic-demographic features could alert clinicians for a close monitoring on these disability aspects of the disorder.

Methods: In this mono-centric cross-sectional study, we collected clinico-demographic and neuropsychological data for each MS patients. Neuropsychological assessment included BICAMS battery, Beck Depression Inventory and Modified Fatigue Impact Scale. We employed a latent profile analysis (LPA) to unveil latent neuropsychological phenotype in MS patients clustering individuals in unobserved groups.

Results: We enrolled 600 MS patients. Using LPA, we unveiled five neuropsychological phenotype: 1) unaffected patients, with normal cognitive and psychological scores; 2) mild Cognition Impairment,

showing mild reduction in cognitive scores; 3) mild-to-severe psychological impairment, showing increased psychological scores with normal cognitive scores; 4) mild neuropsychological impairment, showing mildly reduced cognitive scores, and increased psychological scores; 5) severe neuropsychological impairment, showing severely reduced cognitive scores, and increased psychological scores vs unaffected patients. Overall, cognitive and psychological impairment increases with physical disability. Older age is a determinant for psychological impairment independent from cognitive impairment. Relapsing-remitting and paediatric-onset patients are more likely in the unaffected and mild cognition impairment class, whilst progressive patients were mostly allocated in neuropsychological impaired class.

Conclusion: We identified five neuropsychological phenotypes in patients with MS that showed distinct clinical features. Clinicians should closely monitor neuropsychological disability level in patients with that specific characteristic.

Disclosure: All authors have nothing to disclose.

EPO-174 | Effect of siponimod on lymphocyte subsets in active secondary progressive multiple sclerosis and clinical implications

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Background and Aims: Circulating immune cells play a pathogenic role in multiple sclerosis (MS). However, the role of specific lymphocyte subpopulations is not unveiled yet. We aimed to investigate lymphocyte changes during siponimod treatment in active secondary progressive MS (aSPMS) and their associations with clinical outcomes.

Methods: We enrolled 46 aSPMS patients with 2-year follow-up after the start of siponimod treatment and 14 healthy controls (HCs). Clinical and laboratory data were collected at baseline, 3rd, 6th, 12nd, and 24th month for MS patients, and at baseline for HCs.

Results: At baseline SPMS patients presented with increased naïve regulatory T lymphocytes vs HCs. Over time, SPMS patients showed decreased T CD4+ (coeff.range = −24/−17), B (coeff.range = −3.77/−2.54) and CD4/CD8 ratio (coeff.range = −4.44/−0.67) from month 3 thereafter vs baseline, and reduced CD3+CD20+ lymphocytes from month 12 thereafter (coeff.range = −0.32/−0.24). Patients not experiencing disability progression while on siponimod treatment showed B reduction from month 3 (coeff.range = −4.23/−2.32) and CD3+CD20+ lymphocyte reduction from month 12 (coeff.range = −0.32/−0.24) vs patients experiencing progression.

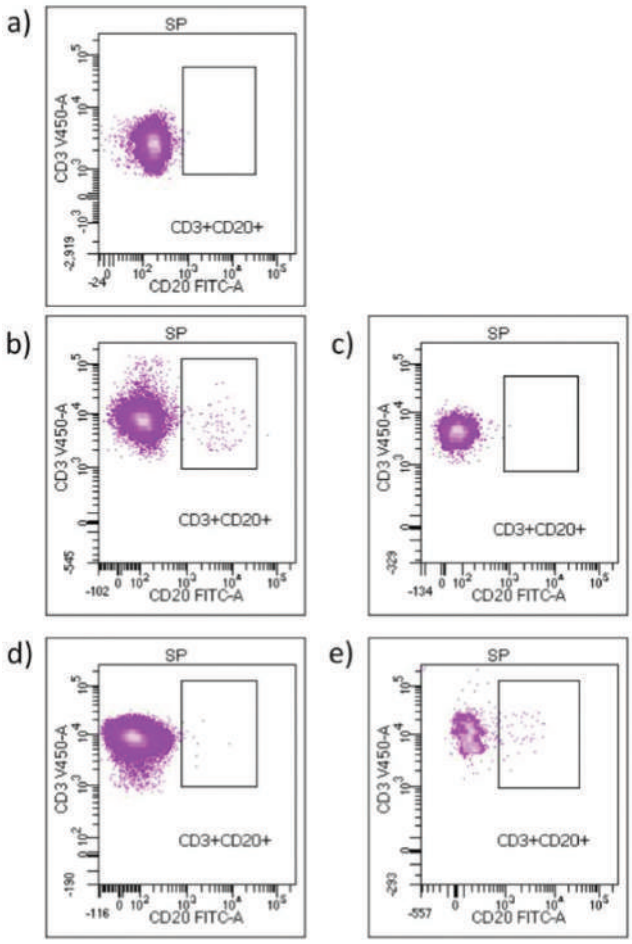

FIGURE 1 Flow cytometer dot plots. Plot of CD3+CD20+ cells in one male healthy control with no detectable cells (a), an aSPMS patient not progressing while on siponimod treatment at baseline with 0.9% CD3+CD20+ cells (b) and after 6 months from treatment

Conclusion: Patients treated with siponimod showed a T and B lymphocyte reduction, especially CD4+, CD3+CD20+, naïve regulatory T and memory regulatory B cells. Disability progression while on siponimod treatment was associated with a less pronounced effect on B and CD3+CD20+ lymphocytes.

Disclosure: MM has received research grants from the ECTRIMS-MAGNIMS, the UK MS Society, and Merck; honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. AC has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen and Novartis. MP has received research grants from Italian MS Foundation and Baroni Foundation, honoraria from HEALTH&LIFE S.r.l. and Biogen and sponsorship for travel/meeting expenses from Novartis, Roche and Merck. DC has received research grant from Merck. RL has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. VBM has received research grants from the Italian MS Society, and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. ALS, GS, VC, AF have nothing to disclose.

EPO-175 | An atypical case of macular oedema in ozanimod

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Department of Translational Biomedicines and Neurosciences, University of Bari Aldo Moro, Bari, Italy

Background and Aims: Macular edema (ME) is a well-established side effect of fingolimod (FTY), the first oral sphingosine 1 receptor S1PR modulator approved for MS. Ozanimod is a second-generation S1PR modulator, and it is thought to avoid some of the side effects associated with this class of drugs for its good bioavailability, high specificity and dose titration.

Methods: Our patient is a 48-year-old woman, diagnosed with RMS in 2009. She was treated with interferon beta 1a until 2013 when she switched to FTY for inefficacy. In 2016 FTY was discontinued for persistent and severe lymphopenia and interferon beta 1a was restarted. In August 2023, the patient began ozanimod after a new and symptomatic cervical lesion. However, in October, she reported a visual discomfort, therefore she underwent a complete ophthalmologic evaluation, including OCT, and was diagnosed as ME leading to ozanimod discontinuation.

Results: The incidence of FTY-associated ME in the population without pre-existing risk factors is approximately of 0.2%. ME was reported in 2882 (0.2%) participants during the ozanimod phase 3 trials, RADIACE and SUNBEAM, and in 0.4% participants during the long-term safety trial DAYBREAK. All cases of confirmed ME had pre-existing risk factors or confounding conditions. However, our patient did not present other risk factors and her pre-ozanimod ophthalmologic evaluation was normal.

Conclusion: This case highlights the risk of developing ME during ozanimod exposure. Further research is needed to better understand whether a long term exposition to different S1PR, with different drug sequencing, may be associated with higher risk of ME.

Disclosure: Dr Iaffaldano received personal fees from Merk, Novartis, Biogen, Roche, Alexion and Genzyme. Dr. Manni received compensation for travel grants, participation in advisory board and/or speakink activity from Biojen, Merck Serono, Sanofi, Novartis, Bristol MS, Janssen and Roche. Dr Paolicelli received personal fees from Sanofi, Merk, Biojen and Janssenn. Dr Bianco, Dr Guerra, Dr Intini, Dr Vitobello and Dr Oggiano have nothing to disclose.

EPO-176 | Validation study of a mobile app-based six-minute walking test compared to smartwatch measurements introduction

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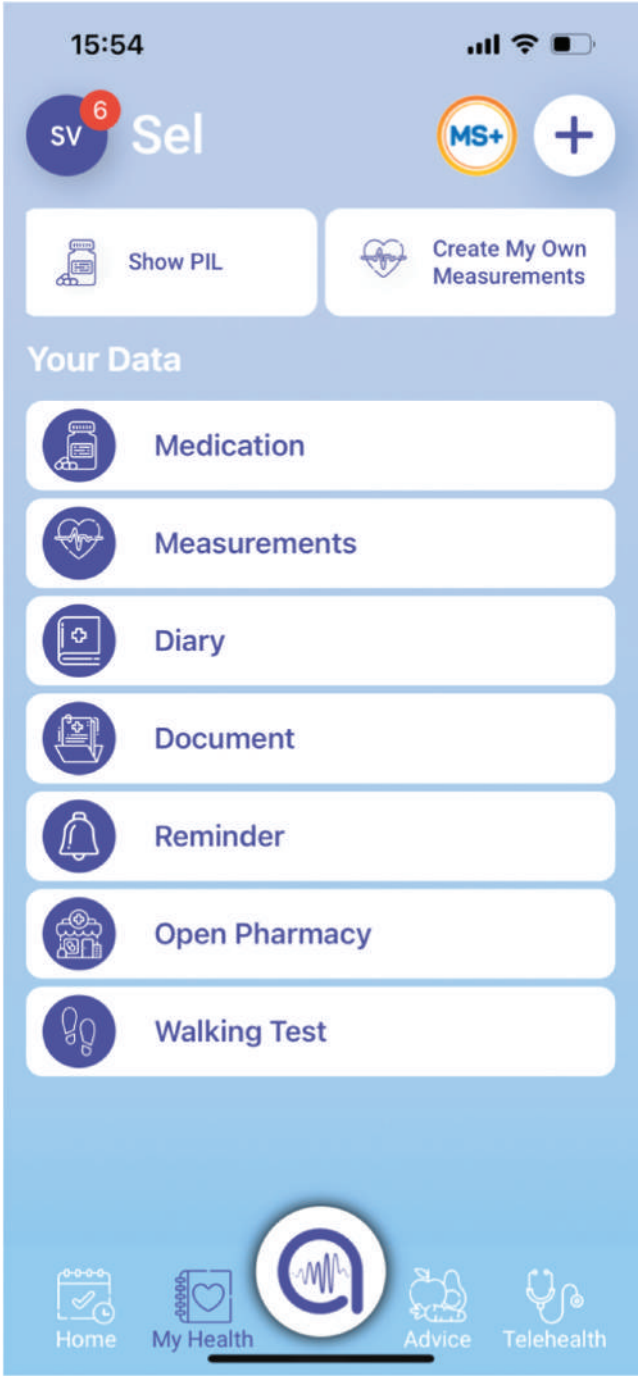
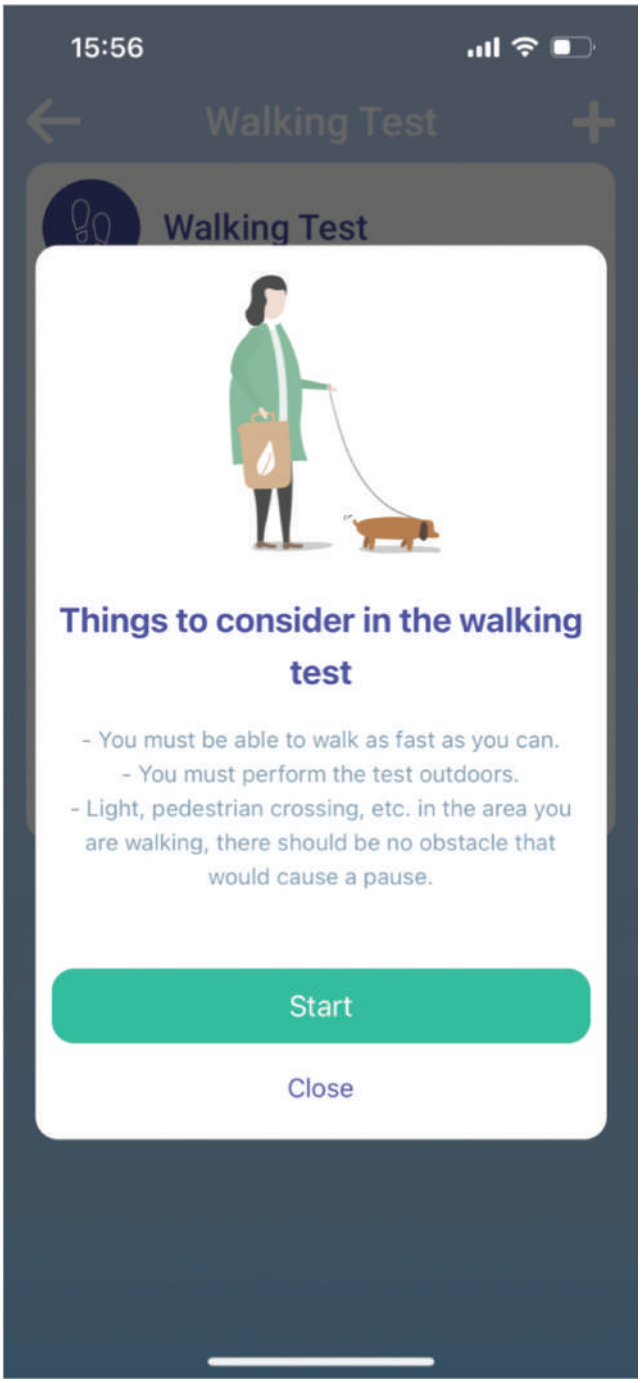
Background and Aims: The study focuses on validating a mobile app-based Six-Minute Walking Test (6MWT) by comparing its results with those obtained from a smartwatch in healthy adults. The aim is to measure the accuracy and reliability of the app-based 6MWT for potential clinical application in monitoring patients with chronic conditions like Multiple Sclerosis (MS)

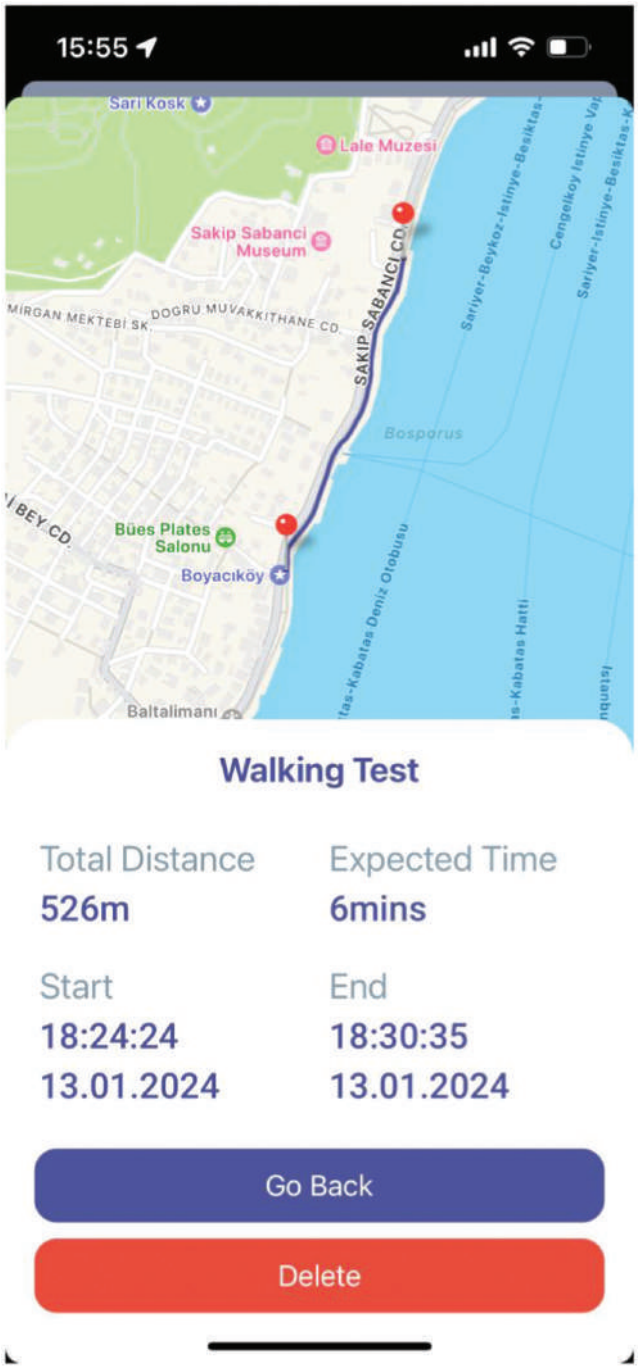
Methods: Twenty-one healthy adults with no comorbidities participated. E 6MWT performed using a mobile app (Albert Health / MS+) and a smartwatch (Apple Watch 7 or higher) two times. The smartwatch's accuracy was validated separately on a 150-meter course. Descriptive statistics and paired t-tests are used to compare the standard deviation and correlation between the app and smartwatch results.



Button of Test at App



Test guideline



Result of a patient

Results: The app-reported walking distance decreased by 13.62 meters on average (SD = 39.99 meters), whereas the smartwatch showed a smaller average decrease of 3.81 meters (SD = 13.22 meters) between the tests. Strong positive correlations were observed between the app and smartwatch in the 6MWT (Test 1: $r = 0.844$; Test 2: $r = 0.865$). Despite a slight decrease in mean walking distances over time, no statistically significant changes were noted (app p-value = 0.134, smartwatch p-value = 0.202).

Conclusion: The findings support that the app can be a reliable and accessible tool for assessing walking capacity, especially in clinical settings for managing chronic diseases like MS. Further research involving patients with MS is recommended to confirm the app's effectiveness in a clinical context.

Disclosure: Nothing to disclose.

EPO-177 | Calf muscles echo intensity in multiple sclerosis patients with lower limb spasticity treated with botulinum toxin

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[1]*Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy*; [2]*Neurology Unit, Sant'Andrea University Hospital, Rome, Italy*

Background and Aims: Lower limb spasticity (LLS) is common in people with multiple sclerosis (PwMS). Previous studies suggested that muscle echo intensity could affect the efficacy of botulinum neurotoxin A (BoNTA) treatment and altered calf muscles echo-intensity was reported in children with cerebral palsy and post-stroke patients with LLS. However, this was not investigated in PwMS.
Methods: Muscle tone and echo intensity of gastrocnemius lateralis (GL), gastrocnemius medialis (GM) and soleus muscles were assessed in 19 PwMS through the modified Ashworth scale (MAS) and the modified Heckmatt scale (mHS), respectively. Patients were dichotomized into those who underwent BoNTA treatment for ≥ 3 sessions (longer group, median duration of treatment 78 months, $N = 11$) or < 3 sessions (shorter group, median duration of treatment 7 months, $N = 8$). The difference between each pair of muscles in terms of MAS and mHS in the overall population and in both subgroups was evaluated.
Results: A significantly higher mHS score in GM compared to soleus was found in the overall population and both subgroups. A significantly higher mHS score in GL than in soleus was found in the overall population and in the shorter group but not in the longer group. No difference was found between GM and GL in terms of mHS and between all pair of muscle in terms of MAS.
Conclusion: In PwMS with LLS, GL and GM showed a higher echo intensity than soleus irrespective of BoNTA treatment duration. This preliminary observation could stimulate research on muscle alterations in PwMS and its potential effect on BoNTA efficacy.
Disclosure: Nothing to disclose.

EPO-178 | Framingham risk score and patient determined disease steps in relapsing remitting multiple sclerosis

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University of Foggia, Italy

Background and Aims: The associations between Multiple Sclerosis (MS) and cardiovascular diseases drawn from epidemiological studies have attracted much attention in the recent years.
Methods: The present study employed a monocentric, observational, retrospective cohort design. The primary study outcome was to describe in a cross-sectional fashion the FRS rate in our cohort of relapsing remitting MS patients regularly followed up and then, if any, to find association with patients. Patient Determined Disease Steps (PDDS). Cardiovascular risk was classified as follow: low if the FRS is less than 10%, moderate if it is 10% to 19%, and high if it is 20% or higher.
Results: s 229 were enrolled. The sample consists of 163 women (71.2%). FRS categories were distributed as follow: 97 (42.3%) patients had low FRS, 84 (36.7%) patients had moderate FRS and 48 (21%) patients had high FRS. In the univariable ordinal regression analysis, one point increase in the PDDS scale was associated with 24% risk of high FRS (vs low) (proportional OR = 2.426, 95% CI 1.660–3.545; $p < .0001$). The results were confirmed also by EDSS score, with one point increase in the EDSS score was associated with 19% risk of high FRS (vs low) (proportional OR = 1.953, 95% CI 1.429–2.669–1.04; $p < .0001$).
Conclusion: the FRS demonstrated an association with the patients 'perception of the disease as indicated by the PDDS. Careful attention should be given to addressing and treating cardiovascular risk factors, in addition to implementing lifestyle changes, when managing MS in the long term
Disclosure: Nothing to disclose.

EPO-179 | Silent progressive brain atrophy in clinically stable neuromyelitis optica a comparative proof-of-concept study

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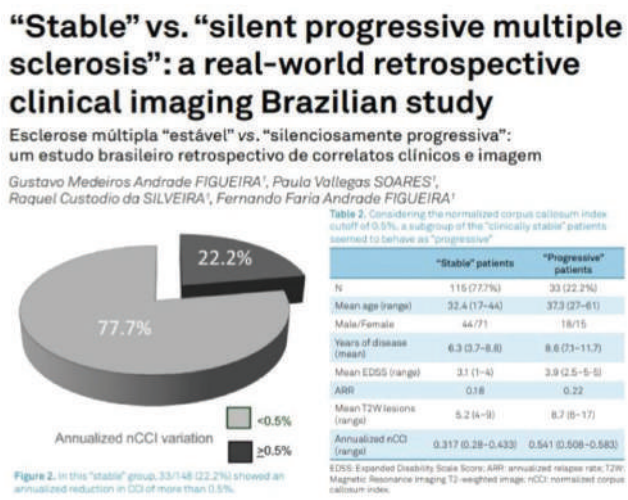
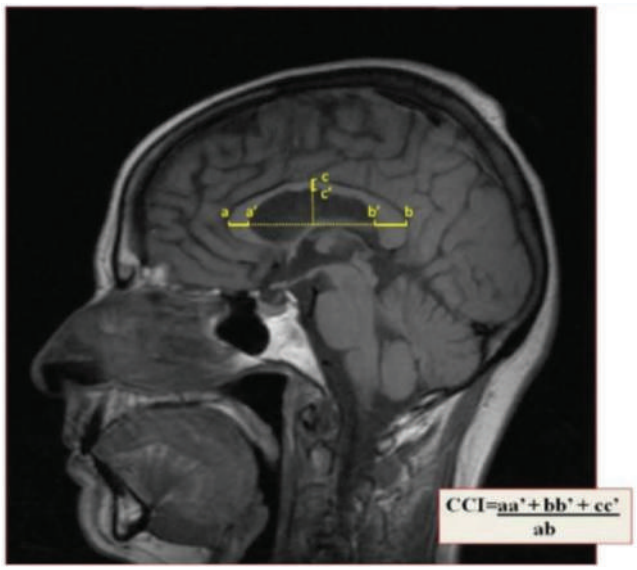
Hospital São Francisco

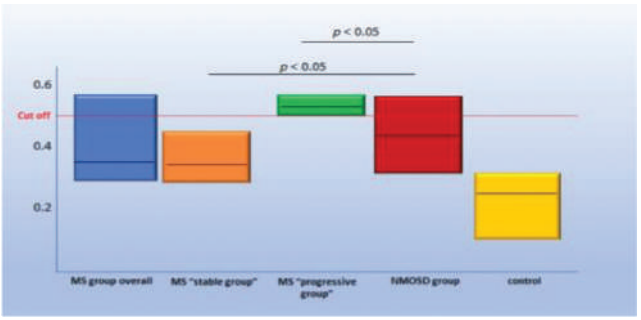
Background and Aims: Recently we demonstrated progressive corpus callosum atrophy occurring even in clinically stable multiple sclerosis (MS) patients, but literature data on brain atrophy in neuromyelitis optica spectrum disorder (NMOSD) patients are still scarce.
Methods: We compared longitudinal MRI data of 14 NMOSD (Wingerchuk, 2015), 148 relapsing remitting MS (McDonald 2001), and 23 control patients, followed regularly with clinical and imaging studies available on baseline and 5 years. All patients had at least 3 conventional MRI available studies with proper protocol leading to a reliable evaluation of activity and progression in at least 5 years. Clinical evaluation included annualized relapses rate and EDSS evolution at least annually, for at least 5 years. MRI data included gadolinium positive lesions or new/enlarging T2W lesion as well as the annualized evolution of corpus callosum index (CCI), measured as previously described.
Results: Patients with NMOSD were older and had EDSS scores higher than MS patients. Their mean CCI annual reduction was 0.477, ranging from 0.372 to 0.569, close to cut off and values situated between the stable and the progressive MS group.



Figueira G., et al. Arq Neuropsiquiatr 2022;80(4):405–409



Corpus callosum index (CCI): a two-dimensional measurement using an orthogonal semi-automated linear model, applied to a conventional mid-sagittal T1W MRI sequence. Figueira F., et al. Arq Neuropsiquiatr 2007;65(4-A):931–935



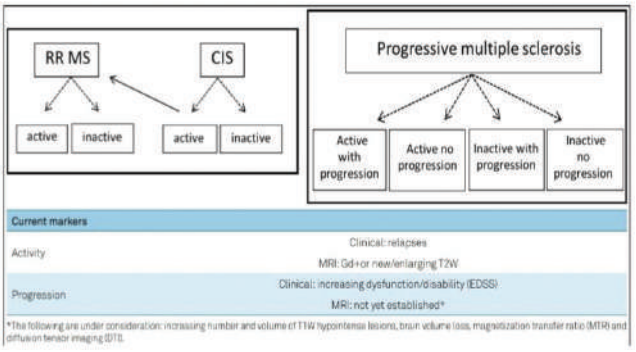
On NMOSD stable group mean CCI annualized reduction was 0.477 (range = 0.372 to 0.569), close to cut off and values were situated between the stable and the progressive MS group

Conclusion: In this small sample of 14 apparently "stable" NMOSD patients over 7 years follow up period, CCI was able to detect a reduction quite similar to that we see on relapsing remitting MS ones. More robust data are required, with a more significant sample, stratifying for clinical phenotypes and serologic status, but it seems reasonable to state that brain volumetry technique might be a useful tool for monitoring the real state of treatment response.
Disclosure: Nothing to disclose.

EPO-180 | "Stable" vs. "silent progressive multiple sclerosis": A real world retrospective clinical imaging Brazilian study

G. Medeiros Andrade Figueira; F. Faria Andrade Figueira; P. Vallegas Soares; R. Custodio Silveira; V. Tavares Carvalho Crelier; M. Nunes Ferreirinha Leite de Castro
Hospital São Francisco

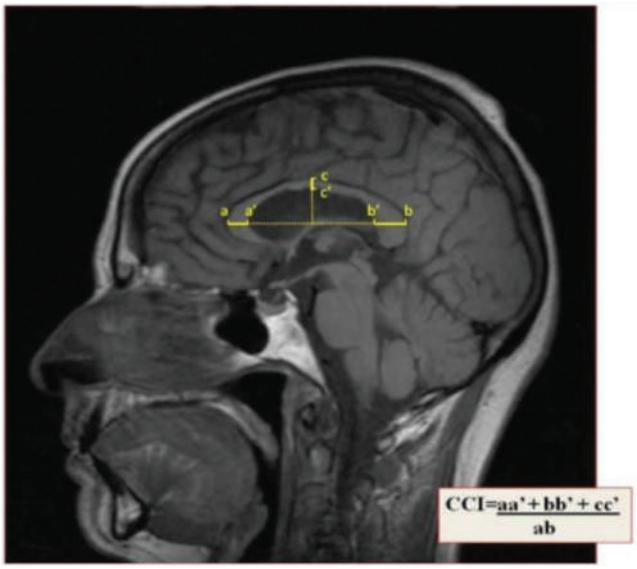
Background and Aims: Clinical and imaging are required to characterize activity and progression in MS. Parameters for activity are well defined but not progression ones. Ideal target for long term treatment includes neither clinical nor imaging signs of disease as well as no brain atrophy.



New MS phenotypes propose clinical and imaging requirements to characterize activity and progression in MS patients.

Methods: Comparative clinical-imaging study focusing on MRI brain volumetry. 174 consecutive relapsing remitting MS patients (McDonald 2001) were studied focusing on activity and progression. Annual clinical evaluation (relapse rate and EDSS) and MRI data as well as annualized evolution of corpus callosum index (CCI) were compared.

Results: From 174 patients 148 were considered clinically "stable" based on EDSS. However, 33 (22.2%) out of this group showed annualized reduction of more than 0.5% on CCI, cut-off to define significant brain atrophy.



Corpus callosum index (CCI): a two-dimensional measurement using an orthogonal semi-automated linear model, applied to a conventional mid-sagittal T1W MRI sequence.

N = 115 (77.7%)	N = 33 (22.2%)
32.4 (17 - 44)	37.3 (27 - 61)
44/71 *	18/15 *
6.3 (3.7-8.8) **	8.6 (7.1-11.7) **
3.1 (1-4)	3.9 (2.5-5.5)
0.18	0.22
5.2 (4-9)	8.7 (6-17)
0.317 (0.28-0.433) **	0.361 (0.308-0.583) **

Among 148 apparently "stable" MS patients over at least 7 years follow up period, 1/5 showed significant progressive brain atrophy.

Conclusion: Among apparently "stable" relapsing-remitting MS patients, 1/5 showed significant brain atrophy over at least 7 years follow up period. We consider reasonable to suggest that MRI volume sequences should be included in follow-up protocols, providing information on the real treatment response status.
Disclosure: Nothing to disclose.

MS and related disorders 2

EPO-181 | Echopraxia, an underrecognized clinical sign in multiple sclerosis: A biological and neuroimaging framework

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[1]University Hospital Dr. Josep Trueta of Girona; [2]Unit of Neuroimmunology and Multiple Sclerosis of Girona

Background and Aims: The study investigates echopraxia, an unrecognized clinical sign, in the context of multiple sclerosis (MS) and explores its potential association with cognitive decline. Echopraxia, a developmental element in social learning, typically disappears with central nervous system maturity. While observed in dementias, Gilles de la Tourette syndrome, and schizophrenia, its occurrence in MS has not been previously documented. The study hypothesizes that echopraxia may serve as a predictor of cognitive impairment in MS patients.
Methods: The research involved 21 patients with relapsing-remitting multiple sclerosis (RRMS) at the University Hospital Dr. Josep Trueta of Girona. Two cohorts, matched for age, gender, and clinical features, were established: one with 13 RRMS patients exhibiting echopraxia (RRMSwE) and another with 11 control RRMS patients. Tractography was used to identify morphological alterations in the cingulate gyrus, a region implicated in echopraxia pathogenesis. Circulating miRNAs in plasma from MS patients with and without echopraxia were also analyzed.
Results: Patients with echopraxia, particularly those with affective disorders had lower cingulate fiber numbers. Circulating miRNA analysis revealed that miR-143-3p and miR-181c-5p were twice less abundant in RRMSwE compared to RRMS patients. These miRNAs have been associated to cognitive impairment in patients with MS.
Conclusion: Atrophy of cingulum measured by tractography might be a radiological marker of echopraxia in patients with affective disorders such as depression. Some miRNAs (miR-143-3p and miR-181c-5p) involved in the cognitive impairment associated to MS could be related to echopraxia. Thus, echopraxia emerges a potential biomarker for predicting cognitive decline in patients with RRMS.
Disclosure: Nothing to disclose.

EPO-182 | Comparing adult-onset and late-onset multiple sclerosis: A real-world study

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Background and Aims: The clinical presentation of multiple sclerosis (MS) may vary according to onset age. This Finnish retrospective registry study compares clinical characteristics of older adults (65+) with adult-onset MS (AOMS, onset at 18–49 years) and late-onset MS (LOMS, onset after 50 years).

Methods: Utilizing the Finnish MS registry, we analysed data of all older adults with MS in the catchment area of Tampere University Hospital (TUH, approximately 500,000 inhabitants) as of November 5th, 2023. Exclusions comprised patients with paediatric onset MS or unknown onset age.

Results: Altogether 248/1395 (17.8%) individuals from the catchment area of TUH were included, with 207/248 (83.5%) classified as having AOMS and 41/248 (16.5%) as having LOMS. Demographic details are presented in Table 1, age distribution in Figure 1 and MS diagnoses in Figure 2. At data acquisition, most patients had a progressive disease course (160/248, 64.5%), but primary progressive MS (PPMS) was more common in LOMS (15/41, 36.6%) compared to AOMS (26/207, 12.6%). No difference in disability outcomes emerged after 65 years. Among individuals with a current or previous relapsing-remitting disease course, those with LOMS exhibited more relapses after 65 years (6/15, 40.0% of RRMS patients) than those with AOMS (11/130, 8.5% of RRMS patients). Disease-modifying therapies had been used by 49/130 (37.7%) and 8/15 (53.3%) of relapsing remitting AOMS and LOMS patients, respectively.

TABLE 1 Demographic details. AOMS, adult-onset MS; LOMS, late-onset MS; CIS, clinically isolated syndrome; RRMS, relapsing-remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS; EDSS, Expanded Disability Status Scale.

		Data available AOMS, LOMS	AOMS (n=207)	LOMS (n=41)
Age				
At disease onset	years, mean (SD)	207; 41	36.5 (8.4)	55.2 (5.4)
At diagnosis (excluding CIS)	years, mean (SD)	207; 41	43.7 (9.9)	56.8 (7.0)
At data acquisition	years, median (min-max)	207; 41	71.7 (65.0-91.9)	77.4 (65.1-90.1)
Disease duration from onset	years, mean (SD)	207; 41	35.9 (9.7)	21.1 (8.0)
Sex category		207; 41		
Female	n (%)		147 (71.0)	26 (63.4)
Male	n (%)		60 (29.0)	15 (36.6)
Smoking		155; 28		
No	n (%)		91 (58.7)	19 (67.9)
Yes	n (%)		27 (17.4)	4 (14.3)
Quit	n (%)		37 (23.9)	5 (17.9)
Diagnosis / phenotype				
Initial		207; 41		
CIS	n (%)		42 (20.3)	8 (19.5)
RRMS	n (%)		100 (48.3)	12 (29.3)
SPMS	n (%)		25 (12.1)	2 (4.9)
PPMS	n (%)		22 (10.6)	15 (36.6)
Unspecified	n (%)		18 (8.7)	4 (9.8)
At data acquisition		207; 41		
RRMS	n (%)		56 (27.1)	8 (19.5)
SPMS	n (%)		105 (50.7)	12 (29.3)
PPMS	n (%)		26 (12.6)	17 (41.5)
Unspecified	n (%)		20 (9.7)	4 (9.8)
EDSS				
last available visit after the age of 65 years	median (min-max)	114; 29	6.25 (0-9.0)	6.5 (1.5-8.0)

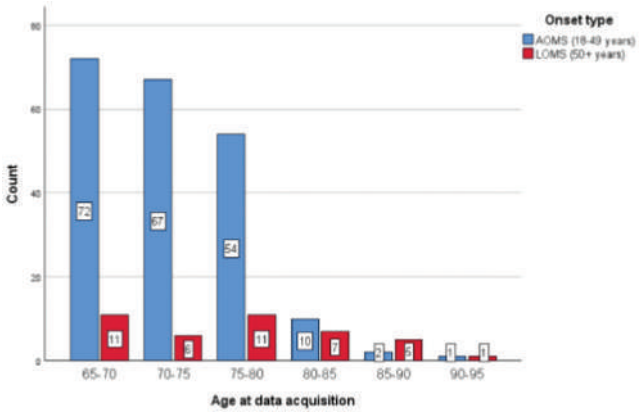

FIGURE 1 Age distribution in the study sample at data acquisition. AOMS, adult-onset MS; LOMS, late-onset MS.

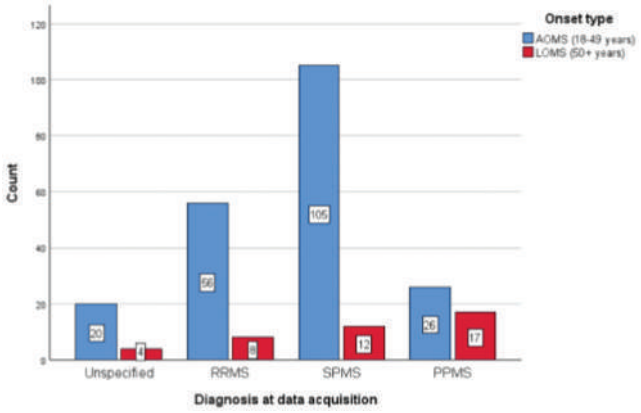

FIGURE 2 Distribution of diagnoses at data acquisition. AOMS, adult-onset MS; LOMS, late-onset MS; RRMS, relapsing-remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS.

Conclusion: Older adults with MS frequently exhibit a progressive disease course, and PPMS is particularly common in people with LOMS. However, in those with relapsing-remitting LOMS, relapses may sometimes persist beyond 65 years.

Disclosure: KA, IK and IR have no disclosures relevant to this study. HK is the chair of the Finnish Multiple Sclerosis Current Care Guidelines working group. IR and HK contributed equally.

EPO-183 | Clinical presentation of multiple sclerosis in older adults

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Background and Aims: Older adults (65+) with multiple sclerosis (OAwMS) may carry substantial disease burden from prior activity or progression. However, limited data exists on their characteristics. We aimed to assess the clinical presentation of OAwMS in Finland.
Methods: OAwMS treated in Tampere University Hospital (TUH), Finland, were identified from the Finnish MS registry as of 5th December 2023. Clinical variables were analysed using summary statistics.
Results: At data acquisition, the Finnish MS registry included 13,037 subjects (26.8% aged 64 or older) of which 1395 were treated in TUH. Of these, 264/1395 (18.9%) were identified as OAwMS. Table 1 and Figure 1 present clinical characteristics and age distribution. Most patients exhibited a progressive disease course at data acquisition (170/264, 64.4%). Disease-modifying therapy (DMT) had been used by 60/150 (40.8%) patients with relapsing-remitting MS (RRMS), as well as 3/40 (7.7%) patients with secondary progressive MS who lacked a previous RRMS diagnosis and 1/46 (2.2%) patients with primary progressive MS. Only one patient with RRMS was currently on disease modifying therapy (DMT). After 65, relapses occurred in 18/150 (12.0%) patients with a current or previous RRMS. The median Expanded Disability Status Scale (EDSS) at the last available visit after the age of 65 years was 6.5 (range 0–9.0). Comorbidities were present in 205/264 (77.9%) patients.

TABLE 1 Demographic details of the study sample. SD, standard deviation; CIS, clinically isolated syndrome; RRMS, relapsing-remitting MS; SPMS, secondary progressive MS; PPMS, primary progressive MS; EDSS, Expanded Disability Status Scale.

		Data available		
Age				
At disease onset	years, mean (SD)	255	38.9	(11.2)
At diagnosis (excluding CIS)	years, mean (SD)	264	45.4	(10.8)
At data acquisition	years, median (min-max)	264	72.5	(65.0-91.2)
Disease duration from onset	years, mean (SD)	255	32.4	(11.8)
Sex category		264		
Female	n (%)		185	(70.1)
Male	n (%)			
Smoking		193		
No	n (%)		116	(60.1)
Yes	n (%)		32	(16.6)
Quit	n (%)		45	(23.3)
Diagnosis / phenotype				
Initial		264		
CIS	n (%)		51	(19.3)
RRMS	n (%)		117	(44.3)
SPMS	n (%)		28	(10.6)
PPMS	n (%)		40	(15.2)
Unspecified	n (%)		28	(10.6)
At data acquisition		264		
RRMS	n (%)		64	(24.2)
SPMS	n (%)		125	(47.3)
PPMS	n (%)		45	(17.0)
Unspecified	n (%)		30	(11.4)
EDSS				
last available	median (min-max)	243	6.0	(0-9.0)
last available after the age of 65 years	median (min-max)	152	6.5	(0-9.0)

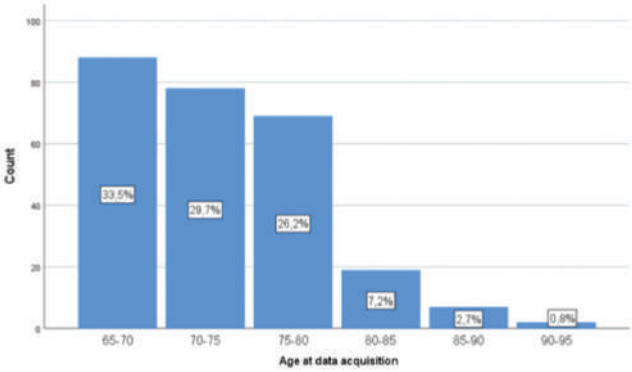

FIGURE 1 Age distribution in the study sample.

Conclusion: Most OAwMS had a progressive disease course, marked disability and comorbidities. Only one subject was on DMT. Treatment of OAwMS should adopt a multidisciplinary approach, focusing on rehabilitation, symptomatic treatment, and management of comorbidities in contrast to DMT.
Disclosure: IK, KA and IR have no disclosures relevant to this study. HK is the chair of the Finnish Multiple Sclerosis Current Care Guidelines working group. IR and HK contributed equally.

EPO-184 | Follow-up of NMOSD course by using sensor-based gait analysis

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[1]*Movement Analysis Laboratory, Koç University Research Center for Translational Medicine (KUTTAM), Koç University, Istanbul, Turkey;* [2]*Department of Neurology, School of Medicine, Koç University, Istanbul, Turkey*

Background and Aims: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune astrocytopathy affecting the central nervous system. Despite advancements in targeting pathogenic factors like AQP4-IgG, understanding the clinical course during relapse-free periods and the impact on gait and balance remains underexplored. This pilot study employs sensor-based gait analysis to assess NMOSD progression over one year.
Methods: Patients diagnosed with NMOSD underwent gait and balance assessments at initial, six-month and one-year visits using APDM OPAL sensors performing 2 MWT, T25FW, and various balance tasks. Paired Student t-tests compared the first visit to six months and one year, while mixed-effects analysis and Holm-Sidak's tests assessed changes across three visits.
Results: Thirteen NMOSD patients participated, with four completing six months and three completing one-year visits. Paired t-test

showed no change in gait and balance, but a trend emerged in mixed-effect analysis, suggesting decreased double support ($p=0.09$), increased midswing elevation ($p=0.09$), increased single limb support ($p=0.07$) and decreased terminal double support phase ($p=0.08$). Most parameters were successfully matched except toe-out angle, coronal ROM, and turn angle during gait analysis. Balance parameters when eyes were closed, feet apart on foam, and feet together did not change throughout a year of analysis in three visits conducted with mixed-effect analysis.

Conclusion: This ongoing study aims to reveal sensor-based gait analysis to monitor disability in NMOSD. Continuous tracking of the disease course is essential due to unpredictable prognosis. Highlighting parameters with matching success is crucial for effective disease follow-up, urging an increase in participant numbers for robust outcomes.

Disclosure: Nothing to disclose.

EPO-185 | Seizures in inflammatory demyelinating disorders of the central nervous system

Ö. Ertürk Çetin; İ. Güngör Doğan; Ü. Zanapalıoğlu; F. Yadi; D. Çetinkaya Tezer; S. Demir

Department of Neurology, University of Health Sciences, Sancaktepe Şehit Prof Dr İlhan Varank Training and Research Hospital

Background and Aims: Multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD), may be associated with acute symptomatic seizures and chronic epilepsy as well. The clinical features of the seizures and/or accompanying epilepsy seen in each disease group may vary. We aimed to describe the clinical features of seizures and epilepsy in our demyelinating patient population.

Methods: We retrospectively analyzed patients who were followed up in our tertiary referral center between 2019 and 2024. Those with a definite diagnosis of MS, NMO and MOGAD were identified. Patients who had at least one seizure before, simultaneously or after the diagnosis of demyelinating disease were included in the study.

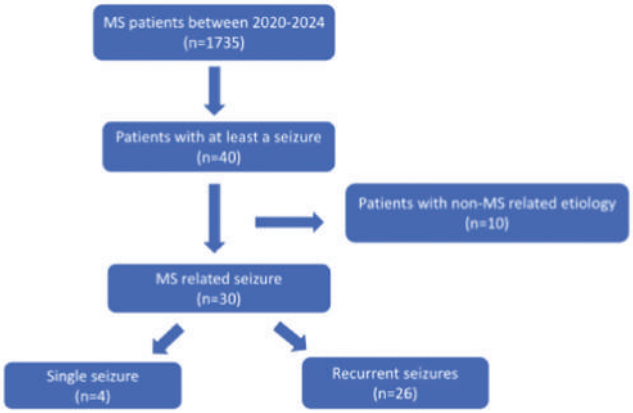
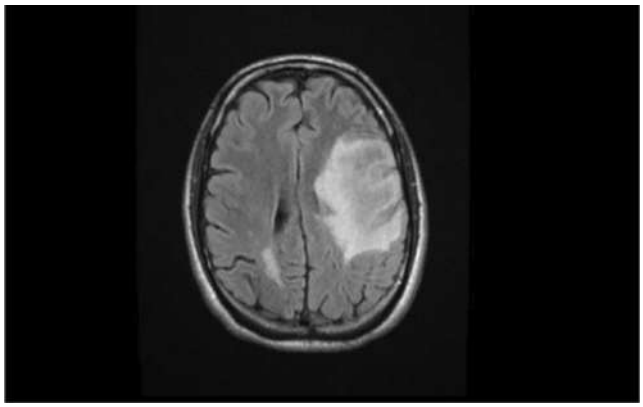
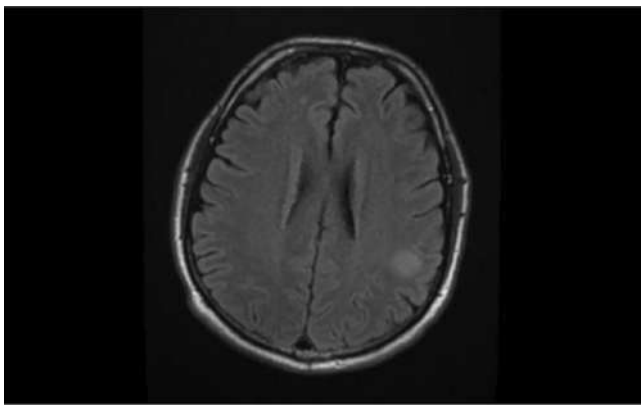


FIGURE 1

Results: Among 1735 patients with MS, 40 had experienced at least one epileptic seizure (2.3%). Thirty patients (1.7%) had seizures that could not be explained by other factor than MS. The interval between MS-epilepsy diagnosis was longer and seizure recurrence was more in SPMS compared to RRMS. However, the prognosis of epilepsy was good in both subtypes. Out of 21 patients with NMOSD, none had a seizure during follow-up. Out of 56 patients with MOGAD seizures were observed in three (5.4%). All of them had status epilepticus either at onset or during the course of the disease.



MRI of patient 1 with MOGAD



MRI of patient 3 with MOGAD

Conclusion: While the seizure seen during the relapses may be related to new cortical lesion formation and acute inflammation, it is more likely to be due to chronic atrophy, especially in SPMS. Prevalence of status epilepticus was common in MOGAD patients.

Disclosure: Nothing to disclose.

EPO-186 | Does natalizumab affect oligoclonal bands in the cerebrospinal fluid of patients with multiple sclerosis?

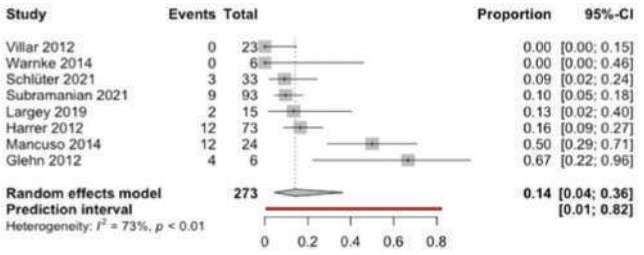
A. Liampas[1]; V. Tseriotis[2]; G. Vavougios[3]; P. Zis[3]; G. Hadjigeorgiou[3]; P. Bargiotas[3]; C. Pourzitaki[2]; A. Artemiadis[3]

[1]Department of Neurology, Nicosia General Hospital, Nicosia, Cyprus; [2]Laboratory of Clinical Pharmacology, Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Department of Neurology, Medical School, University of Cyprus, Nicosia, Cyprus

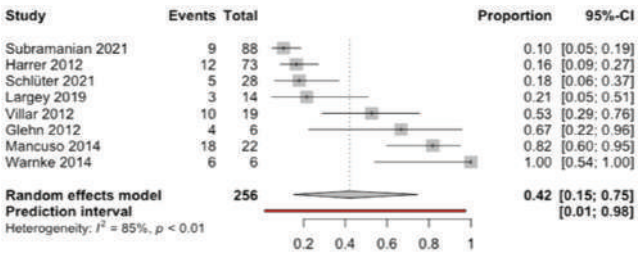
Background and Aims: The pathological role of cerebrospinal fluid (CSF) oligoclonal bands (OCBs) in multiple sclerosis (MS) has been demonstrated. Long-lived plasma cells are the main cells contributing to production of OCBs. Our aim was to demonstrate the quantitative effect of natalizumab (NTZ) on OCBs in the CSF of patients with MS.

Methods: A systematic search on MEDLINE, SCOPUS and Web of Science for English-written and peer-reviewed longitudinal studies on adults was performed. Meta-analysis of the data was also performed.

Results: Eight eligible studies of adequate quality with a total sample of 326 relapsing- remitting MS patients were included. A summary rate of 14.07% [95% CI, 4.48%–36.36%] was observed for complete loss of OCBs and 42.02% [95% CI, 15.23%–74.51%] for reduction in OCB number or intensity was observed, both with considerable heterogeneity. Pooled estimates dropped (11% [95% CI, 0.04%–0.29%] and 34% [95% CI, 0.11%–0.68%] respectively) after the identification of an influential study. Multivariable meta-regression identified IgG index as a factor contributing to heterogeneity (adj. $p = 0.0279$), regarding reduction of OCB number or intensity.



Forest plots of the meta-analysis on the proportion of patients with complete loss of OCBs after NTZ treatment.



Forest plots of the meta-analysis on the proportion of patients with reduction of OCB number or intensity after NTZ treatment.

Conclusion: In conclusion, our systematic review and meta-analysis showed that NTZ can lead to reduction of intrathecal OCBs in MS patients, indicating a possible effect of NTZ on memory plasma cells which are the main source of OCBs in MS.

Disclosure: Nothing to disclosure.

EPO-187 | Identifying definite patterns of unmet needs in patients with multiple sclerosis using unsupervised machine learning

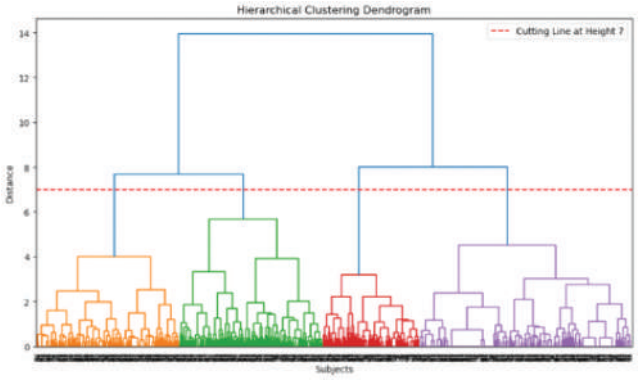
E. Maida[1]; G. Abbadessa[1]; E. Cocco[2]; P. Valentino[3]; A. Lerede[4]; J. Frau[2]; G. Miele[1]; F. Bile[1]; M. Vercellino[5]; F. Patti[6]; G. Borriello[7]; P. Cavalla[5]; M. Sparaco[1]; L. Lavorgna[1]; S. Bonavita[1]

[1]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy; [2]Department of Medical Science and Public health, Centro Sclerosi Multipla, University of Cagliari, Cagliari, Italy; [3]Institute of Neurology, University Magna Graecia, Catanzaro, Viale Europa, Catanzaro, Italy; [4]Department of Brain Sciences, Imperial College London, London W120BZ, UK; [5]MS Center, Department of Neuroscience, City of Health and Science University Hospital of Turin, Turin, Italy; [6]Department "GF Ingrassia", Section of Neurosciences, University of Catania, Catania, Italy; [7]MS Center, Hospital San Pietro Fatebenefratelli, Rome, Italy

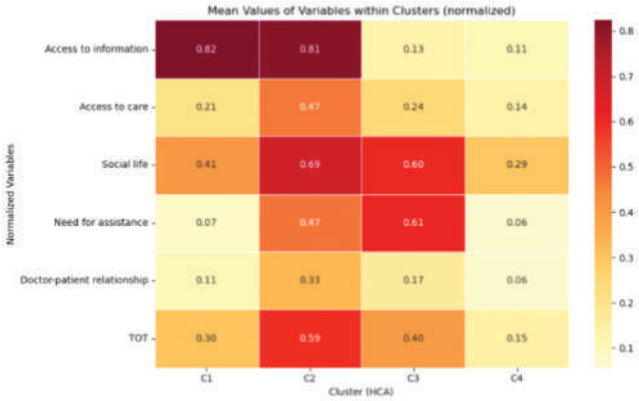
Background and Aims: People with Multiple Sclerosis (PwMS) exhibit a spectrum of needs that extend beyond solely disease-related determinants. Investigating unmet needs from the patient perspective may address daily difficulties and optimize care. Our aim was to identify patterns of unmet needs among PwMS and their determinants.

Methods: We conducted a cross-sectional multicentre study. Data were collected through an anonymous, self-administered online form. To cluster PwMS according to their main unmet needs, we performed agglomerative hierarchical clustering algorithm. Principal component analysis (PCA) was applied to visualize cluster distribution. Pairwise comparisons were used to evaluate demographics and clinical distribution among clusters.

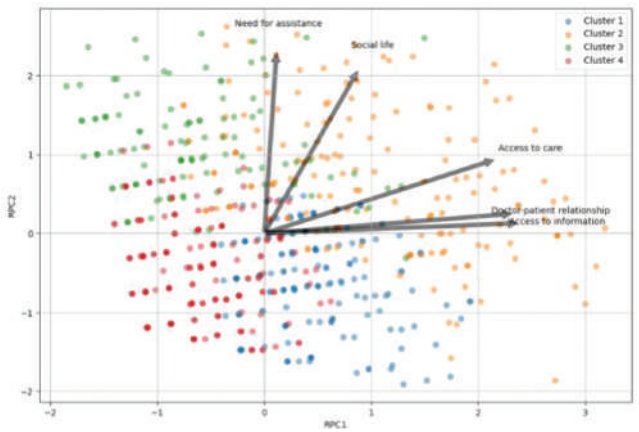
Results: Out of 1,764 mailed questionnaires, we received 690 responses. Access to primary care was the main contributor to the overall unmet need burden. Four patterns were identified: Cluster C1, "Information-Seekers with Few Unmet Needs"; Cluster C2, "High Unmet Needs"; Cluster C3, "Socially and Assistance-Dependent"; Cluster C4, "Self-Sufficient with Few Unmet Needs". PCA identified two main components in determining the patterns: the "public sphere" (access to information and care) and the "private sphere" (need for assistance and social life). Older age, lower education, longer disease duration, and higher disability characterized clusters with more unmet needs in the "private sphere". However, demographic, and clinical factors failed in explaining the four identified patterns.



Hierarchical clustering dendrogram. The figure displays the hierarchical clustering dendrogram generated using the Ward linkage method.



Mean values of normalized variables within clusters generated by hierarchical clustering algorithm (HCA). The heatmap presents the mean values of selected variables within distinct clusters, after the normalization process.



Biplots of principal component analysis (PCA) scores and component loadings with cluster assignments.

Conclusion: Our study identified four unmet need patterns among PwMS, emphasizing the importance of personalized care. While clinical and demographic factors provide some insight, additional variables warrant further investigation to fully understand unmet needs in PwMS.
Disclosure: Nothing to disclose.

EPO-188 | Systemic inflammation biomarkers in multiple sclerosis as potential indicators of underlying inflammatory process

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Background and Aims: The role of systemic inflammation biomarkers has been investigated in several autoimmune diseases. Our study aimed to assess whether inflammatory indices differ between healthy individuals and people with Multiple Sclerosis (PwMS), and explore whether they may correlate with demographic, clinical, and laboratory variables.
Methods: We conducted a retrospective study involving 100 PwMS admitted to our MS Center, and 83 age- and sex-matched healthy controls. Demographic, MS characteristic and laboratory data, including lymphocyte subsets, were collected. Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio, monocyte/lymphocyte ratio, Systemic Inflammation Index and Systemic Immune-Inflammation Index (SIRI) were calculated.
Results: NLR and SIRI values were significantly higher in PwMS than in healthy control group ($p=0.03$, $p=0.02$, respectively). In the linear regression model, NLR was associated with primary-progressive forms (PPMS) ($p=0.03$), higher number of oligoclonal bands ($p=0.03$) and higher frequency of relapses before the diagnosis ($p=0.03$). SIRI was associated with PPMS ($p=0.03$) and higher frequency of relapses before the diagnosis ($p=0.04$). NLR and SIRI were associated with higher absolute CD20+ B cells count at disease onset ($p=0.02$, $p<0.01$, respectively).

	Patient Group (n=100)	Control Group (n=83)	*p*-value
Age, mean (SD), years	38.07 (13.09)	40.96 (15.06)	0.17
Female, No (%)	66 (66)	34 (55.42)	0.15
Duration of MS disease, mean (SD), years	1.4 (9.95)	-	
MS clinical descriptors, No (%)		-	
RRMS	84 (84)		
SPMS	8 (8)		
PPMS	8 (8)		
EDSS, mean (SD)	2.01 (1.47)	-	

Demographic and clinical characteristics of the two groups.

Conclusion: The results may highlight the role of NLR and SIRI as potential indicators of an underlying inflammatory process. The correlation with B cells at onset can further support the evidence in favour of their critical role in MS pathogenesis. Further studies are needed to validate such findings and assess the potential impact of disease-modifying therapies on systemic inflammation biomarkers.
Disclosure: Nothing to disclose.

EPO-189 | Natalizumab efficacy on radiological and clinical parameters in pediatric-and adult-onset multiple sclerosis

M. Puthenparampil[1]; M. Gaggiola[1]; M. Ponzano[2]; G. Scialpi[1]; G. Zanotell[1]; A. Miscioscia[1]; A. Berardi[1]; M. Nosadini[3]; S. Sartori[3]; P. Perini[1]; F. Rinaldi[1]; F. Bovis[2]; P. Gallo[1]

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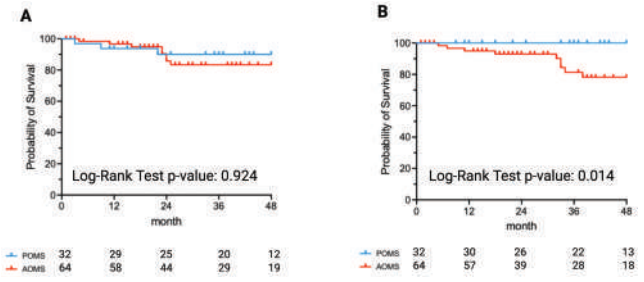
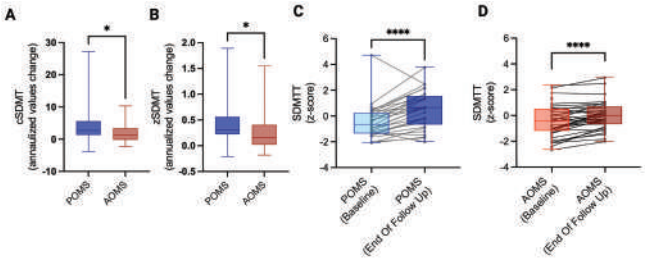
Background and Aims: Pediatric-onset Multiple Sclerosis patients (POMS) is characterized by a more rapid accumulation of CNS inflammation than Adult-Onset MS (AOMS). Therefore, the early use of HET has been highly recommended in POMS.

Methods: All patients who started natalizumab (NTZ) were enrolled in this retrospective single-centre study and were clinically evaluated at baseline and then every six months with EDSS score. The cohort was then divided based on age at onset in Pediatric-Onset (POMS) and Adult-Onset AOMS) MS and were propensity-matched. SDMT was assessed at baseline in all patients and in a sub-cohort of POMS (29) and AOMS (30) at least 2 years after baseline assessment.

Results: From 38 POMS and 122 AOMS, propensity-matching defined a cohort of 36 POMS and 72 AOMS. The effect on inflammatory MRI and clinical was evaluated by survival analysis did not differ between AOMS and POMS ($p=0.924$). PIRA was documented in 9 AOMS (12.5%, $p=0.0278$) during the follow-up (LogRank p-value 0.014). Corrected SDMT values did not differ between POMS and AOMS at baseline (49.43 ± 14.74 and 49.71 ± 10.75, $p=0.639$). While z-score improved in both AOMS and POMS ($p<0.001$), annualized z-score change was significantly higher in POMS than in AOMS (0.41 ± 0.40 vs 0.25 ± 0.34, $p=0.023$).



Survival analysis: NEDA and PIRA



SDMT score at baseline and during the follow up

Conclusion: Evaluation of inflammatory and clinical outcomes did not reveal any significant difference between POMS and AOMS, indicating an excellent response to NTZ in both groups. The favorable outcomes observed in clinical, radiological, and neuropsychological parameters support the use of NTZ as a viable treatment option in POMS.

Disclosure: M.P. reports grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy and Novartis; consultancy for Novartis, Biogen Italy and Sanofi Genzyme; board membership Sanofi Genzyme, Novartis and Biogen Italy. M.G. M.Po, G.S., G.Z., A.M., N.M., and S.S. have nothing to disclose. P.P. reports grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis and Roche; consultant for Novartis, Biogen Italy, Sanofi Genzyme and Roche. F.R. report grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis; consultancy for Novartis, Biogen Italy and Sanofi Genzyme. P. G. reports grant from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche and Bristol Myers Squibb; consultancy for Novartis, Biogen Italy, Sanofi Genzyme, Roche and Bristol Myers Squibb; board membership Sanofi Genzyme, Novartis, Biogen Italy, Roche, Merck Serono and Bristol Myers Squibb.

EPO-190 | Retinal microglia changes in relapsing-remitting multiple sclerosis under natalizumab therapy

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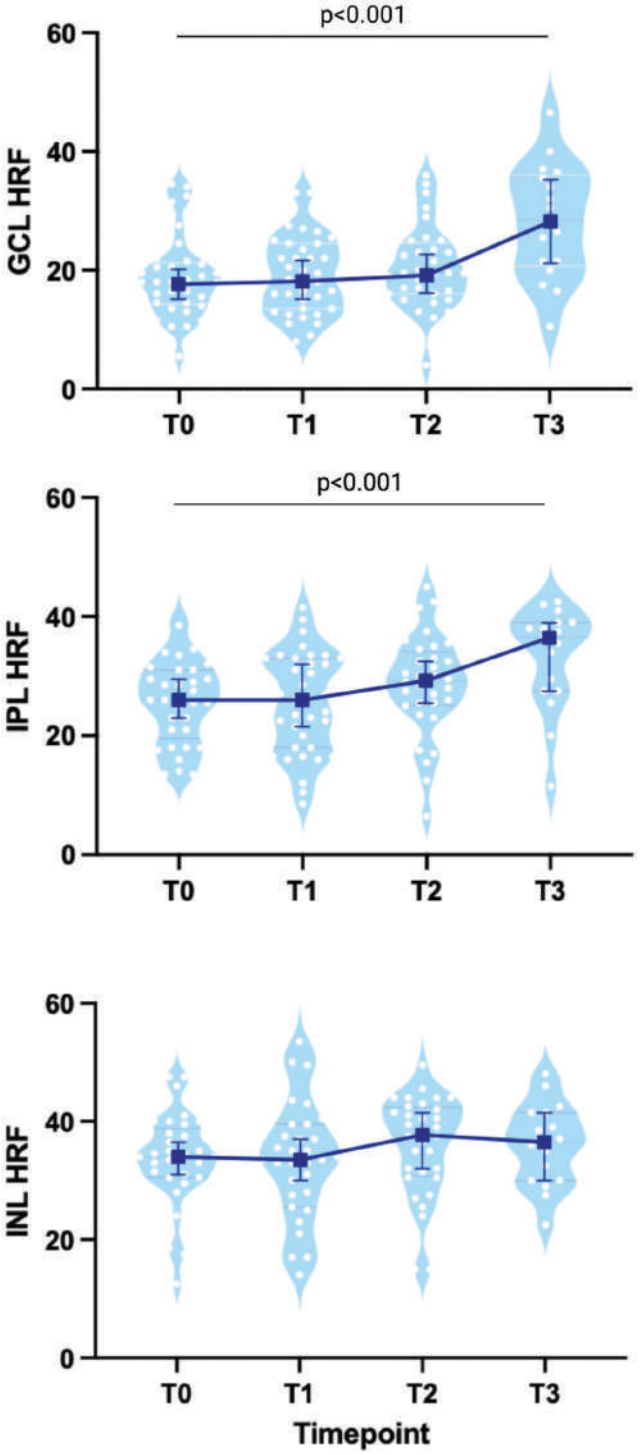
Background and Aims: Microglia (MG) is suggested to play an immunopathological role of in Multiple Sclerosis (MS). In vivo analysis of retinal MG proliferation/activation, evaluating Retinal Hyperreflective Foci (HRF) by Optic Coherence Tomography (OCT), in MS patients under disease modifying therapies may help to clarify MS immunopathology as well as drug's mechanism of intrathecal action.

Methods: The effect of NTZ in retinal MG on 36 Relapsing-Remitting MS (RRMS) patients was investigated in a retrospective, single-centre study. OCT was performed immediately before the first infusion and then between infusion 3 and 4, infusion 6 and 7, infusion 11 and 13. Peripapillary and macular scans were acquired, evaluating peripapillary retinal nerve fiber layer (pRNFL) thickness, macular volumes (vertical scans), and HRF count (horizontal scan) in Ganglion Cell Layer (GCL), Inner Plexiform Layer (IPL) and Inner Nuclear Layer (INL). Clinical examination was performed every six months.

Results: HRF count significantly increased under NTZ therapy ($p<0.001$) in both GCL (18.85 ± 6.93 at baseline, 28.24 ± 9.55 after 12 months) and IPL (25.73 ± 7.03 at baseline, 33.21 ± 8.50 after

12 months) but remained stable in INL (33.65 ± 7.76 at baseline, 36.06 ± 6.86 after 12 months, $p = 0.868$), while no relevant modification of pRNFL and macular volumes were observed during the study.



HRF count in MS patients treated with Natalizumab

Conclusion: In RRMS NTZ affects retinal MG activation (HRF count) in GCL and IPL, but not in INL, suggesting that NTZ does not impact on all the aspects of MS immunopathology.

Disclosure: M.Pu., report travel grants, consultancy, and board membership from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Bristol Myers Squibb, Janssen, and Alexion. E.B., M.Po., A.M., E.P., F.B. have nothing to disclose. V.A.M reports travel grants from Sanofi Genzyme, Biogen, and Viatris. P.P. reports grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche, Alexion, Janssen, Brystol Mayer Squibb; consultancy for Novartis, Biogen Italy, Sanofi Genzyme, Roche, Janssen, Brystol Mayer Squibb. RF report grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, consultancy for Novartis, Biogen Italy, Sanofi Genzyme. P.G. reports grant, consultancy, and board membership for Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche, Bristol Myers Squibb, Janssen, and Alexion.

EPO-191 | PAI mutation 4G/5G-coagulopathy risk factor for multiple sclerosis?

M. Cholakova
Nikolay Mihnev

Background and Aims: Homozygous carrying of the PAI mutation, 4G/4G is clinical significant for thrombotic events. In multiple sclerosis (MS), malfunction of the plasminogen activation system and blood brain barrier disruption are pathological processes that might lead to an abnormal fibrin(ogen) extravasation into the parenchyma.
Methods: Healthy controls, patients with ischemic stroke, patients with MS, MRI, laboratory tests for thrombophilia, neurological examination, statistical analysis
Results: A prospective clinical trial of 54 patient with multiple sclerosis, 69 healthy controls and 101 patients with ischemic stroke. A total of number of 101 patients with ischemic stroke under 50 years were screened, 67 were examined for PAI mutation. The healthy control group consists of 44 women and 25 men. Homozygous carrier of the PAI mutation 4G/4G variant was found to increase the chance of stroke 3.00 times [OR = 3.00; CI: (0.70–12.93)]. Patients with multiple sclerosis were 54, with the majority of female – 39, and male – 15. We compared the groups of patients with stroke and multiple sclerosis to evaluate prevalence of PAI-1 mutation in both cohorts. According to our study, PAI-1 mutation could be a risk factor for the development of multiple sclerosis (p-value < 0.00001) and ischemic stroke at a young age ($p < 0.05$), and the difference between the two groups and healthy controls is statistically significant.

TABLE 1

Gender	n	%	Age		
			average	Standard deviation	Min
Female	32	31,7	41,66	7,196	19
Male	69	68,3	42,55	6,388	18
Total	101	100	42,27	6,632	18

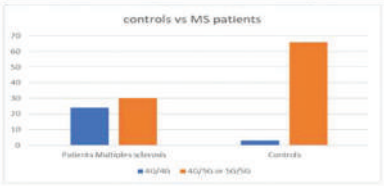
TABLE 2, 3

Group	N	Age				t	df
		Mean	Standard deviation	Min	Max		
Healthy controls	69	40,45	8,23	18,00	50,00	5,09	168
Patients with stroke	101	42,27	6,63	18,00	50,00		
Total	170	39,91	7,84	18,00	50,00		

iroup	count	Age		
		Mean	Standard deviation	Min
Control	69	40,45	8,23	18,00
MS	54	32,796296	10,51572	18,00

TABLE 4 Graphic 1

	Mutant 4G/4G	Normal 4G/5G or 5G/5G	Marginal Row Totals
MS	24	30	54
Control	3	66	69



Conclusion: PAI mutation could play a role as a risk factor for development of demyelinating disease like MS. In the future examination of patients with MS for PAI mutation could play role for the choice of treatment and prevention of invalidation.

Disclosure: No.

EPO-192 | Efficacy and safety profile of ocrelizumab in primary progressive multiple sclerosis patients from Montenegro

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Clinic for Neurology, Clinical Center of Montenegro, Ljubljanska bb, 81000 Podgorica, Montenegro

Background and Aims: As only registered drug for patients with primary progressive multiple sclerosis (PPMS), ocrelizumab is in use in Montenegro since March 2019. Efficacy and safety of ocrelizumab in PPMS patients was confirmed in ORATORIO trial, as well as in several real-world studies. Our aim is to evaluate efficacy and safety of Ocrelizumab in PPMS patients in Montenegro.

Methods: We retrospectively examined data of PPMS patients treated with ocrelizumab in Montenegro from March 2019 to September 2023.

Results: During the abovementioned period, we treated 73 PPMS patients, mean aged 51.6 ± 10.6 years. In 61.6% of patients baseline Expanded Disability Status Scale (EDSS) was 5.5 or higher. During the follow-up period, no EDSS worsening was observed in 70.3% of treated-patients, while treatment was stopped in 16 patients: due to EDSS progression in 6 patients; due to death in 3 patients; due to adverse event (AE) in 1 patient; due to other reasons in 2 patients. Treatment discontinuation was choice of 4 patients. Regarding MRI activity during the follow-up period, presence of T1Gd+ lesions was detected in 1 patient, while 4 patients developed new/enlarging T2 lesions. Elevation of hepatic transaminases was observed in 10.6% of patients; lymphopenia grade 2 in 1.5%; one patient developed cervical malignancy. Urinary tract infection was detected in 3% of patients.

Conclusion: Our data, similar to other real-world studies, confirmed good efficacy as well as favorable safety profile of ocrelizumab in PPMS patients.

Disclosure: All authors have received speaker honoraria and/or travel grants.

EPO-193 | Executive dysfunction in multiple sclerosis patients

S. Sellami; N. Farhat; N. Bouattour; K. Moalla; H. Haj Kacem; S. Daoud; S. Sakka; M. Damak; C. Mhiri

Neurology Department and Research Laboratory LR12SP19, Habib Bourguiba University Hospital, Sfax, Tunisia

Background and Aims: Executive dysfunction occurs in 15%–28% of Multiple Sclerosis (MS) patients. The aim of this study is to identify characteristics of Executive Function Disorders (EFD) in a clinical cohort of Tunisian patients with MS.

Methods: A group of patients diagnosed with definite MS according to the 2017 McDonald criteria and followed up in the department of Neurology of Habib Bourguiba Hospital-Tunisia and a group of control subjects were assessed with a battery of classical executive tests which included semantic and phonemic verbal fluency test (SVFT/PVFT), Go/no-Go, digit-span-backwards and Delis Kaplan Executive Function System (D-Kefs).

Results: 70 MS patients with an average age of 34,6 years and 50 control subjects were included. As compared to controls, 74% of MS patients had executive disorders perceived by the D-Kefs ($p = 0.03$). The planning ability and the mental flexibility were disrupted as evidenced by impaired verbal fluency in all MS patients. The phonemic verbal fluency was clearly more affected ($p = 0.049$). There were no significant alterations regarding scores of Go/no-Go test ($p = 0.3$) and digit-span-backwards test ($p = 0.4$) in MS group compared to controls. Patients with SPMS (secondary progressive multiple sclerosis) showed significant EFD than those with RRMS (relapsing-remitting multiple sclerosis). Our study also showed a significant correlation between EFD and the EDSS (Expanded Disability Status Scale) ($p = 0.002$). No impact of DMT (disease modifying therapy) on EFD.

Conclusion: These results suggest that there are executive difficulties that are commonly found among patients with MS. The identification of these profiles in clinical practice could allow for more individualized rehabilitation.

Disclosure: Nothing to disclose.

EPO-194 | Assessment of visual function in multiple sclerosis patients over time

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[1]*Neurology, Hospital Clínico San Carlos, Idissc, Madrid, Spain;* [2]*Ophtalmology, Hospital Clínico San Carlos, Madric, Spain;* [3]*Ciencias de la Computación, Universidad de Coruña, Spain*

Background and Aims: Optic neuritis (ON) is often the first symptom at the onset of MS and can impair visual function. Objective: To longitudinally analyse the visual function in MS patients.

Methods: Stable MS patients over six months were included, with two assessments: baseline (V1) and one year later (V2). Visual acuity (VA), VA2.50% and VA1.25% were measured with ETDRS and low contrast test. Colour vision with Ishihara and Farnsworth-Munsell D28 (FM-D28) test. Contrast sensitivity with Pelli-Robson test. Comparisons were drawn between eyes affected by previous optic neuritis (ON) and those not.

Results: with Pelli-Robson test. Comparisons were drawn between eyes affected by previous optic neuritis (ON) and those not. Results Thirty-two patients, predominantly female (22), average age 43, were studied. Twenty eyes with previous ON. VA, VA2.50%, VA1.25% and contrast sensitivity showed significant differences between both groups (ON vs. no ON) in V1 and V2 ($p<0.05$). After one year a significant worsening in visual function ($p<0.05$) in the non-ON group were observed. The ON group showed significant reductions in VA1.25% ($p=0.005$) and contrast sensitivity ($p=0.000$). In the Ishihara test at V1 and V2, 95.5% of patients without optic neuritis had normal results. Meanwhile, 10% of the patients in the optic neuritis group displayed abnormalities. The non-ON group showed 43.2% altered FM-D28 values in V1 and 47.7% in V2. The ON group showed 80% of altered values in V1 and 85% in V2.

Conclusion: Visual acuity and contrast sensitivity decline as the disease progresses. The FM-D28 test offers a more precise evaluation of color vision.

Disclosure: Nothing to disclose in relation with the abstract.

EPO-195 | Hyperreflective foci in the inner retina in multiple sclerosis: Preliminary results of an external validation study

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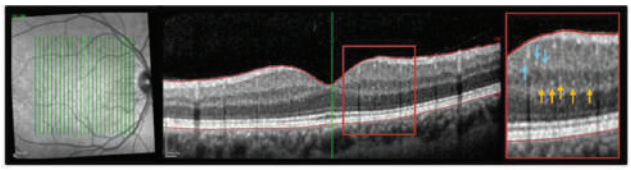
[1]*Department of Neurology, Medical University of Vienna, Vienna, Austria;* [2]*Department of Ophthalmology, Medical University of Vienna, Vienna, Austria*

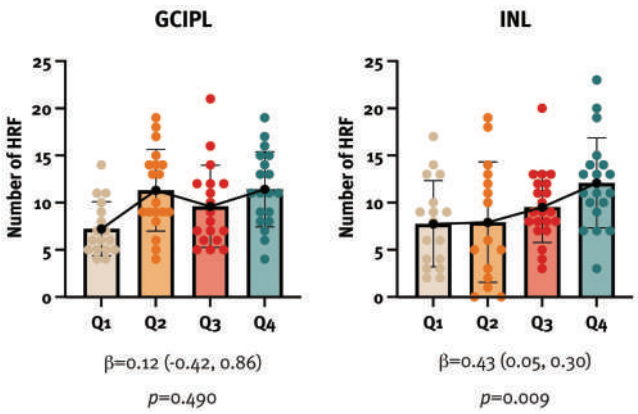
Background and Aims: Microglia, the resident immune cells of the central nervous system, are increasingly recognized to play an important role in the pathophysiology of multiple sclerosis (MS). Retinal microglia may be visualized as hyperreflective foci (HRF) by optical coherence tomography (OCT), but their origin and clinical relevance remain controversial.

Methods: In this cross-sectional retrospective study, we included patients with MS (pwMS) who had undergone an OCT scan. HRF counting was performed separately in the ganglion cell-inner plexiform layer (GCIPL) and the inner nuclear layer (INL). Eyes with a clinical history of ON or asymptomatic ON (interocular asymmetry with cut-off values of ≥5μm for pRNFL and ≥4μm for GCIPL) were excluded from the analysis.

Results: In total, we included 38 eyes of 36 pwMS (47.2% female, median age 31.5 years (24.9–43.8), median disease duration 1.8 years (0.1–10.2), median EDSS 1.0 (0–2.5)). Mean GCIPL and INL thicknesses were 67.3 μm (7.2) and 34.7 μm (2.2), respectively. The mean GCIPL HRF count was 10.8 (3.9), and the mean INL HRF count was 9.5 (5.5). The INL HRF count was associated with the INL thickness (β = 0.43; 95% CI 0.05, 0.30; $p=0.009$), whereas the GCIPL HRF count was not associated with the GCIPL thickness (β = 0.12; 95% CI −0.42, 0.86; $p=0.490$).



HRF Protocol. Macular scan and HRF visualization in a patient with MS. HRF were defined as isolated, small sized (<30 μm), punctiform elements with moderate reflectivity but without any back shadowing.



The INL HRF count was associated with the INL thickness, whereas the GCIPL HRF count was not associated with the GCIPL thickness.

Conclusion: This study demonstrated that HRF can be assessed by OCT and confirmed that the INL HRF count is associated with the INL thickness, providing indirect evidence that HRF may indeed represent activated microglia. Further studies are needed to confirm their clinical relevance.

Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 1

EPO-196 | Advancing clinical practice: Impact of online education on implementation of novel therapies for myasthenia gravis

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Background and Aims: We developed an online CME activity titled: "Navigating the Changing Landscape in Myasthenia Gravis: An Expert Case-Based Discussion". We hypothesized that participation in this education would lead to improved knowledge of implementing targeted MG treatments.
Methods: Neurologists participated in a 30-min expert discussion educational activity (www.medscape.org/viewarticle/993422). Educational effect was assessed using a repeated-pair design with pre-/post-assessment. Three multiple choice questions assessed knowledge and 1 question (Likert-type scale) assessed confidence. A paired samples t-test was conducted for significance testing on overall average number of correct responses and for confidence rating, and a McNemar's test was conducted at the learning objective level (5% significance level, $p < .05$). Cohen's d with correction for paired samples estimated the effect size of the education on number of correct responses (<.20 modest, .20–.49 small, .59–.79 moderate, ≥.80 large). Data were collected from 7/14/2023 to 10/25/2023.
Results: A total of 789 neurologists participated of which 104 completed all the pre- and post-activity questions during the study period. Overall 64% neurologists improved their knowledge and competence related to implementing novel targeted therapies in the management of MG (average knowledge/competence pre: 33% vs post: 68%) $p < .001$, Cohen's d = 1.02) (see Table). 56% had increased confidence in appropriately integrating novel targeted therapies for MG.

TABLE Impact of education on neurologists' knowledge and competence

Learning Objective	Aggregated data		Linked Learning Results[a]	
Knowledge	Average % of correct responses Pre- vs. Post-education	P-value	% Improved[b] learners Pre- vs. Post-education	% Reinforced[c] learners Pre- vs. Post-education
Regarding novel targeted therapies for the management of MG	23% vs 56%	<.001	35%	21%
Competence				
Related to individualizing therapy for patients with MG	38% vs 74%	<.001	56%	33%
Confidence	Mean Pre- vs. Post-education (1 – not confident; 5 – very confident)		% Increased learners Pre- vs. Post-education	% Maintained learners Pre- vs. Post-education
In appropriately integrating novel targeted therapies for MG such as FcRn inhibitors in clinical practice	2.00 vs 2.87	<.001	56%	44%

[a]Each individual learner tracked pre and post-education
[b]Incorrect answer pre-education, Correct answer post-education
[c]Correct answer pre-education, Correct answer post-education

Conclusion: This online CME activity significantly improved neurologists' knowledge and competence related to implementing novel targeted therapies in the management of MG; however, substantial gaps remain which should be addressed in future medical education.
Disclosure: Nothing to disclose.

EPO-197 | Impact of myasthenia gravis on patients' daily life: Findings from the ME&MGopen decentralised study

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Background and Aims: Generalised myasthenia gravis (gMG) is an autoimmune disease causing fluctuating and debilitating muscle weakness, profoundly affecting patients' quality of life. Capturing its daily impacts objectively remains a challenge. The ME&MGopen study aims to address this gap. This study describes gMG impact using electronic patient-reported outcomes (ePROs) and potential influencing factors.
Methods: 199 gMG patients were enrolled in ME&MGopen, a multicountry (USA, Canada), decentralised research study. Sociodemographic, clinical and treatment data were collected during baseline remote visit. Participants used the ME&MGopenTM digital tool for up to 8 months and completed questionnaires on a monthly basis (MG-QOL-15r, MG-ADL, ISI, Chronic Pain, PHQ-8).
Results: Of the 199 participants, 65% were female, with a mean age 57 ± 16 years. 60 self-reported their MGFA Disease Class, with the following distribution: 55% Class III, 28% Class II, 17% Class IV. Across all participants, PHQ-8, ISI, Chronic Pain, MG-ADL, MG-QOL-15r baseline scores indicated a meaningful gMG impact on their lives [6.5 ± 5.1, 9.0 ± 6.0, 2.5 ± 2.4, 5.2 ± 3.7, 12.0 ± 8.0 respectively]. PHQ-8, MG-ADL, MG-QoL-15r scores were significantly higher when disease control was considered inadequate [9.8 ± 4.0 ($p < 0.05$), 10.6 ± 3.2 ($p < 0.0001$), 21.0 ± 6.0 ($p < 0.01$)] versus controlled patients. PHQ-8 and MG-QoL-15r scores were significantly increased in patients unable to work [10.0 ± 5.0 ($p < 0.05$), 20.0 ± 5.7($p < 0.001$)] versus working or unemployed patients.
Conclusion: These findings show the impact of gMG on quality of life, consistent with literature of gMG. The reliability of ME&MGopenTM to collect ePROs will be confirmed during upcoming longitudinal analyses.
Disclosure: Carolina Barnett Tapia: Research funding (paid to her institution) (Ad Scientiam, Alexion AstraZeneca (AZ) Rare Disease, Cartesian Therapeutics, US Department of Defence, Muscular Dystrophy Canada, MGNet, Grifols and Octapharma); Honoraria

(consulting and/or Advisory board) fees (AcademicCME, Alexion AZ Rare Disease, argenx, Sanofi, UCB Pharma and Janssen). Sophie Lehnerer: Lecturing activity (Alexion (AZ Rare Disease), argenx, Hormosan, UCB); Consultancy work (Alexion (AZ Rare Disease), Argenx, Biogen, Roche, UCB); Research support (Alexion (AZ Rare Disease), Argenx, Hormosan, UCB (at Charité – Universitätsmedizin Berlin)) Clarissa Gorin, Dellini Ravindra, Noura Sellami, Emma Touré Cuq: employees of Ad Scientiam. Martin Keller, Emrah Aras: employees of Alexion Pharmaceuticals Inc. James Howard: Research funding (paid to his institution) (Alexion AZ Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, UCB Pharma); honoraria/consulting fees (AcademicCME, Alexion AZ Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc, Medscape CME, Merck EMD Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, Zai Labs); non-financial support (Alexion AZ Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs).

EPO-198 | The ME&MGopen study: Analysis of 8-month adherence trends to a smartphone application in generalized Myasthenia Gravis

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Background and Aims: Generalised Myasthenia Gravis (gMG) is a debilitating, chronic, autoimmune disease characterized by fluctuating fatigable muscle weakness. The ME&MGTM smartphone application is a research tool enabling the unsupervised data collection of gMG symptoms as well as quality of life and mental health measures. Improving users' long term adherence will optimize data quality for research. We evaluated patient adherence to ME&MGTM digital tests and e-questionnaires in this fully decentralized ME&MGopen study.

Methods: Patients diagnosed with anti-AChR autoantibody positive gMG were enrolled in the USA and Canada. Five active digital tests and five e-questionnaires were completed at baseline and on a monthly basis for one year. App adherence was assessed until Day-240.

Results: After their remote baseline inclusion visit, 176 participants complied to the ME&MGTM tasks (adherence rate = 91%). Adherence rate dropped at Day 30 for both digital tests (78%) and e-questionnaires (79%) and remained above 60% until Day-240. Once a digital test or e-questionnaires was initiated, it was generally brought to completion. The most demanding task (sit-to-stand test) was interrupted in less than 4% of evaluations.

Conclusion: These results show promising immediate and lasting adherence to ME&MGTM, persisting beyond 6 months, a critical turning point in digital studies. Additional subgroup analyses will inform on specific adherence profiles and offer avenues to maintain patients' long-term engagement.

Disclosure: Carolina Barnett Tapia: Research funding (paid to her institution) (Ad Scientiam, Alexion AstraZeneca (AZ) Rare Disease, Cartesian Therapeutics, US Department of Defence, Muscular Dystrophy Canada, MGNet, Grifols and Octapharma); Honoraria (consulting and/or Advisory board) fees (AcademicCME, Alexion AZ Rare Disease, argenx, Sanofi, UCB Pharma and Janssen). Sophie Lehnerer: Lecturing activity (Alexion (AZ Rare Disease), argenx, Hormosan, UCB); Consultancy work (Alexion (AZ Rare Disease), Argenx, Biogen, Roche, UCB); Research support (Alexion (AZ Rare Disease), Argenx, Hormosan, UCB (at Charité – Universitätsmedizin Berlin)) Clarissa Gorin, Dellini Ravindra, Noura Sellami, Emma Touré Cuq: employees of Ad Scientiam. Martin Keller, Emrah Aras: employees of Alexion Pharmaceuticals Inc. James Howard: Research funding (paid to his institution) (Alexion AZ Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, UCB Pharma); honoraria/consulting fees (AcademicCME, Alexion AZ Rare Disease, argenx, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc, Medscape CME, Merck EMD Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, Zai Labs); non-financial support (Alexion AZ Rare Disease, argenx, Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs).

EPO-199 | Efficacy and safety of nusinersen and risdiplam for adult spinal muscular atrophy: A systematic review and meta-analysis

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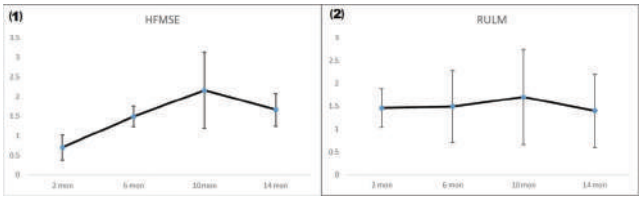
Background and Aims: Nusinersen and risdiplam were approved by the US food and drug administration (FDA) for adult SMA patients. However, clinical evidence for their efficacy in adults are still inconclusive. We conducted this meta-analysis to establish the clinical efficacy and safety of them on the adult patients.

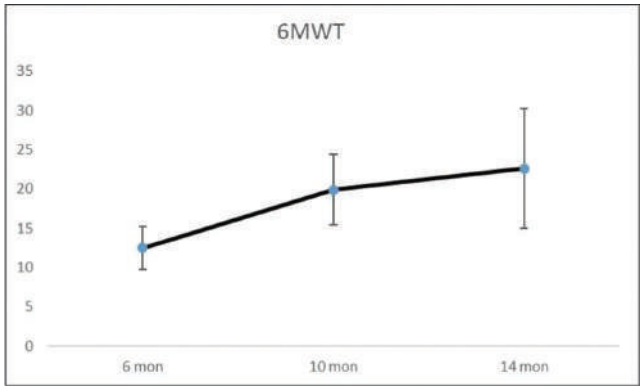
Methods: A literature search was conducted using the Web of Science Library, Scopus, PubMed, Wiley, and Cochrane up to August

2023. Data were pooled for analysis using OpenMeta Analyst software for Windows.

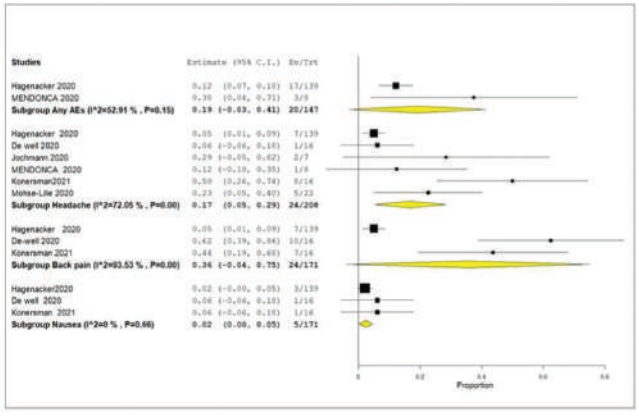
Results: 29 studies met the eligibility criteria, including 25 studies related to nusinersen and only 4 studies related to risdiplam. After 6 months of follow-up, nusinersen showed a statistically significant improvement of the HFMSE and the 6MWT. However, its effect on the RULM was not statistically significant. Regarding risdiplam, the findings of RULM showed a significant improvement during a year of follow-up. Frequent adverse events included headache, back pain, nausea, infections, and vomiting, which were more likely related to the disease progression or the lumbar puncture procedure as in nusinersen treatment rather than the drugs themselves. No significant serious adverse effects were reported for either.



Linear graphs of the changes in the mean during the follow-up periods of nusinersen on HFMSE and RULM.



Linear graphs of the mean change during the follow-up periods of nusinersen on 6MWT



Reported Adverse effects at 6 months

Conclusion: Nusinersen can improve motor and respiratory functions in adult patients with SMA, and its effects become more pronounced with extended follow-up periods. Risdiplam has shown promising results, but more clinical trials on adults with more sample size are needed. Both of nusinersen and risdiplam are generally tolerated and have an acceptable safety profile.

Disclosure: Nothing to disclose.

EPO-200 | Efficacy and safety of anti FcRN treatment in refractory MG: The UK experience of the Efgartigimod EAMS

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Background and Aims: We report our experience of patients with generalised MG (gMG) treated with Efgartigimod an FCRN antagonist, under the early access to medicine scheme (EAMS) in the UK.

Methods: Data from all UK patients treated with Efgartigimod under the EAMS June 22-July 23 were collected retrospectively. Efgartigimod was administered as per the ADAPT protocol (treatment cycle of 4 infusions at weekly intervals with further cycles given according to clinical need).

Results: 49 patients with AchR antibody positive gMG were treated in 12 centres. Most (76%) were female and most had a disease duration of over 10 years. The average MG-ADL score at baseline was 11.2 (SD 3.2). Most (73%) patients had undergone thymectomy. 71.4% were taking prednisolone at baseline. All patients had utilized non-steroidal immunosuppressant treatments, the average number tried was 4.3 (range 1–7) and 51% had received Rituximab. 57% of patients required regular IVIg/PLEX and 38% had required rescue IVIg/PLEX in the year before starting Efgartigimod. 77% of patients

had a mean reduction in the MG-ADL of ≥2 points in the first cycle and this remained stable throughout the study. The mean reduction in the MG-ADL score in the 1st, 2nd, 3rd and 4th cycles were −4.5, −6.3, −6.9 and −7.8 respectively. Side effects were generally mild though one patient stopped treatment due to severe hypokalemia. No rescue treatments were required. At the end of the study 96% of patients remained on Efgartigimod.

Conclusion: Efgartigimod is a safe and effective treatment for patients with refractory, treatment resistant gMG.

Disclosure: J. Spillane: speaker fees and travel support from Argenx; advisory services to UCB.

EPO-201 | Navigating the triggers of fear and anxiety after diagnosis of Myasthenia Gravis

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Background and Aims: As individuals living with Myasthenia Gravis (MG) have high rates of anxiety, we aimed to understand the experience of anxiety and its triggers among individuals discussing a recent diagnosis of MG online.

Methods: A research study was conducted using a proprietary AI-powered methodology to examine English-language public domain online conversations about MG from August 2022–August 2023.

Results: Of 9901 online conversations about MG, 33% ($n=3268$) were immediately after diagnosis. Self-described anxiety was expressed in 36% of posts ($n=1177$) at diagnosis, which was 25% lower than at pre-diagnosis (48%). Fear was discussed by 43% ($n=1405$), an increase of ~13% from pre-diagnosis (38%). Unknowns surrounding their future were discussed. Uncertainty (18%) was the most common anxiety trigger ($n=1177$) and could be sub-categorized into anxiety about diagnosis severity, not knowing the prognosis, and if symptoms will worsen. Symptom discomfort (13%) and fatigue (5%) were also important anxiety triggers. Fear ($n=1405$) was primarily triggered by catastrophizing thoughts (21%), including fear of loss of function, limitations in lifestyle, and death. The fear about physical impact (14%) was driven by physical symptoms, discomfort, and fatigue. Other fears included financial impact (3%) and impact on relationships (5%).

Conclusion: Anxiety and fear are frequently experienced by individuals recently diagnosed with MG, primarily due to physical symptoms, uncertainty about the future, lifestyle impacts, and catastrophizing thoughts. These observations provide important insight that healthcare practitioners can consider when treating newly-diagnosed MG, particularly the need for early symptom alleviation and mental health support.

Disclosure: Dr. Raghav Govindarajan is employed by HSHS Medical Group Multispecialty Care – St. Elizabeth's, O'Fallon, IL, USA. Rachelle Rodriguez, Jacqui Pesa, Zia Choudhry, Sindhu Ramchandren, Kavita Gandhi, and Kristin Heerlein are employees of Janssen Pharmaceuticals US, Inc., Titusville, NJ, USA. Caroline Brethenoux is employed by Human Dot Plus, TX, USA. Dr. Nizar Souayah is employed by Rutgers NJMS – Department of Neurology, Newark, NJ, USA.

EPO-202 | The impact of depression on quality of life for individuals with Myasthenia Gravis

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Background and Aims: Individuals with myasthenia gravis (MG) have a higher prevalence of depression than the general population (1–4). Therefore, we aimed to evaluate the occurrence of online discussions related to MG, depression, and depression triggers.

Methods: A research study was conducted using a proprietary AI-powered methodology to examine English-language public domain online conversations about MG from August 2022–August 2023.

Results: Nearly 10,000 online conversations about MG were identified. One-third of posts (33%; $n=3268$) discussed experiences immediately following diagnosis. Self-described depression was indicated in 21% ($n=686$) of posts regarding recent diagnosis, representing a 50% increase from the period prior to diagnosis (14%). Out of all conversations ($n=3268$), the progressive worsening of MG symptoms was the most common depression trigger (9%), and the impact of MG on quality of life (QoL) was the second most frequent depression trigger (6%). One individual shared a sentiment, "I long for my life as it used to be". A lower portion (4% of 3268) stated their depression was related to lack of control over various aspects of their life as a result of MG. Depression related to ineffective treatment experiences was also discussed (2%).

Conclusion: An increase in reported depression was observed at diagnosis compared to the pre-diagnosis stage of MG in this social listening study. Depression was attributed to progressive worsening of symptoms and QoL, loss of control, and ineffective treatments. Healthcare practitioners can use this information to guide treatment decisions to improve symptom control and provide emotional support resources.

Disclosure: Dr. Neelam Goyal is employed by Stanford Neuroscience Health Center, Palo Alto, CA, USA, and reports advisory and consulting engagements from Alexion, Argenx, UCB/Ra Pharma, Janssen, Amgen, Lycia, as well as grant support from Argenx. Rachelle Rodriguez, Jacqui Pesa, Zia Choudhry, Sindhu Ramchandren, Kavita Gandhi, and Kristin Heerlein are employees of Janssen Pharmaceuticals US, Inc., Titusville, NJ, USA. Caroline Brethenoux is employed by Human Dot Plus, TX, USA. Dr. Ashley E.L. Anderson is employed by Houston Methodist Hospital, Houston, TX, USA.
References: 1. WHO 2023. https://www.who.int/publications/i/item/depression-global-health-estimates. 2. SAMHSA 2022. https://www.samhsa.gov/data/report/2021-nsduh-annual-national-report. 3. Nadali J, et al. Brain Behav. 2023;13(1):e2840. 4. Dewilde S, et al. BMJ Open. 2023;31;13(1):e066445.

EPO-203 | Interactive application for the study of neuromuscular jitter

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Background and Aims: This work presents a software application that incorporates the necessary features to perform jitter studies off-line in a precise and efficient manner, so that comparative studies using manual jitter extraction procedures or new automatic methods can be conducted.
Methods: JitterAnalizer is a Matlab-based application for manual jitter analysis (Fig. 1). Time alignment and jitter estimation (MCD, MSD, etc.) of motor unit potential trains (MUPTs) can be performed either by the peak method or by the flank method. Other functionalities include: selection of sampling frequency, elimination of non-valid potentials, visualization of MUPTs in shimmer and raster modes, and results exportation.

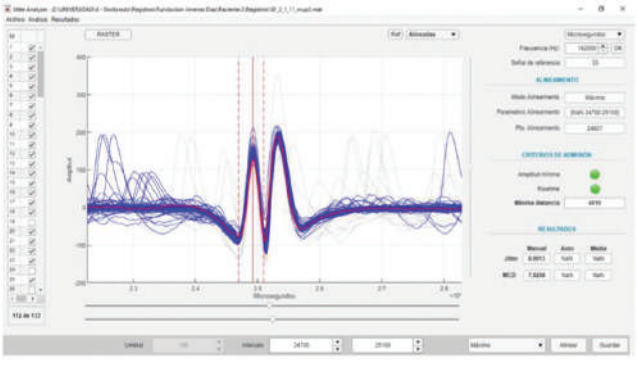

FIGURE 1 Interface of JitterAnalizer

Results: As a test example, EMG signals were recorded from 7 patients with pathologies of the neuromuscular junction or neuropathies. These signals were acquired using concentric facial needles and a Keypoint system. Jitter (MCD) measurements were then obtained from the Keypoint and from JitterAnalizer, using the peak method. Table 1 shows the statistical values of the jitter measurements obtained by each method from the 71 MUPTs that were taken as valid for the comparative study.

TABLE 1 Statistical results of the jitter measurements

EMG System	Mean (µs)	Standard deviation (µs)
Keypoint	32,92	23,65
JitterAnalyzer	36,91	35,05

Conclusion: JitterAnalizer has proved easy-to-use and fast. The statistical values of the jitter measurements obtained with the Keypoint and with JitterAnalizer are comparable. Their differences can be explained considering that the MUPTs presented to the two systems were not composed by exactly the same potentials.
Disclosure: This work has been funded by the Department of Health of the Government of Navarra (project GN2022/29) and by the Spanish Ministry of Science and Innovation (project PID2022-136620OB-I00).

EPO-204 | Comparison of manual methods in the measurement of neurophysiological jitter

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[1]*Electrical, Electronics and Communication Engineering Department, Public University of Navarra, Spain;* [2]*System Design Engineering Department, University of Waterloo, Waterloo, Canada;* [3]*Neurophysiology Service, Jiménez-Díaz Foundation University Hospital, Madrid, Spain*

Background and Aims: The goal of this work is to compare the jitter measurements obtained by the peak method and the flank method in both small and large muscle recordings, in order to evaluate the equivalence of the two methods.
Methods: 238 EMG recordings taken from 22 patients were used for the study, following two different protocols: 1) single fiber EMG protocol, small muscles (frontalis), facial-concentric electrodes; and 2) a similar protocol, large muscles (biceps, tibialis anterior, etc.), conventional concentric electrodes.
Results: Table 1 and Fig. 1 show statistical results of the jitter measurements obtained with both protocols, using the two methods. The Wilcoxon test was applied (0.05 significance level) and *p*-values of

0.0002 and 0.0001 were obtained for protocol 1 and protocol 2, respectively, suggesting significant differences between the measurements obtained with the two methods. Linear regression models were also obtained, yielding high coefficients of determination (0.994 for protocol 1. and 0.991 for protocol 2), slope values close to 1 (0.989 and 0.992), and small intercept values (1.35 and 2.35 μs, respectively) (Fig. 2).

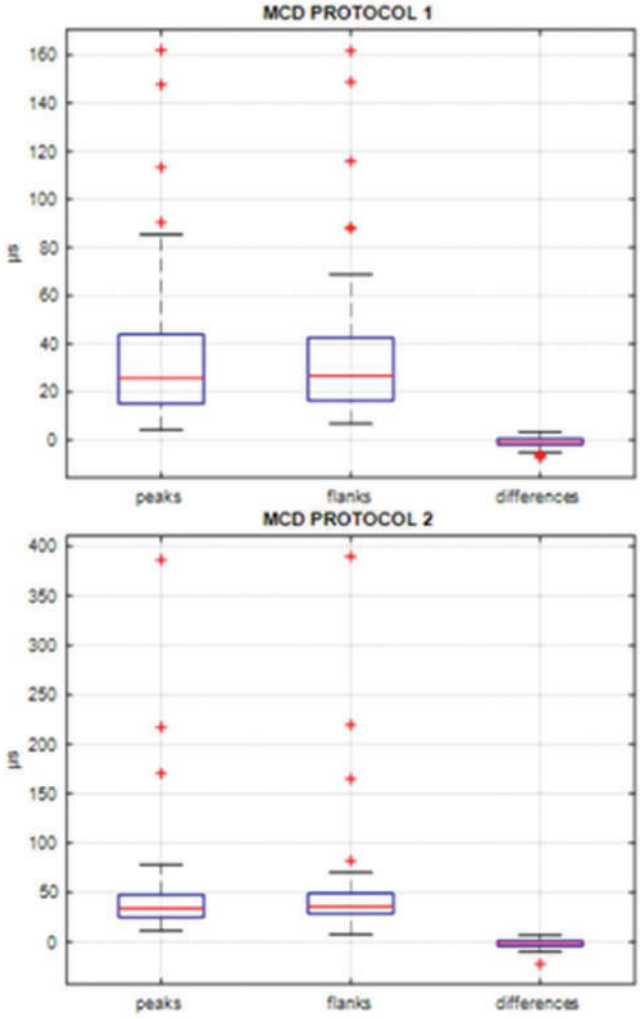

FIGURE 1 Boxplots of the jitter measurements obtained with the peak and the flank methods and the differences between them, for EMG recordings obtained from protocols 1 and 2.

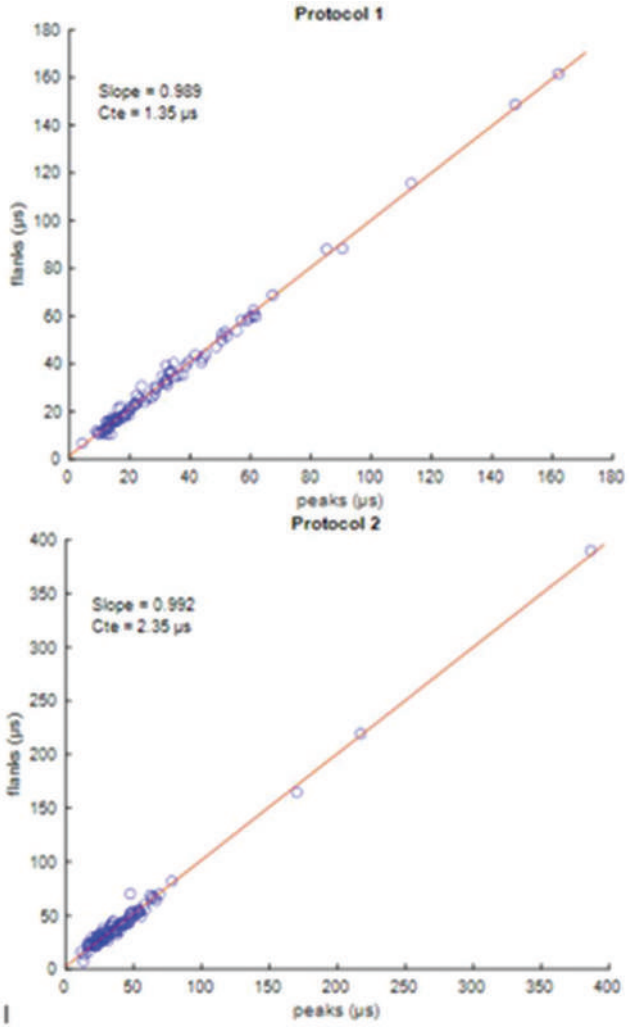

FIGURE 2 Regression models of the jitter measurements obtained with both methods in the two protocols.

TABLE 1 Statistical parameters of jitter measurements obtained by the peak and the flank methods and their differences, for EMG recordings obtained from protocols 1 and 2.

PROTOCOL 1				
	Median (μs)	[25th, 75th] percentiles (μs)	[5th, 95th] percentiles (μs)	Range (μs)
Peaks	25.78	[15.1, 43.9]	[10.5, 87.6]	[4.3, 161.9]
Flanks	26.76	[16.4, 42.6]	[10.9, 88.1]	[6.8, 161.7]
Differences	-0.92	[-1.9, 0.0.5]	[-5.1, 2.1]	[-7.3, 3.2]
PROTOCOL 2				
	Median (μs)	[25th, 75th] percentiles (μs)	[5th, 95th] percentiles (μs)	Range (μs)
Peaks	35,08	[24.8, 47.7]	[16.3, 71.7]	[11.4, 386.4]
Flanks	35.73	[28,2, 49.6]	[19.5 ,73.7]	[7.4, 389.9]
Differences	-1,47	[-4.5, 0.9]	[-9.0, 4.9]	[6.3, -22.6]

Conclusion: Although the jitter measurements obtained with the two methods were statistically different for both protocols, this difference seems to be small and not too relevant from a clinical viewpoint. However, in some isolated cases, the difference in their measurements may be high, which could affect the diagnosis.

Disclosure: This work has been funded by the Department of Health of the Government of Navarra (project GN2022/29) and by the Spanish Ministry of Science and Innovation (project PID2022-136620OB-I00).

EPO-205 | Myocarditis/myositis/myasthenia gravis overlap syndrome: Description of three patients

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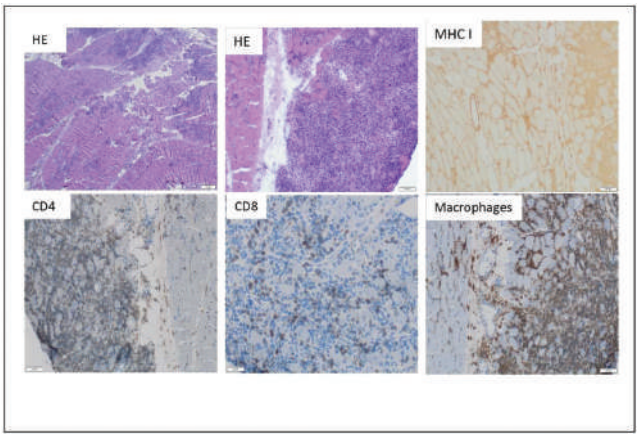
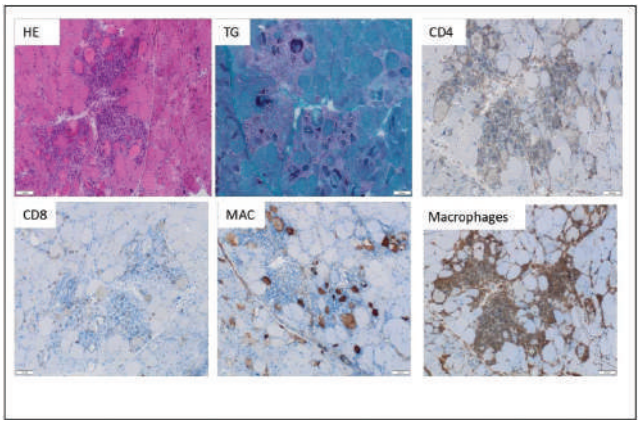
Background and Aims: Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of tumors with a poor prognosis. Despite their high effectiveness, these therapies are associated with a broad spectrum of adverse effects, including the overlap syndrome of myocarditis/myositis/myasthenia gravis (IM3OS Syndrome).

Methods: We report on three patients undergoing treatment with ICIs (pembrolizumab and nivolumab). The first patient presented with binocular diplopia and ptosis. The second patient complained of muscle weakness, diplopia, chest pain, and recurrent syncope. The third patient was asymptomatic but was referred due to elevated CK levels.

Results: In all three patients, serum CK levels (>1000 IU/L) and troponins (>200 ng/L) were elevated. Whole-body muscle MRI was normal. EMG showed spontaneous activity at rest and myopathic patterns suggestive of inflammatory myopathy. The repetitive nerve stimulation test was normal. AntiRACh and anti-MUSK (anti-receptor tyrosine kinase) antibodies were positive only in one of the patients. Muscle biopsy revealed inflammatory myopathy. Two patients received corticosteroid therapy, intravenous immunoglobulins, and pyridostigmine. The second patient also required a pacemaker implantation due to complete atrioventricular block and ultimately succumbed to respiratory failure. The third patient only required corticosteroid treatment.



Patient 1. Biopsy of the right quadriceps



Patient 2. Biopsy of the brachial biceps muscle.

Conclusion: An increased incidence of IM3OS Syndrome has been observed in patients treated with ICIs, associated with high mortality. The presence of any of the symptoms should alert to the possibility of coexistence of others. Early diagnosis is essential for the management and prevention of potentially fatal complications.

Disclosure: Nothing to disclose.

EPO-206 | **Efgartigimod consistently improved health-related quality of life in AChR-Ab+ participants with gMG in IV and SC trials**

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Background and Aims: Myasthenia gravis (MG) causes substantial burdens on patient health-related quality of life (HRQoL). Recent MG guidelines indicate that therapeutic goals should aim for the best possible disease control, with the best possible preservation/restoration of QoL. Here we report HRQoL outcomes from efgartigimod-treated, AChR-Ab+ generalised MG (gMG) participants in the completed, placebo-controlled, Phase 3 ADAPT (IV) and ongoing, open-label extension ADAPT-SC+ (SC) trials.

Methods: Efgartigimod was administered via IV infusion (10mg/kg) or SC injection (coformulated with recombinant human hyaluronidase PH20; 1000mg), in cycles of 4 once-weekly administrations. Subsequent cycles were initiated >=5 weeks (ADAPT) or >=4 weeks (ADAPT-SC+) from last dose based on clinical evaluation. HRQoL was assessed by validated MG-specific (MG-QoL15r) and general (EQ-5D-5L VAS) scales.

Results: Demographics/baseline characteristics for AChR-Ab+ participants are in Table 1. In ADAPT, efgartigimod-treated AChR-Ab+ participants ($n=63$) showed statistically significant improvements in HRQoL versus placebo ($n=60$). Mean (SE) MG-QoL15r score decreased from baseline to week 4, cycle 1: efgartigimod, –7.3 (0.79); placebo, –2.3 (0.51). Mean (SE) EQ-5D-5L VAS score increased from baseline to week 4, cycle 1: efgartigimod, 15.8 (2.20); placebo, 4.1 (1.64)(Fig.1). Improvements in QoL were consistent in ADAPT-SC+, with peak mean (SE) changes from baseline in MG-QoL15r and EQ-5D-5L VAS scores of –5.1 (0.44) and 13.8 (1.54), respectively, at week 4, cycle 1 (Fig. 1). In ADAPT-SC+, MG-QoL15r and EQ-5D-5L VAS cycle baseline scores improved with subsequent cycles, indicating durable QoL improvements.

Conclusion: Efgartigimod IV/SC demonstrated consistent and meaningful improvements in QoL across clinical trials in AChR-Ab+ gMG, achieving an important treatment goal for these participants.

Disclosure: FS: Agenzia Italiana del Farmaco, Alexion, Almirall, argenx, Dianthus, Friedrich's Ataxia Research Alliance, Genpharm, Immunovant, Leadiant Biosciences, Lexeo Therapeutics, Madison Pharma, Medpharma, Novartis, Prilenia, Reata, Sandoz, Sanofi, Zai Lab. JLDB: Alexion, Alnylam, argenx, CSL, Janssen, Sanofi Genzyme, UCB. KU: Alexion, argenx, Chugai, Horizon, Janssen, Japan Blood Products Organisation, Mitsubishi Tanabe, UCB, Viela Bio. DK: argenx, BIOCAD, Bristol Myers Squibb, Horizon, Janssen, Merck, Novartis Russia, Roche, Sanofi, UCB. SS, BVH, RK and JP: Employees of argenx. AM: Alexion, argenx, German Myasthenia Gravis Society, Grifols, Hormosan, Janssen, Merck, Octapharma, UCB, Vitaccess. RM: Alexion, argenx, Biogen, BioMarin, Catalyst, Merck, Roche, Teva, UCB.

TABLE 1

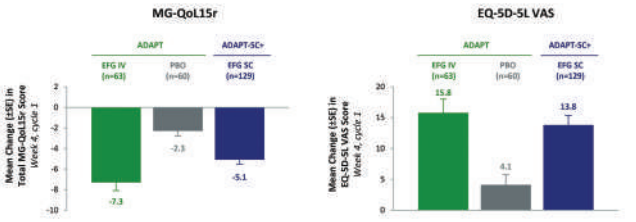
Table 1 Demographics and baseline disease characteristics (AChR-Ab+ participants)

	ADAPT*		ADAPT-SC+*,‡
	Efgartigimod IV (n=65)	Placebo (n=64)	Efgartigimod SC (n=141)
Age, years, mean (SD)	44.7 (15.0)	49.2 (15.5)	51.0 (15.9)
Sex, female, n (%)	46 (70.8)	40 (62.5)	90 (63.8)
Total MG-ADL score, mean (SD)	9.0 (2.5)	8.6 (2.1)	7.6 (3.4)
Total MG-QoL15r score, mean (SD)	16.1 (0.7)	16.8 (0.6)	13.1 (6.8)
EQ-5D-5L VAS score, mean (SE)	58.0 (1.9)	57.2 (1.9)	61.0 (1.6)
Concomitant MG therapy, n (%)			
Any steroid	46 (70.8)	51 (79.7)	103 (73.0)
Any NSIST	40 (61.5)	37 (57.8)	67 (47.5)
Any AChEI	57 (87.7)	57 (89.1)	122 (86.5)
Steroid + NSIST§	34 (52.3)	31 (48.4)	53 (37.6)
AChEI only	13 (20.0)	6 (9.4)	23 (16.3)

AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor antibody–seropositive; EQ-5D-5L VAS, EuroQoL 5-Dimension, 5-Level visual analogue scale; IV, intravenous; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; NSIST, nonsteroidal immunosuppressive therapy; SC, subcutaneous; SD, standard deviation; SE, standard error.

*Concomitant therapy received at a stable dosage during screening and throughout the study. ‡Concomitant therapy received during the first year of the study. ‡Open-label extension of ADAPT-SC trial. §As dual or triple therapy, in combination with AChEI.

Figure 1 HRQoL improvements in AChR-Ab+ participants



AChR-Ab+, acetylcholine receptor antibody–seropositive; EFG, efgartigimod; EQ-5D-5L VAS, EuroQoL 5-Dimension, 5-Level visual analogue scale; HRQoL, health-related quality of life; IV, intravenous; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; PBO, placebo; SC, subcutaneous; SE, standard error.

FIGURE 1

EPO-207 | Eculizumab as rescue therapy in two gMG patients with worsening symptoms while on Efgartigimod

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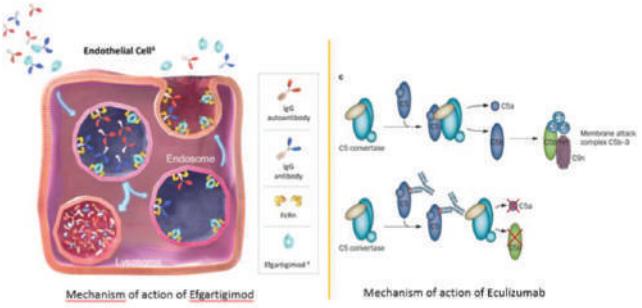
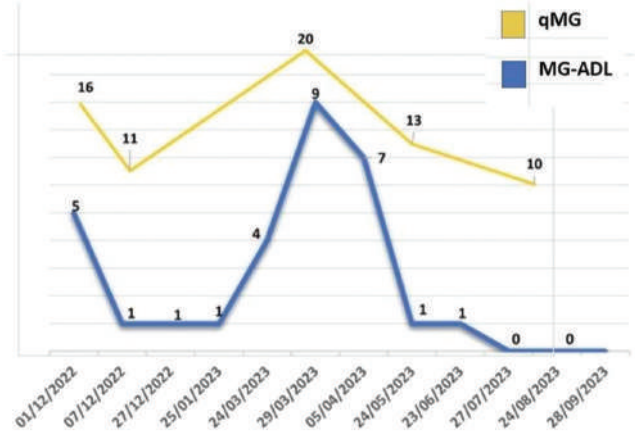
Background and Aims: Eculizumab and Efgartigimod are available for refractory anti-AChR+ gMG. We describe two cases who suffered a relapse while on Efgartigimod, rescued with Eculizumab.



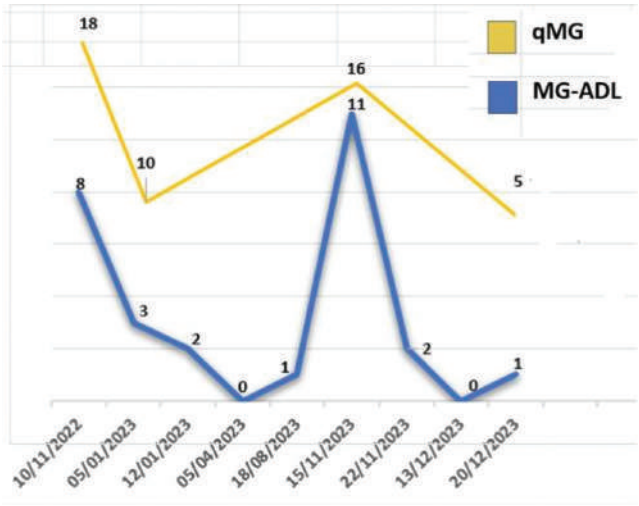
Efgartigimod and Eculizumab mechanisms of action

Methods: Case 1: A 46 yo woman treated with thymectomy, pyridostigmine, prednisone, azathioprine, IVIg. In December 2022 she started Efgartigimod IV (10 mg/kg weekly for four weeks, every two months). Her MG-ADL and qMG were 5 and 16. Case 2: A 47 yo woman treated with thymectomy, pyridostigmine, prednisone and azathioprine. In November 2022 she started Efgartigimod. Her MG-ADL and qMG were 8 and 17.

Results: Case 1: After the first cycle her MG-ADL and qMG dropped to 1 and 11 and remained stable, until, during the third cycle (18th week) she worsened (MG-ADL 9, qMG 20). We discontinued Efgartigimod and started Eculizumab (900 mg iv weekly for 4 weeks, followed by 1200 mg from the fifth week and every two weeks). Her MG-ADL dropped to 5 and at the fifth week her MG-ADL and qMG were 1 and 14. Case 2: After the first Efgartigimod cycle her MG-ADL and qMG were 2 and 10. 48 weeks later her symptoms worsened (MG-ADL 11 and qMG 16). We stopped Efgartigimod and started Eculizumab: after the first infusion her MG-ADL was 2 and at the beginning of the maintenance phase her MG-ADL and qMG were 0 and 5.



Case 1 – MG-ADL and qMG scores



Case 2 – MG-ADL and qMG scores

Conclusion: As far as we know, these are two of the first reports of Eculizumab as rescue therapy in patients not responding to Efgartigimod.

Disclosure: Nothing to disclose.

EPO-208 | Dysferlinopathies: Insights from two Portuguese tertiary centers

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Background and Aims: Dysferlinopathies constitute a subgroup of rare autosomal recessive muscular dystrophies characterized by high phenotypic and genetic heterogeneity. We aimed to characterize the adult patient population with dysferlinopathy from two Portuguese centers.

Methods: Retrospective analysis of patients with a molecular diagnosis of dysferlinopathy followed in an outpatient setting. Recording of demographic, clinical, laboratory, imaging and molecular data were used.

Results: Twenty-one patients from 19 families were identified (male-to-female ratio 1.65:1) with an average age of 48.3 years and symptom onset at 23 ± 9 years. Fifteen different pathogenic variants were identified in the DYSF gene (2 homozygous, 9 compound heterozygous). Most patients reported symptoms in the 20 years preceding molecular diagnosis. Eleven (52%) underwent muscle biopsy, with most showing absence of dysferlin staining. Fourteen patients presented with limb-girdle muscular dystrophy type R2 (LGMDR2) phenotype, two with Miyoshi myopathy, two with distal anterior compartment myopathy, two with hyperCKemia, and one with proximodistal. Fifteen patients progressed to generalized weakness. At an average of 26 years of disease progression, 11 patients (52%) were unable to walk, and 14% required walking aids. Four patients reported dyspnea, 8 with abnormal respiratory function tests, and 3 with cardiomyopathy. Initial CK levels were globally elevated (average 4,953 U/L). Muscle MRI, performed in 4 patients, revealed a similar pattern of adipose infiltration.

Conclusion: Our findings are consistent with the existing literature, demonstrating a diverse spectrum of phenotypes, onset patterns, and progression rates. Given the described clinical and molecular heterogeneity, the ongoing progress in molecular genetic techniques have facilitated a more rapid and definitive diagnosis.

Disclosure: Nothing to disclose.

EPO-209 | Efficacy and safety of Efgartigimod IV and PH20 SC in gMG: analysis of AChR-Ab− participants in ADAPT+/ADAPT-SC+

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Background and Aims: Efgartigimod, a human IgG1 antibody Fc fragment, reduces IgG autoantibody levels by blocking the neonatal Fc receptor. AChR-Ab− patients comprise 15–20% of the generalised myasthenia gravis (gMG) population but have limited treatment options. Efficacy (AChR-Ab− participants) and safety (overall population) from the completed, Phase 3 ADAPT+ (IV) and ongoing, open-label extension ADAPT-SC+ (SC) trials are reported.

Methods: Efgartigimod was administered via IV infusion (10mg/kg [ADAPT+]) or SC injection (coformulated with recombinant human hyaluronidase PH20; 1000mg [ADAPT-SC+]) in cycles of 4 once-weekly administrations. Subsequent cycles were initiated based on clinical evaluation. Efficacy was assessed using MG-ADL scores from final (ADAPT+) and interim (ADAPT-SC+; cut-off December 2022) analyses.

Results: Demographics/baseline characteristics were similar between AChR-Ab− and AChR-Ab+ populations (Table 1). Efgartigimod improved total mean (SE) MG-ADL scores in AChR-Ab− participants (week 3, cycle 1): ADAPT+, −5.3 (0.74); ADAPT-SC+, −3.5 (0.51), with most achieving clinically meaningful improvements (ADAPT+: 79.4%; ADAPT-SC+: 67.6%). MG-ADL score improvements were consistent across multiple cycles (Fig.1). A subset of AChR-Ab− participants achieved minimal symptom expression (MSE) at any time during cycle 1 (ADAPT+: 26.5%; ADAPT-SC+: 13.2%). Proportions achieving MSE were consistent across multiple cycles in both trials. Efgartigimod was well tolerated, and most adverse events (AEs)

were mild/moderate in severity. The most frequent AEs were headache (24.8%, 20.1%), nasopharyngitis (13.8%, 15.6%) and COVID-19 (12.4%, 22.3%) in ADAPT+ and ADAPT-SC+, respectively (Table 2). Reported deaths (ADAPT+: $n = 5$; ADAPT-SC+: $n = 4$) were unrelated to treatment.

TABLE 1

Table 1 Demographics and baseline disease characteristics (AChR-Ab− and AChR-Ab+ participants)

	ADAPT+*		ADAPT-SC+	
	AChR-Ab− (n=34)	AChR-Ab+ (n=111)	AChR-Ab− (n=38)	AChR-Ab+ (n=141)
Age, years, mean (SD)	46.7 (12.2)	47.1 (15.5)	49.7 (14.2)	51.0 (15.9)
Sex, female, n (%)	28 (82.4)	75 (67.6)	29 (76.3)	90 (63.8)
Weight, kg, median (Q1, Q3)	78.1 (65.2, 93.9)	74.0 (62.8, 94.0)	76.1 (67.7, 85.6)	77.0 (63.0, 92.0)
Total MG-ADL score, mean (SD)	10.7 (3.4)	9.5 (3.1)	8.9 (3.4)	7.6 (3.4)
Concomitant MG therapy,† n (%)				
Any steroid	26 (76.5)	85 (76.6)	25 (65.8)	103 (73.0)
Any NSIST‡	22 (64.7)	67 (60.4)	22 (57.9)	67 (47.5)
Any AChEI§	22 (64.7)	100 (90.1)	28 (73.7)	122 (86.5)
Steroid + NSIST‡	19 (55.9)	57 (51.4)	16 (42.1)	53 (37.6)
AChEI only§	4 (11.8)	16 (14.4)	6 (15.8)	23 (16.3)

AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor antibody–seropositive; AChR-Ab−, acetylcholine receptor antibody–seronegative; EFG, efgartigimod; MG-ADL, Myasthenia Gravis Activities of Daily Living; NSIST, nonsteroidal immunosuppressive therapy; PBO, placebo; Q1, first quartile; Q3, third quartile; SD, standard deviation.

*Combined EFG-EFG and PBO-EFG populations. †During the first year of the study. ‡Azathioprine, cyclosporine, cyclophosphamide, methotrexate, mycophenolate and/or tacrolimus. §Ambenonium chloride, distigmine bromide, pyridostigmine and/or pyridostigmine bromide.

TABLE 2

Table 2 Summary of AEs (overall population)

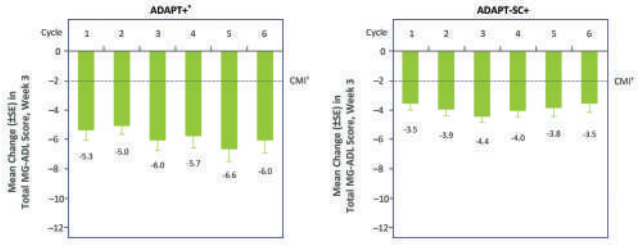
	ADAPT+ (N=145) [228.9 PYFU]		ADAPT-SC+ (N=179) [193.4 PYFU]	
	ER*	Overall Population, n (%)	ER*	Overall Population, n (%)
Any AE	3.53	124 (85.5)	8.95	152 (84.9)
Any grade ≥3 AE	0.33	40 (27.6)	0.39	36 (20.1)
Any SAE	0.24	36 (24.8)	0.26	33 (18.4)
Any ISR	0.09	15 (10.3)	3.25	82 (45.8)
Any infection	0.73	80 (55.2)	1.04	91 (50.8)
Fatal event†	0.02	5 (3.4)	0.03	4 (2.2)
Discontinued study treatment owing to AEs	0.06	12 (8.3)	0.03	4 (2.2)
Most commonly observed AEs‡				
Injection site erythema	-	-	1.73	52 (29.1)
COVID-19§	0.10	23 (15.9)	0.24	40 (22.3)
Headache	0.45	36 (24.8)	0.63	36 (20.1)
Nasopharyngitis	0.10	20 (13.8)	0.19	28 (15.6)
Diarrhea	0.08	14 (9.7)	0.18	24 (13.4)
Injection site pain	-	1 (0.7)	0.21	21 (11.7)
Injection site pruritus	-	-	0.24	19 (10.6)
Injection site bruising	-	1 (0.7)	0.24	18 (10.1)

AE, adverse event; ER, event rate; ISR, injection site reaction; PYFU, patient-year(s) follow-up; SAE, serious adverse event; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SC, subcutaneous.

*ER was calculated as number of events per total PYFU. †None of the fatal events were related to efgartigimod treatment, as determined by investigators. ‡Most frequent AEs occurring in >10% of participants receiving efgartigimod IV or efgartigimod PH20 SC. §Includes all preferred terms of COVID-19, COVID-19 pneumonia, coronavirus infection, exposure to SARS-CoV-2 and SARS-CoV-2 test positive.

FIGURE 1

Figure 1 Mean change in total MG-ADL score from study baseline (AChR-Ab− participants)



AChR-Ab−, acetylcholine receptor antibody–seronegative; CMI, clinically meaningful improvement; IgG, immunoglobulin G; MG-ADL, Myasthenia Gravis Activities of Daily Living; SE, standard error.

*No data captured at week 4 in ADAPT+ (when maximal IgG reduction and clinical improvement may have occurred).

†≥2 point improvement in the total MG-ADL score.

Conclusion: Efgartigimod was well tolerated and provided clinically meaningful improvements in AChR-Ab− gMG participants across IV and SC trials.

Disclosure: SH: Alexion, argenx, UCB JFH: Academic CME, Ad Scientiam, Alexion, AstraZeneca Rare Disease, argenx, Biologix, Cartesian Therapeutics, Centers for Disease Control and Prevention, CheckRare CME, F. Hoffmann-LaRoche Ltd, Amgen, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Toleranzia AB, UCB, Zai Lab TV: AbbVie, Alexion, argenx, AstraZeneca, Cartesians Therapeutics, CSL Behring, Dianthus, Horizon, Immunovant, ImmunoAbs, Janssen, Sanofi Genzyme, UCB JLDB: Alexion, Alnylam, argenx, CSL, Janssen, Sanofi Genzyme, UCB KU: Alexion, argenx, Chugai, Horizon, Janssen, Japan Blood Products Organisation, Mitsubishi Tanabe, UCB, Viela Bio HM: Alexion, argenx, AstraZeneca, Chugai, Japan Blood Products Organisation, Ministry of Health, Labour and Welfare of Japan, Roche, UCB FS: Agenzia Italiana del Farmaco, Alexion, Almirall, argenx, Dianthus, Friedrich Ataxia Research Alliance, Genpharm, Immunovant, Lediant, Lexeo therapeutics, Madison, Medpharma, Novartis, Prilenia, Reata, Sandoz, Sanofi, Zai Lab DK: argenx, BIOCAD, Bristol Myers Squibb, Horizon, Janssen, Merck, Novartis, Roche, Sanofi, UCB CT'j, SS, BVH, JP: Employees of argenx AM: Alexion, argenx, German Myasthenia Gravis Society, Grifols, Hormosan, Janssen, Merck, Octapharma, UCB, Vitaccess RM: Alexion, argenx, Biogen, BioMarin, Catalyst, Merck, Roche, Teva, UCB.

EPO-210 | Achievement of minimal symptom expression in participants treated with Efgartigimod in ADAPT+ and ADAPT-SC+

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Background and Aims: Efgartigimod, a human IgG1 antibody Fc-fragment, reduces IgG levels through neonatal Fc receptor blockade. Efgartigimod has been investigated in the treatment of generalised myasthenia gravis (gMG) through intravenous (IV) and subcutaneous (SC, coformulated with recombinant human hyaluronidase PH20) administration in the ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+ studies, respectively. A key efficacy indicator in gMG treatment is MG-ADL score improvement. Minimal symptom expression (MSE, MG-ADL total score of 0 or 1) is explored as a novel proposed treatment target in gMG.

Methods: The proportion of acetylcholine receptor antibody positive (AChR-Ab+) participants in ADAPT+ ($n=111$) and ADAPT-SC+ ($n=141$) to achieve MSE was assessed.

Results: In ADAPT, MSE was achieved in 44.6% of efgartigimod-treated participants vs 10.9% of placebo-treated participants at any time point up to 3 cycles. In ADAPT+, the number of participants achieving MSE at any time in up to 19 cycles was 40.5%. Eighty-one percent of efgartigimod-treated participants who achieved MSE in ADAPT also achieved MSE during ADAPT+; 23% who had not achieved MSE in ADAPT did so in ADAPT+. In ADAPT-SC, 45.5% and 41.3% of participants receiving efgartigimod PH20 SC or efgartigimod IV achieved MSE at any time in cycle 1, respectively. In ADAPT-SC+, the number of participants achieving MSE at any time in up to 9 cycles was 54.6%. Clinical improvements may not have been fully captured in OLEs (ADAPT+/ADAPT-SC+) due to the limited number of assessment timepoints.

Conclusion: Achievement of MSE was consistently seen across cycles in AChR-Ab+ participants of both ADAPT+ and ADAPT-SC+, similar to results demonstrated in ADAPT and ADAPT-SC.

Disclosure: Multiple relationships financial and non-financial nature for authors SH, SP, JFH, HM, GP, CQ, DG, EB, SZ, VB, JV, JVV, and RM stated at point of presentation.

Sunday, June 30, 2024

Ageing and dementia 2

EPO-211 | Knockdown of hippocampal calponin-3 alleviates memory impairment and Aβ deposition in APP/PS1 mice

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Background and Aims: Alzheimer's disease (AD) is characterized by progressive cognitive decline, with senile plaques of beta-amyloid (Aβ). Calponin-3, encoded by CNN3, is highly expressed in the brain and regulates cytoskeletal reorganization and dynamics as well as actin interactions through efficient binding to F-actin, thereby controlling dendritic spine morphology, density and plasticity.

Methods: Adenovirus with calponin-3 knockdown or control virus were injected into the hippocampi of APP/PS1 mice to construct APP/PS1-CNN3-KD or APP/ PS1-CNN3-Ctrl mice. The expression of calponin-3 in the hippocampi of experimental mice were confirmed by western blot and Immunofluorescence (IF). Cognitive function of mice were tested by novel object recognition testing(NOR)for working memory, and object location recognition testing(OLR)and morris water maze (MWM) for spatial memory.

Results: The level of hippocampal calponin-3 of 4-, 6- and 9-month old APP/PS1 mice were significantly higher than those of wide type (WT) mice at the same age. IF revealed that calponin-3 distributed in clusters and colocalized with Aβ in the hippocampi of APP/PS1 mice. 7-month old APP/PS1-CNN3-KD mice showed significantly better the working memory and spatial memory, and reduced Aβ deposition and β secretase enzyme 1 (BACE1) levels than APP/ PS1-CNN3-Ctrl mice.

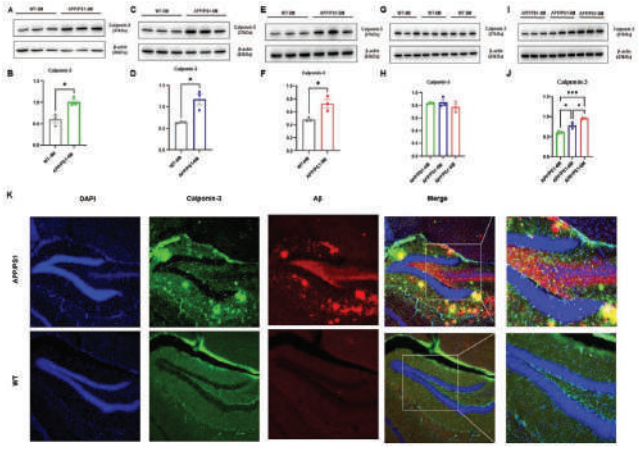

FIGURE 1

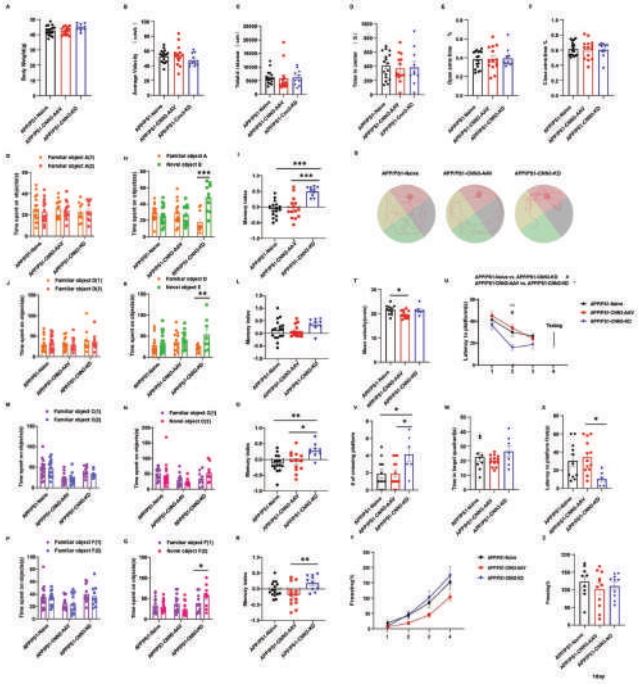

FIGURE 2

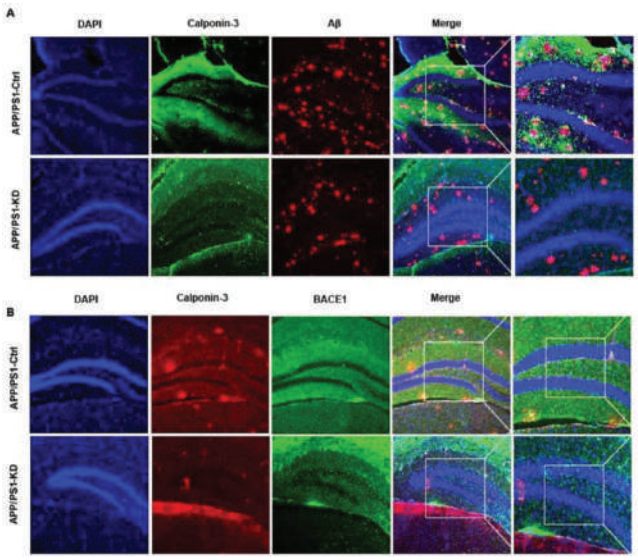

FIGURE 3

Conclusion: Knockdown of hippocampal calponin-3 can improve working and spatial memory and alleviate deposition of Aβ in APP/PS1 mice. Abnormally up-regulation of hippocampal calponin-3 may involve in pathogenesis of AD.

Disclosure: Nothing to disclose.

EPO-212 | Randomized, placebo-controlled, multiple ascending dose study of NX210c safety/tolerability and PK/PD in the elderly

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Background and Aims: Blood-brain barrier (BBB) dysfunction underlies various neurodegenerative diseases (NDD). NX210c is an oligopeptide that reduces blood-brain barrier (BBB) permeability via claudin-5, supports neuroprotection and promotes synaptic transmission in preclinical models. multiple A multiple ascending dose (MAD) study assessed safety and tolerability of intravenously (IV) administered NX210c (at 5 and 10 mg/kg) in healthy elderly volunteers (HEV) with secondary and exploratory objectives to assess blood pharmacokinetics (PK) and pharmacodynamic (PD) parameters, respectively, including blood biomarkers relevant to NDD.

Methods: We report results of a randomized, double-blind, placebo-controlled, MAD study of two doses of NX201c in HEVs run in a single centre with two cohorts of 15 HEVs randomized (4:1 ratio) to NX210c dose or placebo 3x/week (w) for 4w with a follow-up visit 2w after last dosing.

Results: Of 29 HEV randomized, 20 registered 73 treatment-emergent adverse events with all possibly related adverse events mild and no serious adverse events or evidence of NX210c accumulation. According to modelling data, NX210c treatment demonstrated a robust PK/PD relationship, characterized by inhibition of claudin-5, NfL, and SPARCL-1 production, as well as degradation of homocysteine.

Conclusion: NX210c demonstrated a good safety profile following multiple doses in HEV and showed a PD relationship for biomarkers relevant to the BBB, including a reduction of plasma claudin-5. As BBB disruption is a driving feature of NDD, NX210c effect on target biomarkers may represent an important disease-modifying treatment for several neurological disorders and warrants further study in patients with NDD.

Disclosure: DD and PK are employed by CHDR. JLD, SM, SL and AJ are employed by Axoltis Pharma. YG is a shareholder of Axoltis Pharma.

EPO-213 | Neuropathological, clinical and genetic comparison of four peculiar FTLD cases from the Abbiategrasso Brain Bank

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Background and Aims: The spectrum of fronto-temporal lobar degeneration (FTLD) encompasses several proteinopathies and clinicopathological features: (1) heterogeneous clinical presentations; (2) heterogeneous neuropathology; (3) involvement of many genes; (4) atrophy of the frontal and/or temporal cortex. The aim of the study is to present four emblematic cases in order to emphasize the clinical and pathological heterogeneity of FTLD.

Methods: We followed four subjects with major-neurocognitive disorder (major-NCD), belonging to the Abbiategrasso Brain Bank, and analyzed the neuropathology of their brains.

Results: Case 1 – Major-NCD: nfv-PPA/CBS: progressive non-fluent aphasia (nfPPA), apraxia, disinhibition, apathy, hyperorality, severe right hemiparkinsonism and dystonia; neuroimaging: asymmetrical left frontal atrophy; neuropathology: prevalent type A TDP-43 histopathology, limbic co-localization of synuclein pathology and low AD pathology. Case 2 – Major-NCD: behavioral variant FTD (bvFTD): spatial disorientation, wandering, disinhibition, delusions, apathy, hyperorality, postural instability and bilateral parkinsonism; neuroimaging: asymmetrical right temporo-parieto-occipital atrophy; neuropathology: pure type A TDP-43 histopathology. Case

3 – Major-NCD: frontal variant AD (fvAD): logopenic language impairment, progressive memory loss, social withdrawal, apathy, aggressivity, wandering, sleep disturbances, delusions, hallucinations, bilateral rigid-hypokinetic parkinsonism in the advanced stages; neuroimaging: symmetrical fronto-temporal atrophy; neuropathology: predominant AD pathology, limbic co-localization of synuclein pathology and mild TDP-43 pathology. Case 4 – Major-NCD: semantic variant FTD (svFTD): spatial disorientation, fluent aphasia with comprehension and naming deficits, delusions, wandering, aggressivity, postural instability and rigid-hypokinetic parkinsonism; neuroimaging: symmetrical temporal atrophy; neuropathology: predominant AD pathology.

Conclusion: The clinical-pathological comparison of these four cases demonstrates the heterogeneity of FTLD and the essential role of neuropathology in determination of definitive diagnosis of neurodegenerative diseases.

Disclosure: Nothing to disclose.

EPO-214 | CSF biomarkers of Alzheimer's disease, neuropsychological tests and UPDRS-III in patients with Parkinson's disease

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Background and Aims: CSF biomarkers of amyloidopathy (Aβ42 and Aβ42/40), tauopathy (p-tau) and neurodegeneration (t-tau) have been widely used as a measure of Alzheimer's disease (AD) pathology in vivo and as a predictor of cognitive impairment in AD. These biomarkers have been proven to predict cognitive decline in PD as well. We aimed to assess the associations between CSF biomarkers of AD pathology and cognitive/motor impairment in a cohort of PD patients.

Methods: We recruited 45 subjects with diagnosis of PD. A lumbar puncture (LP) was performed and CSF biomarkers of AD were quantified. At the time of LP, a complete neuropsychological battery and UPDRS-III motor scale were used to assess cognitive and motor domains respectively. A 12–24 months follow-up UPDRS-III was available for every patient. Correlations between CSF biomarkers, neuropsychological tests and UPDRS-III at the time of LP and after 12–24 months were carried out.

Results: Our results revealed a significant correlation between biomarkers of amyloidopathy and poorer performances in MMSE, RAVLT delayed recall, Spatial Span, Raven matrices, MFTC, semantic verbal fluency, ROCF delayed. Aβ42/40 was found to predict the change between the UPDRS-III score at the baseline and follow-up.

Conclusion: Amyloidopathy is a frequent PD co-pathology. This study highlighted the role of CSF biomarkers of amyloidopathy as a tool to predict worse performances in some common neuropsychological tests. Furthermore, Aβ42/40 showed potential in identifying PD patients at risk of accelerated motor decline, suggesting a possible synergistic role of Aβ42 with alpha-synuclein in the clinical progression of Parkinson disease.

Disclosure: Nothing to disclose.

EPO-215 | Genetically proxied PDE5 inhibition and risk of dementia: A drug target Mendelian randomisation study

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Background and Aims: Phosphodiesterase-5 (PDE5) inhibitors have gained interest as a potential treatment for dementia. However, current evidence is limited to observational and pre-clinical studies. This drug-target Mendelian Randomisation (MR) study aims to elucidate the on-target effects of pharmacological PDE5 inhibition on dementia subtypes, cognitive traits, and neuro-imaging phenotypes.

Methods: Two independent ($r^2 < 0.001$) blood pressure lowering variants from around the PDE5A locus were used in two-sample MR to assess the effect of genetically proxied PDE5 inhibition on risk of dementia subtypes, cognitive performance, and neuroimaging traits (cortical thickness, surface area and volume of white matter hyperintensities) in large-scale genomic consortia. The instrument's predictive validity was assessed against erectile dysfunction and pulmonary arterial hypertension (PAH) as positive controls.

Results: Following correction for multiple comparisons, genetically proxied PDE5 inhibition was associated with lower odds of erectile dysfunction (OR 0.85, 95% CI 0.83–0.87) and PAH (OR 0.58, 95% CI 0.55–0.61), and higher odds of Alzheimer's disease (OR 1.07, 95% CI 1.04–1.10), Lewy body dementia (OR 1.20, 95% CI 1.17–1.23) and vascular dementia (OR 1.04, CI 1.02–1.07). Furthermore, genetically proxied PDE5 inhibition was associated with reduced cortical thickness (SD change −0.003, 95% CI −0.004, −0.002) and cognitive performance (SD change −0.010, 95% CI −0.013, −0.007), but not cortical surface area or volume of white matter hyperintensities.

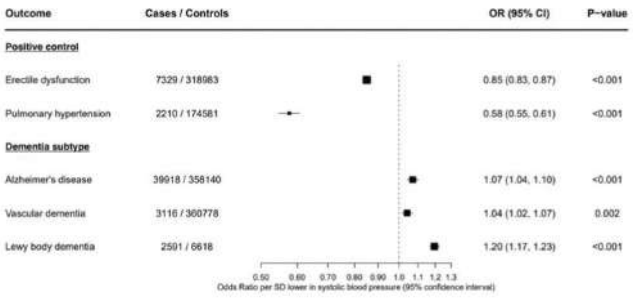

FIGURE 1 Forest plot depicting Mendelian randomisation estimates for genetically proxied PDE5 inhibition and associations with positive controls and dementia subtypes (Bonferroni correction: $p < 0.0036$ for statistical significance)

TABLE 1 Mendelian randomisation estimates for genetically proxied PDE5 inhibition and associations with cognitive traits and neuro-imaging phenotypes (Bonferroni correction: $p < 0.0036$ for statistical significance)

Outcome	Mean (SD)	SD difference (95% CI)	P-value
Cognitive performance	Score 0 ± 1	-0.010 (-0.013, -0.007)	<0.001
Average cortical thickness	2.45 ± 0.11mm	-0.003 (-0.004, -0.002)	<0.001
Average cortical surface area	169,647.43 ± 16,501.45mm²	320.172 (25.464, 614.881)	0.033
White matter hyperintensities	-0.027	-0.027 (-0.050, -0.005)	0.016

Conclusion: In contrast to evidence from observational studies, our findings indicate that inhibition of PDE5 is associated with higher risk of dementia, and an unfavourable neurocognitive profile. This risk should be further investigated prior to clinical trials of pharmacological PDE5 inhibition in the treatment and prevention of dementia.

Disclosure: The author Alexander Tinworth may receive support from the Nuffield Department of Population Health at the University of Oxford or his scholarship benefactor, the British Heart Foundation to attend conferences but has not received financial or academic support in the conducting or writing of the study.

EPO-216 | Identification of novel dysregulated proteins in Alzheimer's disease patients with therapeutic and diagnostic potential

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Background and Aims: Alzheimer's disease (AD) is the most common cause of dementia worldwide. Its pathogenesis has not been well elucidated yet and effective treatments are needed. We aimed to analyze protein dysregulation in AD to identify dysregulated proteins that could be key for the study of AD by two proteomics strategies, TMT (Tandem Mass Tags) 10-plex quantitative proteomics and LFQ (Label Free Quantification).

Methods: For TMT, brain protein extracts from AD patients (Braak IV-VI) were analyzed by tandem mass spectrometry coupled to liquid chromatography (LC-MS/MS) using a Q-Exactive. Protein extracts from VD (vascular dementia) and FTD (frontotemporal dementia) patients, and healthy individuals were used as controls. For LFQ, a pull-down with in vitro synthesized Abeta (Amyloid-beta) fibers was performed, and interacting proteins analyzed by LC-MS/MS. Subsequent analysis of proteomics data was performed with MaxQuant and the R program.

Results: 169 out of 3281 proteins identified by TMT were found statistically significant ≥1.5-fold dysregulated in AD in comparison to controls, with the dysregulation of 10 of them confirmed using a different cohort of tissue and plasma samples. Two of these proteins were found associated to Abeta fibers, and two as blood-based biomarkers of AD. Regarding the pull-down, 332 proteins were identified as potential interactors of Abeta fibers, with 18 of them validated in vitro and ex vivo.

Conclusion: Novel proteins associated to AD pathogenesis, with a potential role in AD development and as biomarkers of the disease were described here. In addition, these proteins possess a high potential as therapeutic targets.

Disclosure: This work was supported by the PI17CIII/00045 grant from the AES-ISCIII program to R.B. The A.M-C. FPU predoctoral contract was supported by the Spanish Ministerio de Educación, Cultura y Deporte. The authors declare no competing interests.

EPO-217 | Structure-based discovery of choline acetyltransferase ligands as potential theranostic agents for Alzheimer's disease

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Background and Aims: Choline acetyltransferase (ChAT), is a key cholinergic enzyme that biosynthesizes neurotransmitter acetylcholine, which plays a pivotal role in fundamental brain processes. Gradual loss of cholinergic neurons is observed in the brain with Alzheimer's disease which correlates well with the progressive decline of ChAT levels. This makes ChAT a key biomarker to estimate AD progression. The absence of specific, potent, blood-brain-barrier permeable small molecule ligands motivated us to discover novel ChAT ligands.

Methods: In this study, we have screened a VITAS-M small molecule library containing ~1.4 million compounds by using a structure-based virtual screen protocol based on VinaMPI. The top scoring compounds were manually inspected for their interaction with the active site amino acid residues and fifty compounds were selected.

Results: The fifty structurally diverse hits were identified. All showed potentially good interaction with the hotspot residues in the binding pocket of ChAT. They also showed prominent interaction with the catalytic residue His324 which is necessary for inhibitory activity of ligands. These hits will be validated in an in-house developed fluorimetric assay to evaluate their enzyme inhibition kinetics

and molecular dynamic simulation to understand their dynamic interaction in the process of ChAT inhibition.

Conclusion: The potential ChAT hits identified in this study can be further developed into ChAT PET tracers for the diagnosis of cholinergic dysfunction and to initiate timely therapeutic interventions to prevent or delay the progression of AD.

Disclosure: Nothing to disclose.

EPO-218 | Clinical correlations with diffusion-weighted MRI in probable Creutzfeldt-Jakob Disease

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Background and Aims: Diffusion-weighted imaging (DWI) of the brain is important in diagnosing CJD. Also, elevated CSF total tau (t-tau) is considered a useful CJD biomarker revealing neuro-axonal damage although it is not specific for CJD. In this study, we attempted to find out the association between DWI abnormality and CSF t-tau in CJD patients.

Methods: The patients who had been diagnosed and reported as human prion disease to the Korea Disease Control and Prevention Agency (KDCA) by medical institutions in South Korea from January 1, 2019, to December 31, 2019, were included in the clinical review. A total of 186 patients had been reported as suspected human prion disease during the one year and 53 patients who satisfied the criteria for human prion disease were included in the analysis.

Results: Hyperintense lesions on DWI were observed in 52 patients (98%). The involvement of the neocortex was observed in almost all patients (98%) and asymmetrical and bilateral hyperintensities on DWI were common. Among the neocortex, the most commonly involved region was the parietal lobe, followed by the frontal lobe, temporal lobe, and occipital lobe. DWI abnormality in the striatum and/or thalamus was observed in 65.3% of patients. There was no significant association between the extent of the lesions on DWI and CSF t-tau.

Conclusion: In this study, most of the patients with probable CJD showed DWI abnormality mainly on the neocortex (parietal > frontal > temporal > occipital). The association between the pattern of DWI abnormality and the level of CSF t-tau was not observed.

Disclosure: Nothing to disclose.

EPO-219 | Linking mitochondrial dysfunction with glial and neuroaxonal degeneration in Creutzfeldt-Jakob disease

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Background and Aims: Creutzfeldt-Jakob Disease (CJD) is a rare human prion disease characterized by the aberrant accumulation of a misfolded prion protein in neurons, causing spongiform changes, and neuronal loss. The exact neuropathogenic mechanisms associated with the rapid neuronal death partly remain unclear, with mitochondrial dysfunction possibly giving a contribution. This study explores the serum concentrations of biomarkers of neurodegeneration, glial activation, and mitochondrial dysfunction in CJD and their associations.

Methods: We assessed the serum material of 16 CJD patients [median age 66 years (25th-75th percentile 59.8–77.3)] and 72 healthy controls [HC median age 64 years (25th-75th percentile 56–72)]. Serum neurofilament light chain (sNfL) and serum glial fibrillary acidic protein (sGFAP) levels were assessed with single molecule assay (SIMOA), and serum Growth Differentiation Factor-15 (sGDF-15) with ELISA. Spearman correlation and analysis of covariance, considering age as covariate, were performed.

Results: Significant differences were found in sNfL [median CJD sNfL: 129 pg/ml (25th–75th percentile 102–252), median HC sNfL: 12.1 pg/ml (25th–75th percentile 7.96–16.2); $p < 0.001$] and sGFAP [median CJD sGFAP 586 pg/ml (25th-75th percentile 394–1300), HC 101 pg/ml (25th-75th percentile 50.8–169); $p < 0.001$] between CJD and HC. No difference was shown when sGDF-15 was considered [median CJD sGDF-15: 780 ng/ml (25th-75th percentile 402–2151); median HC sGDF-15 704 ng/ml (25th-75th percentile 444–992)]. In CJD patients, however, we found a significant positive correlation of sNfL with sGDF-15 levels ($p = 0.001$, $r = 0.748$).

Conclusion: Our study suggests a role of mitochondrial dysfunction in the complex process of neurodegeneration in CJD.

Disclosure: Nothing to disclose.

EPO-220 | Unilateral magnetic resonance-guided focused ultrasound thalamotomy for essential tremor and Parkinson's disease

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Background and Aims: Magnetic Resonance-guided focused ultrasound (MRgFUS) thalamotomy is a minimally invasive procedure with proven efficacy in the management of refractory tremor. The objective of this study is to analyse differences of effectiveness in tremor reduction between Essential Tremor (ET) and Parkinson's disease (PD).

Methods: A total of 22 patients, 11 with refractory essential tremor (ET) and 11 with PD, who underwent MRgFUS thalamotomy in our center were included. The Clinical Rating Scale for Tremor of the

treated hemibody (CRST A+B) and functional disability (CRST C) were compared before and 6 months after MRgFUS thalamotomy, as well as adverse effects at 1 and 6 months.

Results: At baseline, mean (±SD) age was 71.1 1±8.53 for ET patients and 70.1±12.89 years for PD patients ($p=0.832$). Before treatment, CRST A+B scores were 21.45±5.94 and 19.64±5.89 ($p=0.438$) and CRST C were 17.18±5.4 and 14.09±6.46 ($p=0.365$), respectively. After 6 months of MRgFUS thalamotomy, a significant improvement in tremor severity and disability was observed (CRST A+B: 1.82±2.44 and 3.45±3.53 ($p=0.003$); CRST C: 1.82±2.18 and 4.09±4.23 ($p=0.003$)), although there were not significant differences between both groups ($p=0.193$ and $p=0.065$, respectively). Dysarthria and unsteadiness were the most common adverse effects reported, which were mild and transient.

Conclusion: Unilateral MRgFUS thalamotomy is safe and effective for refractory tremor in ET and PD. Further studies with larger sample sizes are needed to address possible differences in efficacy.

Disclosure: Nothing to disclose.

EPO-221 | Obstructive sleep apnoea and cognitive decline: Quest for new biomarkers

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Background and Aims: Obstructive sleep apnea (OSA) is the most common type of sleep-related breathing disorder. The underlying chronic intermittent hypoxia and sleep fragmentation are pointed out as the main mechanisms leading to cognitive decline. Apnea-hypopnea index has been used to evaluate severity of OSA, but oxygen desaturation index (ODI) is a relevant parameter, reflecting hypoxia. We aim to explore the link between different OSA markers and CSF biomarkers related to Alzheimer's disease (AD).

Methods: Transversal and retrospective study. We selected patients with cognitive complaints followed in a neurology appointment from a tertiary health center that met criteria for OSA through polysomnography (PSG). We gathered demographic and clinical data, including PSG parameters and CSF biomarkers of dementia. Statistical analysis comprised univariate and multivariate analysis adjusted for potential confounding variables. Statistical significance was set at $p<0.05$.

Results: A total of 81 patients were included (mild OSA 29.6%, moderate OSA 35.8%, severe OSA 21.0%). Forty-six (56.8%) were women, mean age of 69.2 years, 7.3 years of education, mean MMSE of 23.6, mean AHI of 22.0 events/h and mean ODI of 20.6 events/h. The univariate analysis showed a positive correlation between ODI and pTau ($r=0.29$; $p=0.033$). In stepwise multivariate regression analysis, the best predictors of pTau were Tau ($\beta=0.161$, 95% CI=[0.143, 0.178], $p<0.001$), Aβ42 ($\beta=-0.023$, 95% CI=[−0.036, −0.011], $p=0.001$) and ODI ($\beta=0.446$, 95% CI=[−0.011, 0.903], $p=0.055$).

Conclusion: We found an association between ODI and CSF pTau levels, suggesting that severe nocturnal hypoxemia might contribute to neurodegeneration. These findings further emphasize the possible role of OSA treatment in preventing further neuronal damage.

Disclosure: Nothing to disclosure.

EPO-222 | Repetitive transcranial magnetic stimulation and mild cognitive impairment

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Background and Aims: Repetitive transcranial magnetic stimulation (rTMS) can be used to improve cognition in mild cognitive impairment (MCI) and Alzheimer's disease (AD). Possible neurobiological mechanisms underlying the rTMS therapeutic effects are maladaptive plasticity, glial activation and neuroinflammation, including metalloproteases (MMP) activation. Our aim was to evaluate the effects of bilateral rTMS over the dorsolateral prefrontal cortex (DLPFC) on plasmatic levels or MMP1, -2, -9 and -10, MMPs-related tissue inhibitors TIMP1 and TIMP2, and cognitive performances in MCI patients.

Methods: MCI patients ($n=18$) were randomly assigned to two groups: one group received high frequency rTMS daily four weeks and the other received sham stimulation. Cognitive and psychobehavioural scores were measured at baseline (T0), after five weeks (T1), and six months after rTMS stimulation (T2). To determine the concentration of MMP1, -2, -9 and -10 and the respective inhibitors, TIMP1 and TIMP2, we used commercially available ELISA kits.

Results: We observed reduction in plasmatic levels of MMP-1, -9, and -10 in the MCI-TMS group and an increased in plasmatic levels of TIMP1 and TIMP2. We also detected an improvement in visuospatial performances.

Conclusion: Our study showed a possible long-term impact of bilateral rTMS, a non-invasive neuromodulation technique, on plasmatic levels of selected MMPs and TIMPs in MCI patients. These biological effects, after a 4-week course of rTMS, associated with improvement of visuospatial perceptive abilities, prompt us to hypothesize a neuroprotective effect of rTMS.

Disclosure: I have no disclosure.

EPO-223 | Internetworks functional connectivity in Alzheimer's disease and Mild Cognitive impairment patients with Anosognosia

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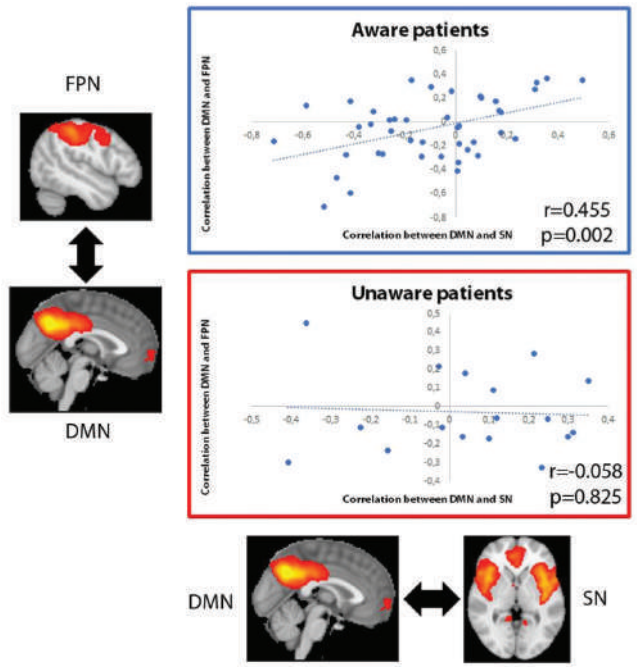
Background and Aims: Unawareness in the Alzheimer's disease (AD) continuum has been hypothesized to arise from an impaired communication between brain regions. Reduced functional connectivity in the default-mode network (DMN) has been demonstrated in AD patients with anosognosia; altered interaction between DMN and Frontoparietal Network (FPN) has been reported in Mild Cognitive Impairment (MCI); stronger connectivity within the salience network (SN) has been linked to anosognosia in prodromal AD. We hypothesized that anosognosia in AD could be associated with an imbalance between the activity of the DMN, the SN and the FPN, detectable using resting state functional magnetic resonance imaging (fMRI).

Methods: Sixty patients with MCI and AD underwent fMRI and neuropsychological assessment. Patients were categorized as aware or unaware of their condition, according to the Anosognosia Questionnaire Dementia. Independent component analysis (ICA) of the fMRI data was used to identify DMN, SN and FPN. Partial correlations were performed on the individual ICA time-courses associated with each network to assess inter-network functional connectivity. Finally, we examined whether the strength of functional connectivity between DMN and SN was a significant predictor of the connectivity strength between DMN and FPN, separately for aware and unaware patients.

Results: Functional connectivity between DMN and SN was positively correlated with functional connectivity between DMN and FPN only in aware patients (Figure 1).

Conclusion: Functional connectivity between DMN, SN and FPN is altered in MCI and AD patients with anosognosia, suggesting that a possible imbalance in these large-scale networks might be associated to anosognosia expression in AD continuum.

Disclosure: Nothing to disclose.



Correlation between internetwork functional connectivity in aware and unaware patients. Images represent average group maps of both aware and unaware patients obtained using independent component analysis.

EPO-224 | Mitigating Alzheimer's: Neurosteroids' effect against mitochondrial dysfunction

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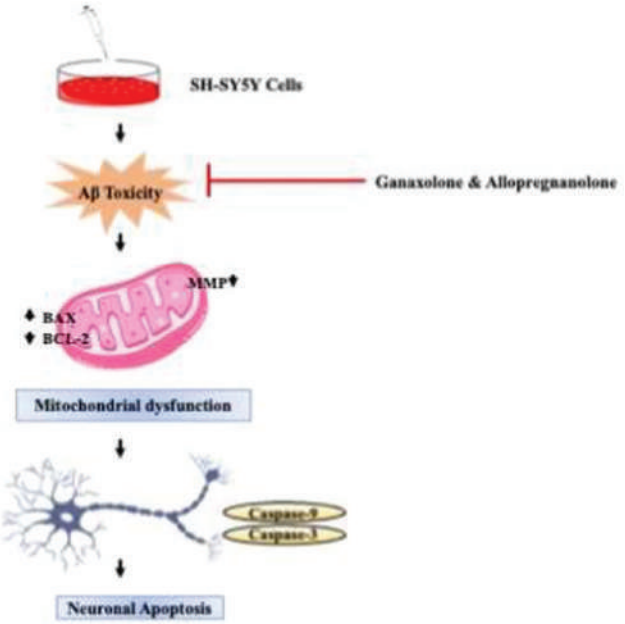
Background and Aims: Introduction: Alzheimer's disease (AD) is a neurological disorder characterized by pathological features such as synaptic and neuronal loss, the accumulation of amyloid-beta (Aβ) deposits, and the formation of neurofibrillary tangles. The disease is closely linked to oxidative stress, stemming from increased reactive oxygen species (ROS), altered mitochondrial biogenesis, and changes in mitochondrial membrane potential (MMP), ultimately leading to disrupted mitochondrial function and cellular apoptosis. Ganaxolone and allopregnanolone have displayed neuroprotective effects; however, their impact on Aβ deposits and mitochondrial dysfunction in AD remains unclear. This study delves into the influence of Ganaxolone and allopregnanolone on Aβ toxicity-induced mitochondrial dysfunction and explores the subsequent cellular processes.

Methods: The SH-SY5Y neuroblastoma cell line was transfected with an amyloid precursor protein (APP) plasmid construct to establish an AD cell model. Cells underwent a 24-hour treatment with Ganaxolone and allopregnanolone, followed by a ThT binding assay and immunoblotting to assess the effects on in vitro amyloid formation. Mitochondrial alterations were monitored using mitosox, and changes in MMP were analyzed through flow cytometry using TMRE. Additionally, apoptotic protein were investigated via Western blotting.

Results: Ganaxolone and allopregnanolone treatment significantly decreased mitochondrial ROS associated with Aβ toxicity and restored altered MMP mitigated apoptosis and amyloid-beta toxicity. We also showed that Ganaxolone decreased the rate of apoptosis in cells by modulating important evolutionarily conserved proteins of apoptosis.

Conclusion: These findings suggest that Ganaxolone and allopregnanolone provide protection against mitochondria to APP-transfected SH-SY5Y cells, proposing Ganaxolone and allopregnanolone as a potential therapeutic agent for AD.

Disclosure: This work was supported by the Indian Council of Medical Research (ICMR) New Delhi, India, for SRF to DG (Ref. No. 45/05/2020-PHA/BMS) and ICMR grant proposal no. IIRP/2023/1050 for financial support.



EPO-225 | Associations between PM2.5 exposure and Alzheimer's disease prevalence among elderly in eastern China

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Background and Aims: Studies showed that PM2.5 might be associated with various neurogenic diseases such as Alzheimer's disease (AD). However, this topic had been little studied in Zhejiang province of China.

Methods: We established a cohort of AD high-risk population with 1,742 elderly aged 60 and above. The average residential exposure to PM2.5 for each participant that in a 5-years period prior to the first survey, was estimated using a satellite-based spatial statistical model. We determined the association between PM2.5 and AD prevalence by cox proportional hazards regression model.

Results: This study showed that an increase in the PM2.5 level was an important associated risk factor that contributed to AD. The average PM2.5 exposure levels among the study population ranged from 32.69μg/m3 to 39.67μg/m3 from 2013 to 2017, which were much higher than 5μg/m3 that specified in the WHO air quality guidelines. There was an association between PM2.5 exposure and AD, and the correlations between PM2.5 and Mini-Mental State Examination, Montreal cognitive assessment scale scores were statistically significant. An increase in the PM2.5 level by 10μg/m3 elevated the risk of AD among residents by 2%-5% (HR model 2-model 4 = 1.02 to 1.05, CI model 2-model 4 = 1.01–1.10). The subgroups of male, with old age, with low education levels, used to work as farmers or blue-collar workers before retirement, overweight and obese were associated with a higher effect of PM2.5.

Conclusion: Reducing PM2.5 exposure might be a good way to prevent AD.

Disclosure: Nothing to disclose.

Table 1. Association between $PM_{2.5}$ exposure (per 10 μg/m³ increment) and incidence of AD

Model	HR	95% CI	*P* values
Model 1	0.85	0.76-1.05	0.06
Model 2	1.02	1.01-1.09	0.04
Model 3	1.05	1.02-1.11	0.03
Model 4	1.03	1.01-1.10	0.04

Abbreviations: HR, relative hazard; 95%CI, 95% confidence interval; AD, Alzheimer's Disease.
* Model 1 was an unadjusted model, Model 2 included $PM_{2.5}$, age, gender; Model 3 added smoking and ETS exposure based on Model 2; Model 4 added educational degree, family income, BMI, and occupation before retirement based on Model 3.

Table 2. Analysis on the Relationship between Cognitive Function Score and $PM_{2.5}$ Exposure

Model	MMSE	MoCA	*P* values for MMSE	*P* values for MoCA
Model 1	0.35 (0.18-0.51)	0.14 (0.08-0.18)	0.03	0.02
Model 2	0.38 (0.19-0.54)	0.15 (0.10-0.22)	0.04	0.03
Model 3	0.36 (0.26-0.47)	0.16 (0.11-0.21)	0.02	0.01
Model 4	0.37 (0.21-0.45)	0.15 (0.08-0.24)	0.03	0.03

* Model 1 was an unadjusted model; Model 2 included $PM_{2.5}$, age, gender; Model 3 added smoking and ETS exposure based on Model 2; Model 4 added educational degree, family income, BMI, and occupation before retirement based on Model 3.

Table 3. Analysis on the association between $PM_{2.5}$ Exposure (Per 10μg/m³) and AD prevalence by subgroups

Variables	Group	HR (95% CI)	*P* values
Gender	Male	1.03 (1.01-1.12)	0.03
	Female	0.94 (0.81-1.08)	0.10
Age group, years	60-64	0.96 (0.72-1.24)	0.13
	65-69	1.04 (0.98-1.12)	0.15
	70-74	1.11 (1.10-1.52)	0.02
	75-85	1.12 (1.11-1.43)	0.02
Education level	Illiteracy	1.13 (1.09-1.20)	0.03
	Primary school	1.01 (0.99-1.15)	0.04
	Junior high school	0.98 (0.77-1.24)	0.23
	Senior high school and above	0.86 (0.26-2.81)	0.31
Marital status	Living alone	1.01 (0.89-1.14)	0.52
	Cohabitation	0.76 (0.58-1.00)	0.78
Occupation	Farmers	1.02 (1.00-1.16)	0.04
	Blue-collar	1.09 (1.01-1.25)	0.02
	White-collar	0.65 (0.43-1.12)	0.42
BMI, kg/m²	Normal, BMI < 24	0.89 (0.76-1.03)	0.36
	Overweight, BMI ≥24 and < 28	1.04 (1.01-1.27)	0.04
	Obese, BMI ≥28	1.03 (1.00-1.12)	0.04

Abbreviations: HR, relative hazard; 95% CI, 95% confidence interval; AD, Alzheimer's Disease.

Autonomic nervous system diseases 2

EPO-226 | Heart rate variability fluctuations within 48 hours following a stroke and their association with symptom severity

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Background and Aims: The impact of cerebrovascular events such as stroke, transient ischemic attack (TIA), and intracranial hemorrhage (ICH) has been the subject of prior publications. However, comprehensive data pertaining to the initial stages of acute cerebral events

is lacking. In this study, we conducted an examination of the fluctuation of heart rate variability, specifically analyzing standard deviation of NN intervals (SDNN), at different intervals after an acute cerebral event.

Methods: Monitoring data from 714 patients treated at the Stroke Unit of University Hospital Tulln were analyzed. For each patient, a 10-minute ECG signal was examined hourly, and heart rate variability and baroreceptor sensitivity were calculated. Heart rate variability fluctuation was quantified as the difference between maximum and minimum values within the specified time frame for each patient.

Results: Stroke patients exhibited the lowest SDNN fluctuation (mean: 16.6, 6 h post-onset), maintaining consistently lower levels over the initial 48 hours compared to individuals with ICH and stroke mimics (ICH: 29.8, stroke mimic: 27.3). Stroke severity influenced SDNN fluctuation, with milder strokes exhibiting increased fluctuation (mean: 26.7) at 6 hours post-onset compared to moderate (mean: 19.8) and severe strokes (mean: 14.9). This effect diminished within 24 h post-onset; however, distinctions between stroke, ICB, and stroke mimic persisted even after 48 h.

Conclusion: Fluctuations in autonomic parameters may suggest autonomic nervous system instability or rigidity during the acute phase following an acute cerebral event. These findings may explain discrepancies in previous analyses, dependent on variances in analyzed datasets and the specific time points considered after symptom onset.

Disclosure: Nothing to disclose.

EPO-227 | Quality indices: A pre-requisite for using automatically monitored electrocardiograms in autonomic dysfunction research

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Background and Aims: While providing indirect assessment of the autonomic nervous system, electrocardiograms (ECG) are often corrupted by noise or irregularities. Gold standard is human expert assessment, which is challenged in large databases. In this study, the performance of two automated, modulation spectrum-based quality indicators were assessed for the detection of corrupted ECG signals in real-life monitoring data.

Methods: Datasets included 1000 ECG-recordings, each 600 seconds, collected at a stroke-unit. ECG quality was evaluated by an expert, including the duration of artefacts and the number of extrasystoles. The modulation spectral based quality index (MSQI) and the Peak Distance Quality Index (PDQI) were calculated, as well as their sensitivity, specificity, accuracy and the area under the curve (AUC) for the detection of high quality ECGs compared to expert rating.

Results: The percentage of ECG signals in the recordings based on the modulation spectrum approach correlates with expert rating ($r = 0.99$, $p < 0.001$). According to expert rating, of 861 recordings, 85 (9.8%) showed more than 15% of extrasystoles and 60 (6.9%) more than 100s of artefacts and were rated as "reduced quality". The AUC for PDQI ranges from 0.758 to 0.916 and for MSQI from 0.728 to 0.834. PDQI is superior in identifying extrasystoles, while the MSQI is better in identifying artefacts.

Conclusion: The large number of artefacts and irregularities makes automated quality indicators indispensable for the use of real-life EGC monitoring data in science. We propose a combination of the MSQI and PDQI to select signals before analyzing data for the evaluation of the autonomic nervous system.

Disclosure: Nothing to disclose.

EPO-228 | Sex-related differences in multiple system atrophy

F. Leys[1]; S. Eschlböck[2]; N. Campese[1]; P. Mahlknecht[1]; M. Peball[1]; G. Goebel[3]; V. Sidoroff[1]; F. Krismer[1]; R. Granata[1]; S. Kiechl[1]; W. Poewe[1]; K. Seppi[4]; G. Wenning[1]; A. Fanciulli[1]

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Background and Aims: Here we aimed at investigating sex-related differences in the clinical presentation of multiple system atrophy (MSA) by means of a literature review and analysis of a retrospective Innsbruck cohort.

Methods: We searched the PubMed database for articles entailing sex-related information in MSA. The baseline to last follow-up clinical demographic differences between female and male individuals of the Innsbruck MSA cohort were investigated with a univariate followed by a multivariable binary regression analysis.

Results: The literature search identified 46 publications. Earlier studies showed comparable survival rates between female and male MSA individuals, while recent ones indicated that a more frequent motor-symptomatic onset and generally less severe autonomic failure may confer female MSA individuals a survival benefit. Fifty-six women and 60 men with a comparable median follow-up of 27 months were included in the retrospective analysis. At baseline, female sex was associated with depression (OR = 4.7; $p = 0.007$), male sex with severe orthostatic hypotension (OR = 5.5; $p = 0.016$). At follow-up, female sex was additionally associated with the intake of CNS-active drugs (OR = 4.1; $p = 0.029$), while male sex also showed an association with the presence of supine hypertension (OR = 3.0; $p = 0.020$) and antihypertensive treatment (OR = 8.7; $p = 0.001$). We also observed an association between male sex and the initiation of antihypertensive regimes over the observational period (OR = 12.4; $p = 0.004$).

Conclusion: Our results indicate dynamic sex-related differences in the clinical presentation of MSA, which need to be taken into account both for therapeutic and research purposes.

Disclosure: Academic study without external funding. Dr Leys and Dr Campese are/were supported by the US MSA Coalition and the Dr. Johannes & Hertha Tuba Foundation throughout conducting this study.

EPO-229 | DA-9701 treatment for gastrointestinal symptoms and quality of life in postural orthostatic tachycardia syndrome

H. Jung[1]; D. Seo[1]; J. Kim[1]; J. So[1]; H. Kim[1]; Y. Lim[1]; Y. Koo[1]; J. Lee[2]; E. Lee[1]

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Background and Aims: Gastrointestinal (GI) symptoms commonly affect patients with postural tachycardia syndrome (POTS), detrimentally impacting their quality of life (QoL). DA-9701, acting on 5-HT1A, 5-HT4, and D2 receptors, may improve GI symptoms and enhance the QoL in patients with POTS.

Methods: This randomized, double-blind, placebo-controlled, pilot trial was conducted at a single center. Patients with POTS were randomized in a 1:1 ratio following a crossover design. Participants received either oral DA-9701 (30 mg) or a placebo thrice daily for eight weeks. This was followed by a four-week washout period and an additional eight-week treatment with the alternate therapy. The primary endpoint was the change from baseline in GI symptoms (total Nepean Dyspepsia Index-Korean version (NDI-K) symptom score) and related QoL (total NDI-K QoL score) over the 8 week-treatment period (cris.nih.go.kr, number KCT0006932).

Results: A total of 24 patients were randomized to initially receive either DA-9701 ($n=12$) or placebo ($n=12$). DA-9701 did not significantly improve the primary endpoints in total NDI-K symptom (Least-squares means, −13.9 vs. −9.5, $p=0.326$) and QoL scores (4.2 vs. 2.4, $p=0.596$). However, there was a tendency for improvement in specific GI symptoms, such as upper abdominal pain (−0.6 vs. 0.7, $p=0.066$) and pressure (−1.4 vs. −0.1, $p=0.061$). A carryover effect was observed in total NDI-K QoL ($p=0.036$), and analysis for the period 1 showed marginally significant treatment difference (-1.3 vs. 9.2, $p=0.067$).

Conclusion: Although DA-9701 was not successful to improve GI symptom and related QoL in this crossover trial, its potential merits warrant further investigation.

Disclosure: Funded by Dong-A Pharmaceutical.

EPO-230 | Painful small fiber neuropathy: A novel mutation in the SCN10A gene

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Background and Aims: We describe the case of a 35-year-old patient with severe painful small fiber neuropathy, early onset of symptoms and a long history of clinical and instrumental examinations who underwent overtime several aggressive and ineffective treatments for a putative rheumatological disease.

Methods: Symptoms started at the age of 21 with paraesthesia and burning pain in pectoral and periscapular area and at the hands. Shortly thereafter pain gradually spread to involve both feet and pelvic area. Twelve years after onset of symptoms, the patient reported generalized burning pain affecting also face and tongue. The pain was so severe he could only walk with the help of crutches. He also complained of gastroesophageal reflux, early satiety, bloating and severe constipation. Neurological examination was normal except from mechanical allodynia at both feet. He underwent functional and morphological assessment of small fibers.

Results: Spine and brain MRI, nerve conduction study, blood examination for dysmetabolic and dysimmune disorders were not relevant. Quantitative sensory testing showed abnormal thermal thresholds. Sympathetic skin response was abnormal and dynamic sweat test showed a non-length-dependent hypohidrosis. Cardiovascular reflexes were normal. Skin biopsy revealed a moderate non-length dependent loss of sensory and autonomic nerves. Exome sequencing revealed a heterozygous VUS mutation (c.4852A>C; p.Met1618Leu) in the SCN10A gene. The same clinical and instrumental features were present in a sister and in the father of our patient who carried the same mutation.

Conclusion: Awareness of the genetic causes of SFN is crucial for providing correct diagnosis and treatment for patients and their family.

Disclosure: Nothing to disclose.

EPO-231 | Cardiac 123I-MIBG Scintigraphy in the differential diagnosis of parkinsonian syndromes – monocentric cohort

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Background and Aims: Cardiac [123I]metaiodobenzylguanidine scintigraphy (123I-MIBG) reflects postganglionic cardiac sympathetic denervation (CSD). It is used for the differential diagnosis of parkinsonian syndromes, particularly between Parkinson's Disease (PD) and Multiple System Atrophy (MSA). We aimed at knowing whether there were clinical features that predict a 123I-MIBG without CSD.

Methods: Retrospective study of a cohort of patients followed in the Neurology department of a tertiary university hospital, who performed 123I-MIBG. Clinical data were retrieved from individual clinical registries. Patients with and without postganglionic cardiac autonomic denervation were compared to find factors associated to absence of CSD. A significant *p*-value was considered below 0.05.

Results: From the thirty patients who performed 123I-MIBG between 2018 and 2023 in our center, twenty-seven did so for differential diagnosis between parkinsonian syndromes (22.2% presumed PD, 51.9% presumed MSA, 25.9% others). Only 44.4% of patients performed a Schellong test. The median time from the onset of the disease to the 123I-MIBG was 3.0 (2.0–6.0) years. 44.4% exhibited cardiac denervation, while 55.6% did not. Univariate analysis revealed statistically significant differences between groups in terms of MDS-UPDRS-III, cardiovascular symptoms, isolated urinary symptoms (without cardiovascular symptoms), cardiovascular plus urinary symptoms, constipation, and presumed MSA diagnosis (Table 1). According to the logistic regression (Table 2), predictors of absence of CSD were isolated urinary symptoms (OR 8.1), constipation (OR 11.7), and a presumed MSA diagnosis (OR 21.2).

TABLE 1 Statistically Significant Differences Between Groups: Univariate Analysis Results

	^{123}I-MIBG with cardiac denervation n=12 (44.4%)	^{123}I-MIBG without cardiac denervation n=15 (55.6%)	p-value
MDS-UPDRS-III (mean +/- SD)	43.2 +/- 20.8	24.3 +/- 13.4	0.029
Cardiovascular symptoms	10 (83.3%)	6 (40.0%)	0.023
Isolated urinary symptoms	1 (8.3%)	9 (60.0%)	0.006
Cardiovascular plus urinary symptoms	8 (66.7%)	4 (26.7%)	0.038
Constipation	2 (16.7%)	10 (66.7%)	0.009
MSA Diagnosis	2 (16.7%)	12 (80.0%)	0.001

TABLE 2 Predictors of Absence of Cardiac Sympathetic Denervation: Logistic Regression Analysis

Logistic regression (p=0.0002)	
MDS-UPDRS-III	OR 8.1 (CI 95% 0.4 – 162.1), p = 0.170
Constipation	OR 11.7 (CI 95% 0.8 – 181.3), p = 0.079
Isolated urinary symptoms	OR 21.2 (CI 95% 1.5 – 299.2), p = 0.024

Conclusion: In our cohort, individuals presenting with isolated urinary symptoms, constipation, and a presumed MSA diagnosis are more likely to exhibit an absence of CSD.

Disclosure: Nothing to disclose.

EPO-232 | Cardiovascular autonomic disorders following COVID-19 infection or vaccination

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Background and Aims: Cardiovascular autonomic disorders have been reported both after coronavirus-disease-2019 (COVID-19) infection and COVID-19 vaccination, but are not well characterized to date. Here we studied the type, frequency and clinical outcome of newly-diagnosed cardiovascular autonomic disorders following COVID-19 infection or vaccination in a retrospective series from the Innsbruck Dysautonomia Center.

Methods: We reviewed the medical records of all individuals referred between March 2020 and March 2023 for new-onset of orthostatic intolerance (OI) within 6 weeks after COVID-19 infection or vaccination.

Results: 102 individuals were studied ($n=76$ with new-onset OI after COVID-19, $n=26$ post-vaccination). In post-COVID-19-infection cases, postural orthostatic tachycardia syndrome (POTS) was the most common cardiovascular autonomic diagnosis ($n=21$, 86% female, 33 ± 9 years of age). POTS was also the most frequent cardiovascular autonomic disorder in post-COVID-19-vaccination cases ($n=11$, 73% female, 32 ± 10 years of age). In 51 (50%) of all cases with post-infectious or post-vaccination OI, no cardiovascular autonomic cause was found. All newly diagnosed POTS cases were recommended non-pharmacological measures, 33% of post-infectious and 55% of post-vaccination cases received additional pharmacological treatment. At follow-up, 68% of post-COVID-19-infection POTS

($n = 13/19$, 7 ± 4 months follow-up) and 78% of post-COVID-19 vaccination cases ($n = 7/9$, 8 ± 6 months follow-up) reported improvement.
Conclusion: A specialized diagnostic work-up is pivotal to diagnose or exclude autonomic disorders in individuals with newly-developed OI following COVID-19 infection or vaccination. POTS is the most frequent autonomic disorder developing after both COVID-19-infection and COVID-19-vaccination, mainly affecting female individuals in their fourth decade of life. Improvement is observed under multimodal treatment at follow-up.
Disclosure: Nothing to disclose.

EPO-233 | Indices of cardiovascular autonomic failure in multiple system atrophy

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Background and Aims: Multiple system atrophy (MSA) is a rare and progressive neurodegenerative disorder. Severe cardiovascular autonomic failure (CAF) is one of the main clinical features with prognostic implications. Moreover, little is known about gender differences in CAF. In this study, we sought 1) to compare heart rate variability (HRV) and baroreflex sensitivity (BRS) as CAF indices between MSA and control patients, and 2) to determine the gender differences in these markers.
Methods: 193 MSA patients (88 men and 105 women) and 88 control patients (32 men and 56 women) were included in the study. HRV was assessed in time (pNN50, SDNN, RMSSD), frequential (LF, HF, LF/HF) and non-linear (SD1, SD2) domains. BRS was estimated by the sequence method. Mann-Whitney test was performed to analyze data between MSA and control patients. To compare men and women, we used two-way ANOVA (condition × gender) with Tukey's method post-hoc.
Results: Mean disease duration from symptom onset was 4.5 ± 2.3 years. Reduced overall variability (SDNN, LF, LF/HF, SD2), parasympathetic activity (pNN50, RMSSD, HF, SD1) and BRS were observed in MSA patients. No gender differences were observed.
Conclusion: Our results indicate a severe impairment in HRV and BRS in MSA patients. These additional markers may be considered as an index of CAF. However, there is no gender difference in the manifest of CAF. Further studies are needed to assess the prognosis value of these markers.
Disclosure: Nothing to disclose.

EPO-234 | Sudomotor function in multiple system atrophy, Parkinson's disease and four-repeat tauopathies: A cross-sectional report

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Background and Aims: Autonomic dysfunction is a well-established feature of Parkinson's disease (PD) and multiple system atrophy (MSA). Sudomotor dysfunction may occur in both diseases and underlying pre- and postganglionic pathology have been suggested. We aimed to non-invasively assess sudomotor function in PD and atypical parkinsonism and explore possible discriminative features.
Methods: In an ongoing longitudinal study, controls and patients with PD, MSA and four-repeat tauopathies were prospectively included. Assessments included clinical rating scales, questionnaires, orthostatic blood pressure and quantification of electrochemical skin conductance in feet and hands using Sudoscan®. Non-parametric testing was performed to explore group differences, and associations with measures of disease burden.
Results: An overview of the study population ($n = 63$) is shown in Table 1. No significant group differences were seen with regard to sex and age. Significant differences in skin conductance were evident between groups ($p = 0.012$ (hands); $p = 0.0068$ (feet)), reflecting reduced conductance in MSA (Figure 1). In a subgroup analysis, significant strong associations between skin conductance in feet and clinical rating scales were demonstrated in MSA (rho = −0.72, $p = 0.0087$; rho = −0.61, $p = 0.034$) (Table 2). No significant associations were evident in other groups (data not shown).

TABLE 1 Clinical and demographic characteristics of the study cohort ($n=63$). Significant group differences with regard to skin conductance are shown. Group comparisons were performed with Fisher's exact test and Kruskal-Wallis H-test.

	PD (n=20)	MSA (n=12)	4R (n=11)	HC (n=20)	p
Age at examination (y), median (IQR)	63.2 (14.2)	59.3 (12.7)	68.6 (10.5)	62.9 (6.3)	0.08
Sex (M/F)	7/13	3/9	4/7	7/13	0.95
Smoking (n, % yes)	1 (0.050)	1 (0.091)	0 (0)	1 (0.050)	1.0
Disease characteristics					
Disease duration (y), median (IQR)	6.5 (4.9)	5.8 (1.6)	4.4 (3.1)	.	**0.046**
L-dopa duration (y), median (IQR)	4.1 (4.4)	2.7 (4.3)	0.2 (2.6)	.	**0.02**
LEDD (mg), median (IQR)	593 (549)	688 (1201)	200 (600)	.	**0.049**
mHY (stage), median (IQR)	2.0 (0)	4.0 (2.0)	4.0 (2.0)	.	**<0.001**
MDS-UPDRS part III (p), median (IQR)	23 (15)	.	.	.	.
UMSARS part II (p), median (IQR)	.	29.5 (18)	.	.	.
UMSARS part IV (p), median (IQR)	.	3.0 (1)	.	.	.
PSP-CDS (p), median (IQR)	.	.	11 (9)	.	.
Assessments					
SCOPA-AUT (p), median (IQR)	10.5 (10)	31.5 (20)	13 (20)	5.5 (7)	**<0.001**
Max systolic BP fall (mmHg), median (IQR)	8.5 (7)	16 (18)	5 (20)	9.5 (15)	0.34
Max diastolic BP fall (mmHg), median (IQR)	0.0 (8)	8.5 (10)	1.0 (12)	0.5 (11)	**0.033**
Mean conductance hands* (μS), median (IQR)	69.5 (29)	55.5 (28)	75.8 (19.9)	67.5 (13)	**0.012**
Mean conductance feet** (μS), median (IQR)	81.8 (14)	57.5 (39.9)	82.3 (15.8)	76.5 (15.9)	**0.0068**
UENS (p), median (IQR)	5.0 (5)	3.0 (3)	3.0 (4)	2.0 (2)	**0.0036**

Abbreviations: PD – Parkinson's disease; MSA – Multiple system atrophy; 4R – four-repeat tauopathy defined as possible corticobasal degeneration or probable progressive supranuclear palsy; HC – healthy control; IQR – interquartile range; LEDD – L-dopa equivalent daily dose; mHY – modified Hoehn and Yahr; MDS-UPDRS – Movement Disorders Society Unified Parkinson's Disease Rating Scale; UMSARS – Unified Multiple System Atrophy Rating Scale; PSP-CDS – Progressive Supranuclear Palsy Clinical Deficits Scale; SCOPA-AUT - Scales for Outcomes in Parkinson's Disease-Autonomic questionnaire; BP – blood pressure; UENS – Utah Early Neuropathy Scale. **3 missing values; **1 missing value*

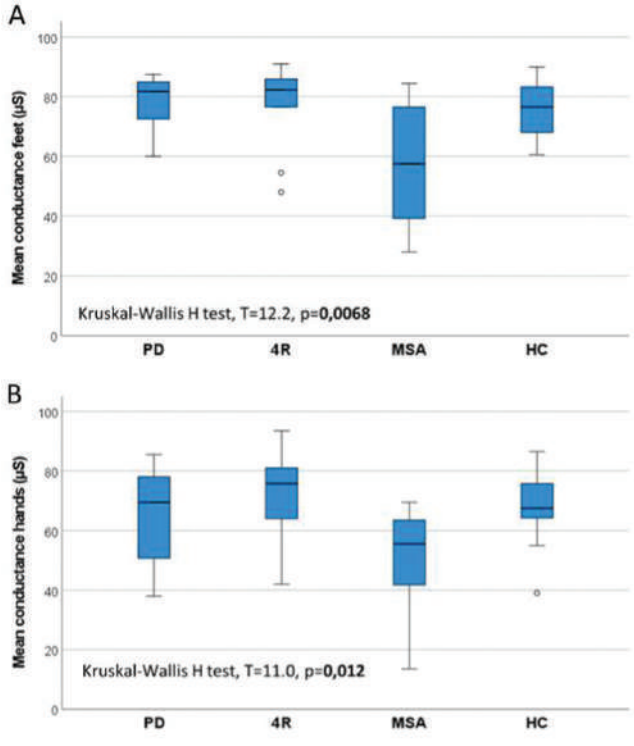

FIGURE 1 Mean skin conductance measured from feet (A) and hands (B). Post-hoc comparisons with Bonferroni correction demonstrate: (A): MSA vs PD, $p=0.010$; MSA vs 4R, $p=0.019$; MSA vs HC, $p=0.12$ (B): MSA vs PD, $p=0.054$; MSA vs 4R, $p=0.018$; MSA vs HC, $p=0.033$

TABLE 2 Associations between skin conductance and measures of disease burden in MSA. Negative associations were demonstrated between skin conductance in feet and UMSARS part II, and mHY stage (rho = −0.72, $p=0.0087$; rho = −0.61, $p=0.034$ respectively).

	Mean conductance hands* (μS)	Mean conductance feet (μS)
UMSARS part II (p)	ns	**-0.72**
UMSARS part IV (p)	ns	ns
mHY (stage)	ns	**-0.61**
SCOPA-AUT (p)	ns	ns

Abbreviations: ns – not significant; UMSARS – Unified Multiple System Atrophy Rating Scale; mHY – modified Hoehn and Yahr; SCOPA-AUT - Scales for Outcomes in Parkinson's Disease-Autonomic questionnaire. **1 missing value*

Conclusion: Reduced electrochemical skin conductance, as measured with Sudoscan®, may be a prevalent finding in MSA relative to PD and four-repeat tauopathies, and possible associations with clinical measures of disease burden may indicate prognostic properties. Further studies are needed to determine whether these findings are detectable in early disease or rather reflect an advanced disease stage with more widespread disease pathology.

Disclosure: MA has received funding for this study from NEURO Sweden, Svenska Läkaresällskapet (The Swedish Society of Medicine) and Hjärnfonden. PS has received funding from Region Stockholm and Wallenberg Clinical Scholarship. PK, KS, AJT report nothing to disclose.

EPO-235 | Autonomic testing in children with inflammatory bowel disease and irritable bowel syndrome: In search of dysautonomia

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Background and Aims: The autonomic nervous system (ANS) is an important pathway connecting the brain and the gut. The aim of this study was to investigate the subjective and objective ANS abnormalities in children with irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) compared to healthy controls (HC).

Methods: A total of 58 children were enrolled: 23 in IBS group (mean age 15 years, male $n=7$), 18 in IBD (mean age 14.25 years, male $n=7$) and 17 HC (mean age 14.83 years, male $n=8$). ANS symptoms were evaluated with the Composite Autonomic Symptom Score (COMPASS-31). Heart rate (HR) and blood pressure (BP) responses were monitored with the Task Force Monitor (CNSystems, Austria) and quantitative sudomotor axon reflex test (QSART) were performed. The severity and distribution of ANS function was quantitated using the Composite Autonomic Severity Scale (CASS).

Results: Children with IBS scored highest on the COMPASS 31, followed by patients with IBD and HC (median scores were 10.9, 5 and 1.6, respectively; $p=0.001$). Moreover, children with IBS scored the highest on questions that involved various gastrointestinal symptoms. There was no significant difference between groups in CASS ($p>0.05$). However, there was a significant difference in symptomatic dysautonomia (defined as COMPASS-31 >7.913 and CASS >0) between children with IBS (56.5%) compared to children with IBD (38.9%) and HC (11.8%), $p=0.015$.

Conclusion: Symptomatic dysautonomia is most frequently observed in children with IBS, indicating important contribution of ANS abnormalities to pathophysiology of IBS.

Disclosure: Founding: Croatian science foundation (IP-2019-04-3028).

EPO-236 | Parasympathetic and cerebral hemodynamic impairment in adults with sickle cell disease and cerebral microangiopathy

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Background and Aims: White matter lesions (WML) on brain imaging are common both in patients with sickle cell disease (SCD). The autonomic nervous system (ANS) is involved in the homeostasis of cerebral hemodynamics. The aim of this study was to evaluate the association between ANS parameters and cerebral microangiopathy in adult patients with SCD.

Methods: We prospectively assessed adult patients with SCD from our cohort for heart rate variability in the frequency domain, baroreflex sensitivity (BRS), cerebral autoregulation using Mx, cerebral arterial compliance (Ca) and cerebral time constant (tau) based on TCD and ABP monitoring. These patients also had cerebral MRI. Patients with history of stroke were excluded.

Results: Forty-one patients (F/M:25/16) were included. Median age was 37.5 years (range 19–65). Twenty-nine (70.7%) patients had SS genotype. Eleven patients had cerebral microangiopathy (26.8%). These patients were older (44.5 vs 30.6 years; $p<0.001$), had a lower HF (HF 157 ms2 vs HF 467.6 ms2; $p<0.005$) and impaired Ca (15.4 vs. 37.3 cm3/mmHg $p<0.014$). AUC for the model with age as single predictor was of 0.876. For age and HF model, AUC was of 0.946.

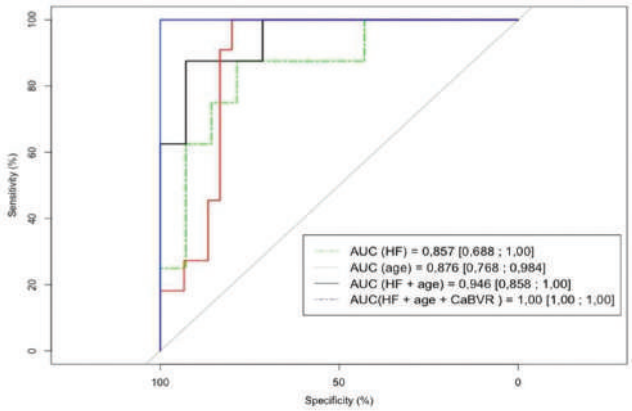

Figure AUC for the model with age as single predictor was of 0.876. For age and HF model, AUC was of 0.946. For age, HF and cerebral compliance model, AUC was of 1.

Conclusion: Lower parasympathetic activity was associated with cerebral microangiopathy in adults in SCD. Cardiovascular prevention including non-drug treatment and physical activity could improve cerebrovascular function and parasympathetic activity. HF monitoring can help assess the cardiovascular impact of such interventions. Including novel hemodynamic parameters such as Ca could yield better understanding of integrative cardiovascular and cerebrovascular hemodynamic regulation in SCD.

Disclosure: Nothing to disclose.

EPO-237 | Pain in multiple system atrophy: A community-based survey

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Background and Aims: According to a meta-analysis pain affects approximately 60% of individuals with multiple system atrophy (MSA), but its prevalence and characteristics remain poorly characterized. Here we assess prevalence, features, risk factors and treatment options for pain in MSA.

Methods: We performed a community-based cross-sectional study. Following a whole population sampling approach, MSA individuals and their informal caregivers were invited via patient advocacies, to complete a survey, available online between February and May 2023. The survey was accessed by 264 MSA individuals and 178 caregivers. After checking for data completeness and plausibility, questionnaires from 194 MSA individuals and 114 caregivers were retained for final analysis.

Results: Pain was reported by 87% of MSA individuals, more frequently by women [OR: 6.38 (95% C.I. 1.27–32.08), $p=0.025$] and subjects with a self-reported annual income below the average of the country [OR: 5.02 (95% C.I. 1.32–19.08), $p=0.018$]. Pain was mostly located in the neck and shoulders (58%), back (45%) and legs (45%). Among individuals with pain, 69% received any kind of treatment, mostly non-steroidal anti-inflammatory drugs (30%), acetaminophen (25%) and opioids (17%) but only 52% of them was at least partially satisfied with pain management. Pain mostly affected patients' work, household activities, and hobbies and caregivers' social activities.

Conclusion: Pain is more common than previously reported in MSA, is mostly located in the neck, shoulders, back and legs, and especially affects women and individuals with lower income. Despite the frequent occurrence, pain remains undertreated or not satisfactorily managed, pinpointing an important unmet need in MSA.

Disclosure: Academic study supported by a grant of the MSA Coalition.

EPO-238 | Autonomic dysfunction in fibromyalgia: A skin biopsy and tilt testing study

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Background and Aims: Fibromyalgia patients frequently report autonomic symptoms, with previous studies suggesting sympathetic nervous system dysfunction, the pathophysiological mechanisms of which remains unknown [1]. Recent findings indicate sympathetic denervation in a subgroup of fibromyalgia patients with small fiber pathology (SFP) [2]. Our study aims to confirm the existence of cardiovascular autonomic dysfunction in fibromyalgia patients, examining its connection with peripheral autonomic denervation and the manifestation of autonomic symptoms.

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2. Autonomic Small-Fiber Pathology in Patients With Fibromyalgia. Falco P, Galosi E, Di Stefano G, Leone C, Di Pietro G, Tramontana L, De Stefano G, Litewczuk D, Esposito N, Truini A. J Pain. 2024 Jan;25(1):64-72. doi: 10.1016/j.jpain.2023.07.020. Epub 2023 Jul 29.

Methods: We enrolled 35 fibromyalgia patients and assessed them using autonomic symptom scale (COMPASS-31), skin biopsy, analyzing intraepidermal (IENFD) and dermal autonomic nerve fibers densities, and a battery of cardiovascular autonomic function tests: tilt test, Valsalva maneuver (VM), deep breathing (DB), heart rate (HR) power spectral analysis, blood pressure (BP) short-term variability with baroreflex sensitivity (BRS) calculation. Based on distal IENFD, patients were divided into two subgroups: with and without SFP (Figure 1). Autonomic test results were compared with 35 sex and age- matched healthy controls and between the two patient subgroups. Correlations to skin biopsy data and autonomic symptoms were studied.

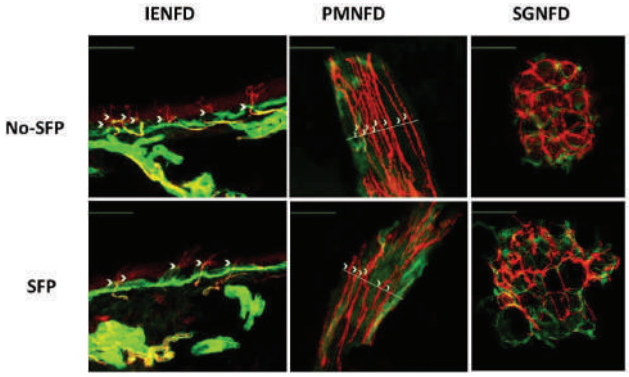

Figure 1: Representative skin biopsy images from fibromyalgia patients with and without SFP, showing nerve fibre counting examples for intraepidermal nerve fibre density (IENFD), piloerector muscle (PMNFD), and sweat gland (SGNFD) nerve fibre density evaluation. Red staining represents PGP9.5 marking nerve fibres, while green staining corresponds to collagen IV. All morphometric variables were reduced in patients with SFP respect to patient without SFP. Intraepidermal nerve fibre density calibration bars: 200 µm; PMNFD and SGNFD: 100 µm.

Representative skin biopsy images from fibromyalgia patients with and without SFP, showing nerve fibre counting examples for intraepidermal nerve fibre density (IENFD), piloerector muscle (PMNFD), and sweat gland (SGNFD) nerve fibre density evaluation.

Results: Fibromyalgia patients exhibit a reduced BP difference between phase IIb and IIa of VM ($p<0.001$), a decreased HR difference in DB ($p<0.001$) and a greater reduction of BRS during tilt ($p<0.004$) compared to healthy subjects, without differences between the two patient subgroups. There isn't correlation between functional and morphometric variables with clinical scales.

Conclusion: Fibromyalgia patients display cardiovascular autonomic dysfunction, which doesn't correlate with peripheral autonomic denervation. This suggests that multiple mechanisms (central and peripheral) contribute to autonomic symptoms complaint by patients.

Disclosure: Nothing to disclose.

EPO-239 | The spectrum of autonomic responses to focal seizures

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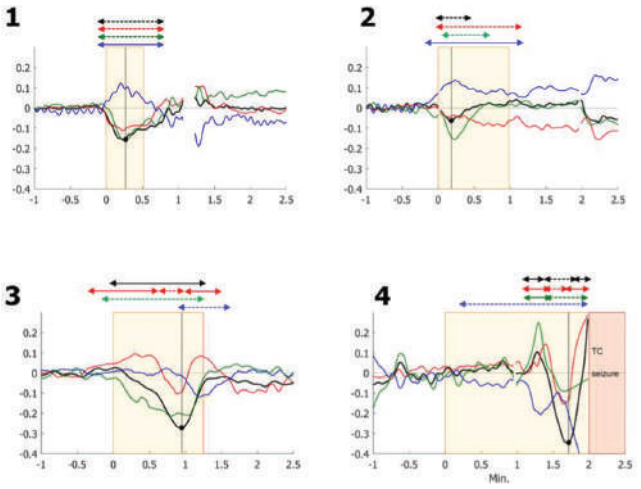
Background and Aims: The cardiovascular response to focal seizures is rarely examined in full due to lack of ictal simultaneous heart rate (HR) and blood pressure (BP) recordings. We explored the temporal patterns in three cases using the log ratio method to dissect the main hemodynamic components.

Methods: We identified three subjects who experienced a seizure during a tilt test: one had two focal with impaired awareness seizures (FIAS #1&2), one had one FIAS (#3) one had a focal to bilateral tonic-clonic seizure (fbTCS, #4). All cases were monitored with video, HR and continuous BP (Finapres) recordings. We used the 'log-ratio method' to determine the relative contributions of HR, stroke volume (SV), and total peripheral resistance (TPR) to mean arterial pressure (MAP). A 'phase' was defined as a temporary departure form baseline.

Results: During seizure 1&2 there was one phase, in which HR and TPR decreased and SV increased simultaneously. During seizure #3 we observed one negative phase for MAP and TPR, three phases for HR (positive-negative-positive), and only one late negative phase for SV; hence, HR changed out of phase with TPR and MAP. In seizure #4 there was no autonomic involvement during the first minute, after which MAP and HR showed an asynchronous three phasic course.



Log-ratio results of the four focal seizures (seizure 1,2,3: focal impaired awareness seizure; seizure 4: focal to bilateral tonic-clonic seizure).

Conclusion: This chance sample illustrates that hemodynamic variables may change during focal seizures in different directions, sometimes in phase, sometimes independently. We speculate that these complex autonomic patterns represent different ictal propagation pathways and may include ictal as well as corrective changes.

Disclosure: None.

EPO-240 | Multimodal assessment of neurogenic lower urinary tract symptoms in people with multiple sclerosis

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Background and Aims: During the disease course symptoms of lower urinary tract (LUTS) are present in more than 80% of people with multiple sclerosis (pwMS), significantly impairing the quality of life (QoL). Objectives: to define the association between subjective LUTS symptoms, assessed by International Consultation on Incontinence Questionnaire (ICIQ) modules, with the results of neurological and neurophysiological evaluation.

Methods: 102 consecutive pwMS (90 females, age 37.7 ± 9.4 years), were included and Expanded Disability Status Scale (EDSS) with Bowel/Bladder Function System (BFS) was calculated. All participants answered the Croatian version of the ICIQ comprised of three parts (ICIQ – overactive bladder (OAB), ICIQ-OAB QOL, and ICIQ – urinary incontinence (UI)). Somatosensory evoked potentials (SSEP) of median (latency N20, amplitude P15-N20) and tibial (latency P40, amplitude P40-N50) nerve were performed.

Results: Positive correlation was found between the EDSS and BFS with ICIQ-OAB ($r = 0.424$ and $r = 0.741$), ICIQ OAB QOL ($r = 0.462$ and $r = 0.785$), and ICIQ-UI ($r = 0.484$ and $r = 0.705$), all p values < 0.001. Latencies of the right P40 wave on the tibial SSEP positively correlated with OAB (ICIQ-OAB: $r = 0.242$, $p = 0.016$; ICIQ-OABqol: $r = 283$, $p = 0.005$) and latencies of both P40 waves with UI symptoms ($r = 0.350$, $p = <.001$ and $r = 0.291$, $p = 0.004$). Amplitudes of the right P40-N50 wave on the tibial SSEP negatively correlated with OAB (ICIQ-OAB: $r = -0.214$, $p = 0.034$; ICIQ-OABqol: $r = -0.211$, $p = 0.036$) and amplitudes of both P40-N50 waves with UI symptoms ($r = -0.371$, $p = <.001$ and $r = -0.340$, $p = 0.001$).

Conclusion: Subjective affection of the LUTS evaluated with ICIQ Questionnaire modules demonstrated significant association with clinical as well as neurophysiological findings.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

EPO-241 | Can clinical risk scores predict atrial fibrillation in patient with cryptogenic stroke? A retrospective analysis

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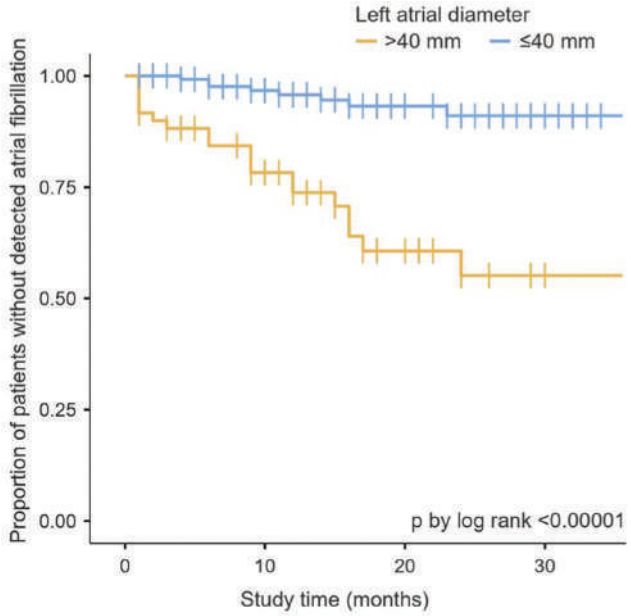
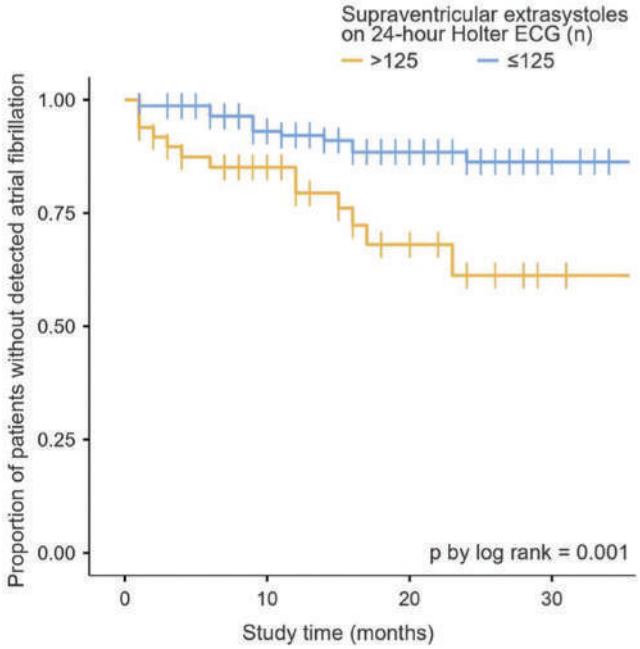
Background and Aims: Atrial fibrillation (AF) is the most common arrhythmia and cause of acute ischemic stroke, often underdiagnosed in cryptogenic stroke (CS), mostly due to inadequate cardiac monitoring. The identification of a clinical risk score to predict AF in CS, could improve patients selection for prolonged monitoring.

Methods: We retrospectively collected data of CS patients discharged from our Stroke Unit from February 2018 to November 2023. A time-to-event analysis was performed to investigate variables associated to AF.

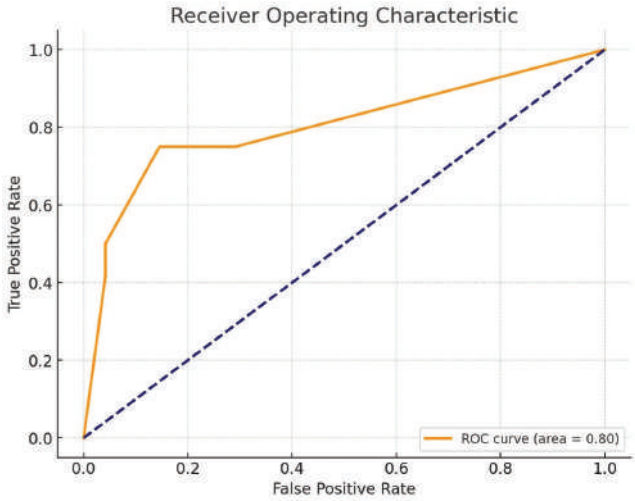
Results: We collected clinical data of 199 CS patients with median age of 70.5 years old. Median follow-up from discharge was 16 months. 52 patients underwent loop recorder implantation of whom, 16 revealed AF after a mean time of 7 months. 14 patients without implantable device discovered AF after a mean time of 15 months. Overall 30 patients (15%) experienced AF. Univariate analysis identified left atrial (LA) dilation with diameter >40 mm ($p<0.001$), supraventricular premature beats (SPB) >125 on 24-hs electrocardiogram ($p=0.03$) and multi-territorial lesions on head TC scan ($p=0.001$) as significant AF predictors. Logistic regression model integrated these three variables and showed: an area under the ROC curve of 0.80, sensitivity of 75.0 % and specificity of 85.4 %.



Left atrial diameter



Supraventricular extrasystoles on 24h ECG



ROC curve (AUC = 0.80)

Conclusion: Our data confirmed studies reporting a significant association between AF and LA dilation, SPB and multi-territorial lesions. For the need to select CS patients for expensive cardiac long-term monitoring, we suggest to integrate these three variables with specificity and reasonable sensitivity in a new clinical risk score.

Disclosure: Nothing to Disclose.

EPO-242 | Does amyloid cerebral deposits influence delayed cognitive impairment after stroke?

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Background and Aims: Amyloid deposits in has been shown to be associated with post-stroke cognitive impairment (PSCI) at baseline. Long-term outcomes have only been examined in a single study and remain to be documented.
Methods: We included 91 stroke patients (age: 63.3 ± 10.7; NIHSS: 5.6 ± 5.8; infarct: *n* = 81): 40 (44%) had subjective cognitive decline (SCD), 44 (47.2%) mild CI and 7 (8.8%) major CI) at 6 months PS. After the amyloid PET performed at baseline, they were followed up annually for 5 years using a clinical and neuropsychological battery.
Results: Amyloid PET was positive in 14 patients (15.4%). At this last visit (mean duration: 80.6 ± 27.9 months), SCT was observed in 59 patients, mild CI in 14 patients and major CI in 18 patients. Focusing on the 84 patients without major CI at baseline, Kaplan Meier survival analysis showed that amyloid PET status was associated with cognitive outcome ($p = 0.03$) due to a faster and higher rate of CI in PET-positive patients (PET+: 60%; PET-: 25.7%). The effect was significant for both mild ($p = 0.03$) and major CI ($p = 0.003$). It was independent ($p = 0.5$) from the stroke subtype. Cox regression analysis showed that the effect of amyloid status ($p = 0.004$) survived the 2 significant covariates (age at stroke: [$p = 0.013$] and pre-stroke ADL impairment score [$p = 0.016$]).
Conclusion: In addition to the higher risk of PS CI at baseline, amyloid deposits are associated with a higher risk of developing incident CI during follow-up, particularly dementia, with major consequences for patient outcome.
Disclosure: Scientific board of commercial entities: Biogen, Roche, Bristol-Myers Squibb.

EPO-243 | Early cognitive trajectories after stroke: Still prevalent cognitive impairment despite neurological recovery

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Background and Aims: Early cognitive trajectories after stroke are barely investigated, despite their crucial significance for tailored early intervention in patients at risk for persistent post-stroke cognitive impairment (PSCI).
Methods: We prospectively evaluated non-aphasic patients with a first-ever ischemic stroke without premorbid cognitive decline. Patients underwent a detailed neuropsychological testing in the acute phase and 3 months post-stroke. PSCI was defined as performance < −1.5 SD in ≥ 2 cognitive domains. Cognitive trajectories across 3 months were evaluated using generalized linear models.
Results: Of 257 patients (66 ± 14 years old, 37% female, median NIHSS 24h = 1.00 [0.00, 4.00]) 68% had PSCI 2.8 ± 2.0 days post-stroke. At 3 months post-stroke, despite only minor neurological residual symptoms (NIHSS = 0.00 [0.00, 1.00]), 37% of patients had persistent PSCI and 4% newly developed PSCI. The most often affected domains were verbal episodic memory (43% of patients), constructive abilities (32%), learning (26%), and working memory (24%; Figure 1). The prevalence of PSCI at 3 months post-stroke was comparable between young (<55 years old) and older (>55 years old) stroke adults ($\chi^2 = 0.3$, $p = 0.579$), meaning that this phenomenon could not be explained by covered pre-stroke neurodegenerative processes. Higher stroke severity (NIHSS 24h, OR = 1.14, 95% CI 1.05–1.23) and lower years of education (OR = 0.81, 95% CI 0.73–0.91), but not age (OR = 1.01 95% CI 0.99–1.03), were identified as risk factors of persisting PSCI.

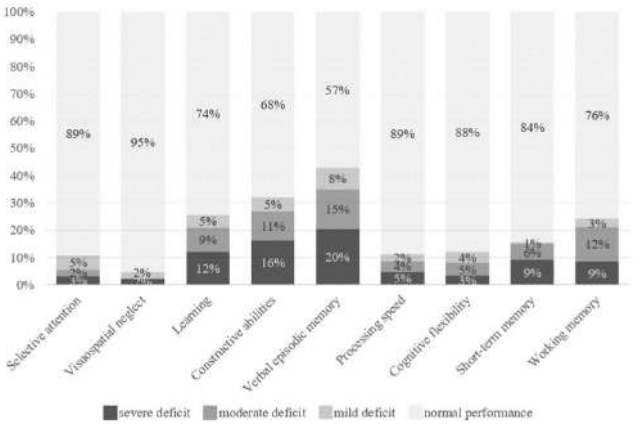

FIGURE 1 Prevalence of cognitive deficits at 3 months post-stroke.

Conclusion: Despite favorable neurological outcome, PSCI still affects every third patient at 3 months post-stroke, even in young adults. New early therapeutic interventions are needed to improve cognitive outcomes.
Disclosure: Nothing to disclose.

EPO-244 | Mechanical thrombectomy vs medical treatment in >85yo patients with acute ischemic stroke from large vessel occlusion

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Background and Aims: The evidence on the benefits of mechanical thrombectomy (MT) in patients older than 85 years is scarce. Our

aim was to compare the functional outcomes of patients treated with MT versus best medical treatment (BMT) exploring potentially related factors.

Methods: Retrospective observational study of consecutive stroke code patients >85 years old with large vessel occlusion attended within 24 hours of stroke onset and NIHSS>5 in a comprehensive stroke center from 1/1/2021 to 1/8/2022. We analyzed baseline characteristics, radiological findings and reperfusion treatments and their association with favorable outcomes (mRS <= 3 at 3 months) univariate analysis and binary logistic regression.

Results: We included 78 patients, 68% women, mean age 88 ± 3 years. 39 (50%) had terminal ICA occlusion-M1, 28 (36%) M2, 3 (4%) BA, 8 (10%) ACA/PCA. Median (IQR) NIHSS was 17 (13–20) and ASPECTS 9 (6–10). Intravenous thrombolysis was administered to 30 (38.5%) patients and 52 received (66.7%) MT. We found no significant differences in the proportion of patients with favorable outcomes between the MT group and the BMT group (30% vs 42.3%; $p=0.283$). Univariate analysis showed that higher NIHSS, longer onset-to-door time, higher glycemia and lower ASPECTS were related to worse outcomes. Logistic regression showed that only baseline NIHSS and ASPECTS were independently related to functional outcomes.

Conclusion: In patients older than 85 years with large vessel occlusion, we failed to demonstrate a benefit of MT over BMT. NIHSS and ASPECTS remain the most determinant prognostic factors.

Disclosure: Nothing to disclose.

EPO-245 | Survival and functional outcomes of patients aged ≥ 85 years treated with mechanical thrombectomy after ischemic stroke

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Background and Aims: Age is no longer an exclusion criterion for endovascular treatment of ischemic stroke. However, the progressive aging of the population raises questions about the efficacy and safety of mechanical thrombectomy (MT) in the older population.

Methods: Retrospective study of a prospective database of patients treated with MT at our center between 2017- 2023. We compared our experience using MT in patients aged ≥85 years to those aged < 85 years.

Results: Among the 647 patients treated with MT, 94 (14.5%) were ≥ 85 years old (median age, 87.4 ± 2.4). Both groups had similar stroke severity evaluated by the NIHSS scale (16.5 in ≥85 years old vs 16 in the younger group, $p=0.116$) and had a similar proportion of fibrinolysis treatment (50% vs 53.7%, $p=0.526$). We found no significant differences in the complete recanalization rate (87.7% vs 87.7%, $p=0.903$) or symptomatic hemorrhagic transformation (4.3% vs 4.9%, $p=0.792$) between both groups. However, there were significant differences in the functional outcome at 3 months with a smaller proportion of independence (38% vs 53.9%, $p=0.014$) and higher mortality (21% vs 13.3%, $p=0.029$) in older patients. In this group, we also found higher hospital mortality differences close to significant (17% vs 10.7%, $p=0.07$).

Conclusion: In our experience, treatment with MT in the older population has a high rate of recanalization with no increment in the risk of hemorrhagic transformation but with higher mortality and worse functional outcome at 3 months comparing it with the younger population.

Disclosure: Nothing to disclosure.

EPO-246 | MicroRNAs as biomarkers of carotid atherosclerotic disease in ischaemic stroke patients

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Background and Aims: MicroRNAs are small non-coding RNA molecules regulating gene expression at the posttranscriptional level. The carotid atherosclerotic disease (CAD) is an important cause of ischaemic stroke. MicroRNAs play a complex role at different stages of atherosclerotic plaque development. Both upregulation and downregulation of different microRNAs were described in patients with CAD and ischaemic stroke. The study aims to describe the association of selected microRNAs and biochemical biomarkers with CAD and plaque stability in ischaemic stroke patients.

Methods: Case-control study of consecutive ischaemic stroke patients with CAD admitted to a comprehensive stroke center. A control group consisted of ischaemic stroke patients with no presence of CAD. Plaques were described as unstable (symptomatic) and stable (asymptomatic). Serum levels of microRNAs (mir-21, mir-29b, mir-133b, mir-142-5p, mir-150, mir-499, mir-223-3p) and biochemical biomarkers (lipid profile, glycated hemoglobin, fibrinogen, antithrombin III, creatinine, CRP) were analyzed at admission. The predictive accuracy was assessed by calculating the AUC.

Results: The data of 117 patients were analyzed (67 with CAD, 55 with no CAD, 16 with symptomatic plaque, 46% men, median age 73 years, median NIHSS 6). In the CAD group vs. no CAD group, the mean levels of glycated hemoglobin were 43.76mmol/mol vs. 39.06mmol/mol ($p=0.031$), the mean levels of fibrinogen 3.07g/l vs. 2.68g/l ($p=0.015$). All other biomarkers, including microRNA levels, were not associated with CAD. No tested biomarker was associated with plaque instability.

Conclusion: Elevated levels of fibrinogen and glycated hemoglobin but no microRNAs were associated with carotid atherosclerotic

disease in ischaemic stroke patients. All biomarkers failed to predict plaque stability.

Disclosure: Nothing to disclose.

EPO-247 | Predictors of early seizures in patients with cerebral venous thrombosis: A single center analysis of 109 cases

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Background and Aims: Early seizures (ES) are frequent manifestation of cerebral venous thrombosis (CVT) which complicates the course and impacts the outcome of the disease. The aim of our study was to identify predictors of ES in patients with CVT.

Methods: This retrospective observational study included 109 patients diagnosed with CVT over the 13- year period. Demographic, clinical, and radiological findings were collected and their association with seizure occurrence was studied. The impact of ESS on modified Rankin score at discharge was also explored.

Results: Among 109 patients, 30 (27.5%) had ESS. Bilateral motor seizures with or without clear focal onset were the most frequent (23 patients), whereas focal seizures were noted in 7 patients. Epileptic status was observed in 6 (20%) patients. In 30% of patients, ESS were the presenting feature, while the rest of patients developed seizures during the first two weeks following CVT. Patients who suffered ESS were younger (34 (18–63) vs. 41 (19–76), $p<0.05$). Among clinical characteristics, coma at admission stood out as a predictor of ESS (5 (16.7%) vs. 3 (3.9%), $p<0.05$). Parenchymal supratentorial lesion on neuroimaging and infarction with hemorrhagic transformation were associated with higher risk of seizure occurrence ($p=0.01$, $p<0.05$). ESS were not associated with poor outcome (mRS-3). However, epileptic status was an important factor of morbidity.

Conclusion: Coma at admission and structural lesions on neuroimaging such as parenchymal supratentorial changes and infarction with hemorrhagic transformation stood out as predictors of ESS in patients with CVT.

Disclosure: Nothing to disclose.

EPO-248 | Effects of EGFr domain on CADASIL clinical and neuroradiological outcomes: A retrospective study of 115 cases

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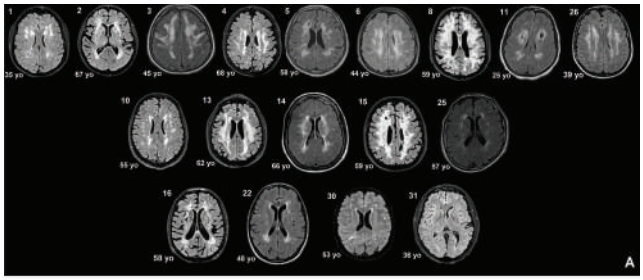
Background and Aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a rare heritable small vessel disease caused by a cysteine-altering mutation in one of the thirty-four epidermal growth factor-like repeat(EGFr)-domains of the NOTCH3 gene. CADASIL has a highly variable disease severity. It is supposed that the strongest known disease-modifier may be the NOTCH3cys variant position. In 2023, a new clinical three-tiered EGFr risk classification was proposed. EGFr domains were classified as either low (LR), medium (MR) or high risk (HR). However, it is still unclear how the location of the variants can play a role in CADASIL clinical and neuroradiological phenotype. Herein, we aimed to investigate the influence of mutation site on the clinical and neuroradiological presentation.

Methods: We included patients with a NOTCH3 mutation. Participants were uniformly characterized with a 3Tesla brain MRI (Figure-1A). For each patient, demographic and clinical data were collected (Figure-1B).



EGFr domain risk	HR (n=71)	MR (n=32)	LR (n=13)
Age at last visit, mean (SD)	49,9 (13,2)	58,1 (12,9)	59,5 (11,7)
Men, n (%)	35 (49,2)	15 (46,8)	5 (38,5)
Clinical symptoms			
Ischaemic stroke, n (%)	24 (33,8)	11 (34,4)	3 (23,1)
Intracerebral haemorrhage, n (%)	5 (7,1)	1 (3,1)	1 (7,7)
Neuroradiological features			
Fakezas score, mean (SD)	2,5 (0,9)	2,4 (0,8)	2,2 (0,9)
Lacune number, mean (SD)	4,8 (6,4)	4,4 (5,2)	2,7 (4,1)

B

FIGURE 1A Representative brain MR FLAIR imaging of one patient for each EGFr domain clustered by high (first line), medium (second line) and low risk (third line) 1B. Demographic, clinical and neuroradiological data of HR, MR and LR patients

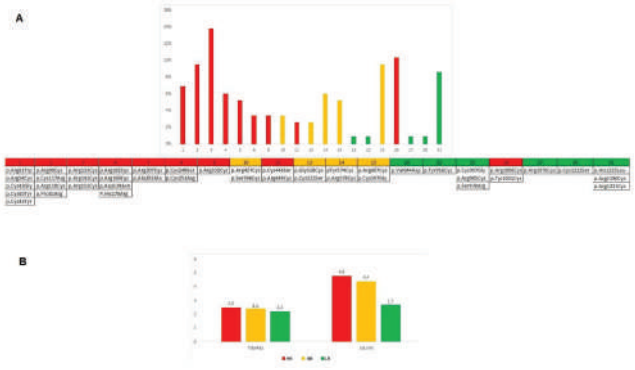


FIGURE 2A Distribution and type of NOTCH3 variants across the three risk groups in our cohort 2B. Average Fazekas score and number of lacuna in the three risk groups.

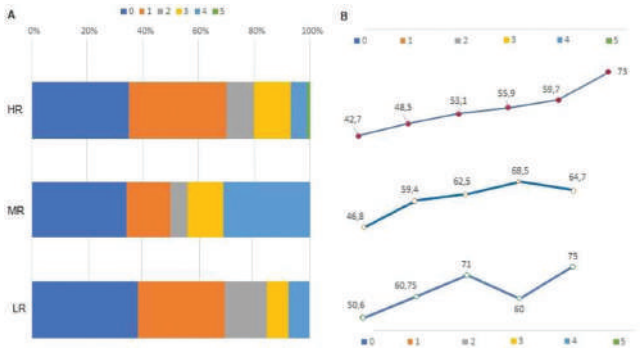


FIGURE 3A Disability for each risk group, according to modified Rankin Scale (mRS) 3B. Mean age for each patient group according to EGFr risk classification and mRS value.

Results: Between 2008 and 2023, a total of 115 individuals with 43 unique NOTCH3 variant were included (Figure-2A). Mutations clustered on the HR-domains were associated with an increased risk of stroke compared to the LR (odds ratio [OR]:1.55; 95% CI: 5.53–0.44) and MR-domains (OR: 1.15; 95% CI: 2.71–0.49) (Figure-1B). On brain MRIs, patients carrying a HR-variants had slightly higher mean Fazekas score and more lacuna than MR and LR-patients (Figure-2B). Furthermore, LR-EGFr individuals had less disability, even though they were significantly older than MR and HR-EGFr patients (Figure-3).

Conclusion: Patients with NOTCH3 HR-EGFr variants had not only an increased risk of stroke and earlier disability but also a more severe neuroradiological picture compared to the LR and MR-domains.

Disclosure: Nothing to disclose.

EPO-249 | Optimal duration of dual antiplatelet therapy after carotid artery stenting: A nationwide cohort study

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Background and Aims: In carotid artery stenosis patients not eligible for carotid endarterectomy, carotid artery stenting (CAS) serves as an alternative. Dual antiplatelet therapy (DAPT) after CAS aims to prevent ischemic stroke, but the optimal duration remains unclear. We aimed to determine the optimal duration of DAPT by identifying differences in clinical events that occur depending on the DAPT maintenance period.

Methods: We obtained all data from the nationwide database of Health Insurance Review & Assessment Service from 2007 to 2020. The patients who received CAS, identified by procedure codes, The patients were divided into two groups according to the duration of DAPT: those who maintained DAPT for at least 90 days but less than 6 months (short-DAPT group) and those who maintained it longer (long-DAPT group). The primary outcome was a composite of ischemic stroke, gastrointestinal bleeding, and intracranial hemorrhage (ICH) within 12 months post-switch to single antiplatelet therapy.

Results: Of 12,034 CAS patients, 2,529 were in the short-DAPT group and 9,505 were in the long-DAPT group. In the short-DAPT group, ischemic stroke, gastrointestinal bleeding, and ICH occurred in 53 (2.1%), 24 (0.9%), and 4 (0.2%), respectively. In the long-DAPT group, ischemic stroke, gastrointestinal bleeding, and ICH occurred in 184 (1.9%), 142 (1.5%), and 6 (0.1%), respectively. The primary outcome did not significantly differ between groups (3.0% vs. 3.4%; adjusted hazard ratio 1.104; 95% CI 0.866–1.406, $p = 0.4252$).

Conclusion: The short-duration DAPT can be recommended as it shows no difference from long-duration in terms of clinical efficacy and adverse events after CAS.

Disclosure: None.

EPO-250 | Non-coding RNA expression profiling of the peripheral blood for patients with cervical artery dissection using RNA-seq

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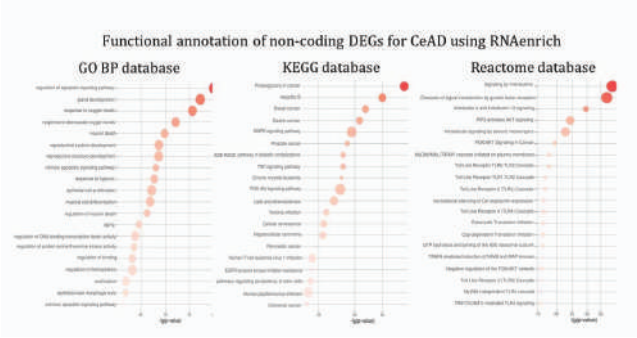
Background and Aims: Cervical artery dissection (CeAD) is the main cause of young ischemic stroke. We performed bulk RNA-seq of the peripheral blood from patients with CeAD and healthy volunteers. As we analyzed previously, the expression profile of protein-coding genes for CeAD was associated with nucleolar stress, senescence-associated secretory phenotype and mitochondrial malfunction. Our new research goal is to evaluate functional properties of differentially expressed non-coding genes (ncDEGs) in peripheral blood for CeAD.

Methods: RNA was extracted from peripheral blood of 19 CeAD patients (37.6 ± 3.95 y.o.) and 18 healthy volunteers (30.1 ± 6.65 y.o.) using the Qiagen© RNeasy Mini Kit. 1000 ng of the RNA (RIN>7.0) were used to prepare each library with the Illumina© TruSeq Stranded Total RNA Library Prep Gold kit. 30–50 million paired-end reads per sample were sequenced on the Illumina© NovaSeq 6000. 80% of the reads were aligned to the human reference genome using STAR. 60% of the aligned reads were counted in the features (genes) using Htseq-count. Differential expression analysis with covariate adjustment (for age, sex and batch factors) was performed in EdgeR (CeAD vs Norma; adj.p-value < 0.05). Enrichment analysis for ncDEGs was performed using RNAenrich against Reactome, KEGG and GO BP.

Results: We identified 62 upregulated and 302 downregulated ncDEGs for CeAD, which are most significantly involved in the pathways relevant to carcinogenesis and angiogenesis: epithelial cell proliferation, cellular senescence, regulation of apoptosis and response to oxygen levels, VEGFA-VEGFR2/PI3K-AKT/MAPK signaling.



Enrichment bubble plots for the top representative pathways enriched in ncDEGs for CeAD. The pathways from GO BP, KEGG and Reactome databases are shown.

Conclusion: Functional profiling of ncDEGs for CeAD confirms our previous results about the probable intersection of CeAD with paraneoplastic mechanisms.

Disclosure: Nothing to disclose.

EPO-251 | Large artery atherosclerosis association with tissue-level collaterals and outcomes in mechanical thrombectomy patients

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Background and Aims: Large artery atherosclerosis (LAA) is responsible for approximately 15% of acute ischemic strokes (AIS). Studies showed that LAA foster leptomeningeal development. We aimed to determine whether LAA is associated with better tissue-level-collaterals (TLC), denoted by lower computed tomography perfusion (CTP)-derived hypoperfusion intensity ratio (HIR), as well as smaller early infarct volume (EIV) and if HIR and EIV affect functional outcomes.

Methods: We retrospectively analyzed 460 consecutive patients with AIS in anterior circulation treated with MT in Comprehensive Stroke Center in Krakow (2019–2023). We included 120 (26.09%) patients with LAA and 340 (73.91%) with cardioembolic AIS etiology. We obtained pre-stroke risk factors and performed CTP followed by post-processing analysis with RAPID software. HIR was defined as ratio of T10max/T6max; EIV as tissue with cerebral blood flow < 30% on admission, good functional outcome (GFO) as modified Rankin Score < 3 at day 90.

Results: LAA was associated with male sex (75% vs 41.2%, $p < 0.001$), smoking history (42.5% vs 14.5%, $p < 0.001$), younger age (66 [59–71 years]vs 76 [69–84 years], $p < 0.001$), lower initial National Institutes of Health Stroke Scale score (15 [10–18] vs 17 [10–20], $p = 0.003$) and lower HIR (0.26 [0.1–0.434] vs 0.386 [0.204–0.521], $p < 0.001$). Despite that, LAA was not associated with lower EIV (8 ml [0–32] vs 7 ml [0–22], $p = 0.502$). LAA etiology predicted GFO in univariate analysis (73.3% vs 60.6%, $p = 0.012$), although significance was lost after adjustment for confounders ($p = 0.394$).

TABLE 1 Characteristics of patients with LAA vs cardioembolic ischemic stroke etiology

	LAA (N=120)	Cardioembolic (N=340)	*P* value
Demographics			
Male, n (%)	90 (75)	140 (41.2%)	<0.001
Age, years, median [IQR]	66 [59-71]	76 [69-84]	<0.001
Stroke risk factors			
Hypertension, n (%)	76 (63.3)	271 (79.7)	<0.001
Diabetes Mellitus, n (%)	22 (18.3)	79 (23.2)	0.474
Hiperlipidemia, n (%)	15 (12.5)	72 (21.2)	0.037
History of stroke/TIA, n (%)	8 (6.7)	47 (13.8)	0.038
Smoking, n (%)	51 (42.5)	49 (14.5)	<0.001
Clinical characteristics			
Baseline NIHSS, median [IQR]	15 [10-18]	17 [10-20]	0.003
Time from LKW to puncture, median [IQR]	324 [245-419.5]	298 [21..25-370]	0.021
Time from LKW to imaging, median [IQR]	256 [197-357]	245 [172-306]	0.032
Intravenous thrombolysis, n (%)	74 (61.7)	157 (46.2)	0.004
Successful recanalization (mTICI 2b), n (%)	103 (85.8)	309 (90.9)	0.12
Stroke localization			<0.001
ICA, n (%)	45 (37.5)	29 (8.5)	
M1, n (%)	45 (37.5)	209 (61.5)	
M2, n (%)	10 (8.3)	85 (25)	
Tandem, n (%)	20 (16.7)	17 (5)	
Stroke-related complications			
Pneumonia, n (%)	22 (18.3)	79 (23.2)	0.265
Urinary tract infection, n (%)	17 (14.2)	56 (1..5)	0.553
No hemorrhagic transformation, n (%)	100 (83.3)	255 (75)	0.061
Outcomes			
90-day good functional outcome (mRS<3), n(%)	88 (73.3%)	206 (60.6%)	0.012
Radiological examination			
Baseline ASPECTS, median [IQR]	8 [7-9]	8 [7-9]	0.459
Penumbra, ml, median [IQR]	94 [65.25-121]	90.5 [53.25-135.75]	0.827
Early infarct volume (CBF<30%), ml, median [IQR]	8 [0-32]	7 [0-22]	0.502
HIR, median [IQR]	0.26 [0.1-0.434]	0.386 [0.204-0.521]	<0.001

*IQR – interquartile range; TIA – transient ischemic attack; NIHSS - National Institutes of Health Stroke Scale; LKW - last known well; ASPECTS - Alberta Stroke Program Early CT Score; CBF – cerebral blood flow; HIR – hypoperfusion intensity ratio

Conclusion: LAA is associated with male sex, smoking history, younger age, lower initial stroke severity and more robust TLC. Despite better TLC, LAA patients have neither smaller EIV nor better prognosis than cardioembolic patients.

Disclosure: ERA-NET-NEURON/21/2020 iBioStroke grant.

COVID-19

EPO-252 | Long-COVID-19: A biomedical model of post-viral chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME)

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Background and Aims: The pathogenesis of post-viral chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is poorly understood. Long-COVID-19 is a post-viral syndrome that shares clinical features of CFS/ME.

Methods: We reviewed the data of 487 adults (age range 16–70 years) with CFS/ME seen in our clinic al unit with the clinical features of adult post-COVID-19 population from literature search.
Results: Symptoms of post-viral CFS/ME and long-COVID-19 were remarkably similar; fatigue, headache, cognitive deficit and chronic pain were common in both groups and tended to be more pervasive for those with longer symptom durations. Quality of life was severely impacted by physical fatigue with post-exertional malaise, cognitive impairment that did not progress over time, and neuropsychiatric symptoms from low mood and anxiety.
Conclusion: Population with CFS/ME and post-COVID-19 experience persistent central fatigue, pain and non-progressive cognitive deficits. Modification of post-translational cell signalling by viral infection and host immune response leading to metabolic reprogramming and consequent alterations in synaptic and ion channel functions is a possible explanation and further work is required for better understanding of biomedical mechanisms of post-viral syndromes to develop effective therapy. Long COVID-19 is a valid biomedical model of post-viral CFS/ME and post-viral syndromes are not primarily a somatoform or functional neurological disorders.
Disclosure: There is no competing interest.

EPO-253 | SARS-CoV-2 impact on disability in Southern Italy's MS patients: Tertiary center findings

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Background and Aims: In Multiple Sclerosis (MS) patients, the occurrence of COVID-19 has been associated with worsening clinical course. This study aimed to assess the incidence of SARS-CoV2 infection during various pandemic waves and evaluate risk factors for clinical disability worsening in the post-COVID-19 era within an MS setting.
Methods: A retrospective study was conducted on patients with MS and neuromyelitis optica spectrum disorder (NMO) at the Multiple Sclerosis Center at the University of Naples "Federico II" between March 2020 and October 2023. Patients were monitored for virologically documented SARS-CoV2 infection during follow-up. Data on Expanded Disability Status Scale (EDSS) scores were collected at MS diagnosis, the latest follow-up before March 2020, and the last available follow-up
Results: Among 276 patients enrolled, 46% (127 patients) were infected with SARS-CoV2, predominantly during the Omicron BA1/2 wave. Infected patients had a lower EDSS at MS diagnosis (3.0 [2.5–3.5] vs. 3.5 [2.5–4.5], $p=0.015$) and at the last follow-up (4.5 [3–6] vs. 5.5 [3.5–6.5], $p=0.03$). No significant differences in EDSS change were observed between infected and non-infected patients. Multivariate Cox analysis revealed that EDSS worsening was associated with age younger than 50 years (HR=3.57, $p=0.03$), while anti-CD20 treatment was protective against disability accrual (HR=0.09, $p=0.04$).
Conclusion: 46% of MS or NMO patients experienced SARS-CoV2 infection while under mAb treatment. Infected individuals exhibited lower motor impairment, suggesting that higher disability might be protective due to increased awareness of fragility status or limited outdoor and social activities. Importantly, COVID-19 infection did not seem to impact the disease course
Disclosure: Lanzillo R received compensations for speaking or consultancy from Biogen, Teva, Genzyme, Merck, Bristol myer squibb, Jansenn, Novartis and Roche Carotenuto A served on advisory boards for: Merk, Novartis, Roche and Almirall Brescia Morra V received funding from Novartis, Roche, Biogen, Teva, Almirall, Sanofi-Genzyme, Merk, Bayer, Mylan, Bristol Myers Squibb Moccia M received honoraria from Biogen, BMS Celgene, Janssen, Merck, Roche, and Sanofi-Genzyme; and serves in the Editorial Board of the Multiple Sclerosis Journal Others authors declare not conflict of interest.

EPO-254 | SARS-CoV-2-induced type I interferon signalling dysregulation in the olfactory-amygdala pathway

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Background and Aims: Previous works from our group have proposed a model where peripheral induction of IFN-I may be relayed to the CNS, even in the absence of fulminant infection. The aim of our study was to identify significantly enriched IFN-I signatures and genes along the transolfactory route, utilizing published datasets of nasal mucosa, olfactory bulb amygdala transcriptomes of COVID-19 patients. We furthermore sought to identify in these IFN-I signature gene networks associated with Alzheimer's disease pathology and risk.
Methods: Gene expression data involving the nasal epithelium, olfactory bulb and amygdala of COVID-19 patients and transcriptomic data from Alzheimer's disease patients were scrutinized for enriched Type I interferon pathways. Gene set enrichment analyses and gene – Venn approaches were used to determine genes in IFN-I enriched signatures. The Agora web resource was used to identify genes in IFN-I signatures associated with Alzheimer's disease risk based on its aggregated multi-omic data.
Results: Pathways associated with type I interferon signalling were found in all samples tested. Each type I interferon signature was enriched by IFITM and OAS family genes. A 14 gene signature

associated with COVID-19 CNS and the response to Alzheimer's disease pathology, whereas 9 genes were associated with increased risk for Alzheimer's disease.

Conclusion: Our study provides further support to a type I interferon signalling dysregulation along the extended olfactory network as reconstructed herein, ranging from the nasal epithelium and extending to the amygdala. We furthermore identify the 14 genes implicated in this dysregulated pathway with Alzheimer's disease pathology, conferring increased risk for the latter.

Disclosure: None declared.

EPO-255 | Serum interleukins in children with neurological complications of SARS-CoV-2 infection

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Background and Aims: Neuroinflammation is one of the key mechanisms involved in the pathogenesis of brain lesions associated with SARS-CoV-2 infection. The aim. To estimate the correlation between serum levels of IL-1beta, IL-10, and nervous system damage in children with SARS-CoV-2 infection.

Methods: We evaluated 100 children (age 29 days – 7 years) with neurological manifestations associated with SARS-CoV-2 (moderate and severe form), divided into two groups: (1) acute neurological complications (CN) and (2) post-acute, in which we evaluated the serum values of IL-1beta and IL-10, by the ELISA method. Clinical manifestations were scored to perform statistical calculations. Statistical processing: *t*-student test, 95 CI confidence coefficient, correlation coefficient (rxy).

Results: In the group with acute CN, 89 (89%; 95 CI 92.13 –85.87) cases were registered, and post-acute CN – 11 (11%; 95 CI 7.87–14.13). In the group with acute CN, encephalopathy (72%; 95 CI 67.51–76.49) and seizures (9%; 95 CI 6.14–11.86) prevailed, compared to those with post-acute CN (2%; 95 CI 0.6–3.4) in which headache predominated (90%; 95 CI 87–93). Serum levels of IL-10 and IL-beta were significantly increased in the acute CN group compared to those with post-acute CN. Strong correlations were found between elevated serum levels of IL-1beta and encephalopathy (rxy = 0.786), IL-1beta and seizures (rxy = 0.824), and between IL-10 and encephalopathy (rxy = 0.758), IL-10 and seizures (rxy = 0.806).

Conclusion: Strong correlations between elevated levels of IL-1β and IL-10 and acute CN suggest the presence of pronounced inflammation and the risk of long-term neurological complications in children who were infected with SARS-CoV-2.

Disclosure: Nothing to disclose.

EPO-256 | Cortical and spinal excitability testing in patients with long-term post-COVID myopathy

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Background and Aims: The objective of this study was to investigate cortical and spinal excitability in patients diagnosed with post-COVID myopathy, exploring the possibility of a multisystemic involvement of both muscles and central nervous system (CNS).

Methods: In this case-control study, we compared 32 patients with post-COVID myopathy to 15 age-matched healthy controls. Cortical excitability was assessed using threshold-tracking transcranial magnetic stimulation (TT-TMS), with the following protocols: Short-Interval Intracortical Inhibition (SICI), Short-Interval Intracortical Facilitation (SICF), Long-Interval Intracortical Inhibition (LICI), Intracortical Facilitation (ICF), Short-latency afferent inhibition (SAI). Spinal cord excitability was evaluated by recording H-reflex and long latency reflexes (LLRs). Cognitive status was assessed using Montreal Cognitive Assessment (MoCA) and Symbol Digit Modalities Test (SDMT).

Results: TT-TMS showed a statistically significant decreased SICI across the entire averaged 1–3.5 ms interval range ($t(45) = 2.411$, p-value = 0.01) in patients compared to controls (Fig 1). The most affected ISI was 2.5ms, with values of 9.2% ± 1.9 for patients vs. 21.3% ± 2.3 for controls ($t(45) = 3.761$, p-value = 0.0005). No significant differences were found in SAI, SICF, ICF and LICI between the two groups. Statistically significant differences were observed in

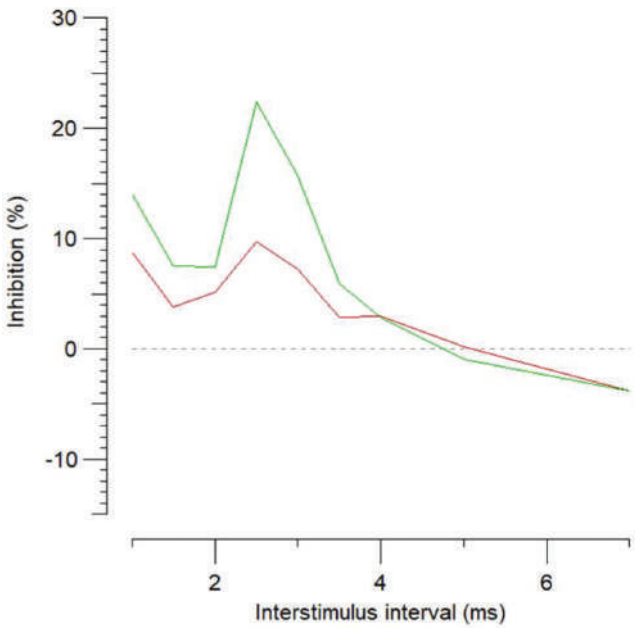
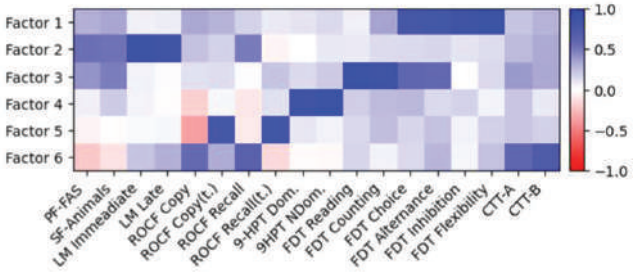


FIGURE 1 Overview of SICI protocol 1–7 ms. Red: patients, Green: healthy controls

LLR II (U = 126.0, *p*-value = 0.02) and LLR III (U = 53.0, *p*-value = 0.03) amplitudes. MoCA median score was 27 for patients and 29 for controls, showing a statistically significant difference between the two groups (U = 96.50, *p*-value = 0.002). We found no differences in H reflex and SDMT score in the two groups.

Conclusion: This study demonstrates that patients with post-COVID myopathy exhibit reduced cortical inhibition and increased LLR amplitudes. These findings point towards a potential concomitant involvement of CNS in individuals with post-COVID myopathy.

Disclosure: Nothing to disclose.



Weighting matrix of the final factor analysis after ObliMin rotation. PF: Phonetic Fluency, SF: Semantic Fluency, ROCF: Rey-Osterieth Complex Figure test, 9-HPT: nine-hole peg test, FDT: Five-Digit test, CTT: Color Trails test.

EPO-257 | The different neuropsychological phenotypes of Post-COVID subjects

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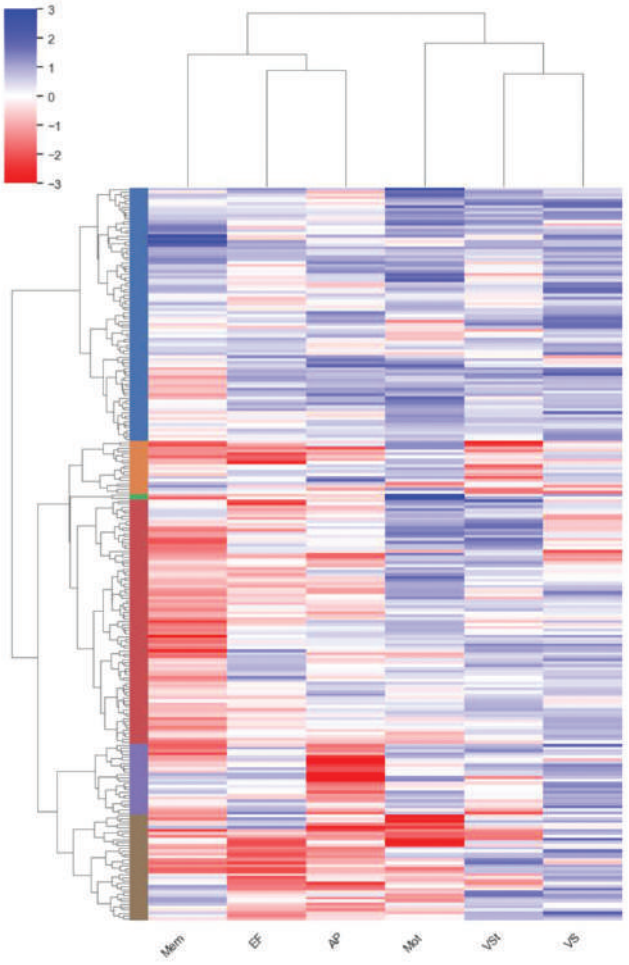
Background and Aims: Although cognitive dysfunction of patients after COVID-19 infection has been described, a systematic search of neuropsychological subgroups has not been conducted. The present study aims to derive the neuropsychological profile of different subgroups using a data-centric hierarchical clustering method.

Methods: We analyzed the data from the NeuroCovid cohort, comprising different neuropsychological tests (comprising multiple cognitive domains). After outlier removal, a factor analysis was performed to derive the latent cognitive factors in the data. Factor-transformed data were renormalized according to the expected population mean and standard deviation and used in hierarchical analysis with Ward's method. Subjects were compared between clusters regarding demographics, illness severity, depression and anxiety scores.

Results: We applied factor analysis to neuropsychological data from 265 subjects. Data were deemed proper for factor analysis (Kayser-Meyerz-Olkin statistic 0.63), and the number of factors was determined to be 6 by parallel analysis. Factors regarding memory, executive functions (EF), automatic processes (AP), motor, visuospatial construction (VSP) and visuospatial construction speed were identified. One was excluded from the six clusters identified due to insufficient subjects (*n* = 2). The remaining clusters were (A) unimpaired (*n* = 86), (B) visuospatial impaired (*n* = 18), (C) memory impaired (*n* = 83), (D) AP impairment (*n* = 24), and (E) EF impairment (*n* = 36). Cluster C comprised older subjects, whereas subjects were younger in Cluster E. Depression scores (Beck's Depression Inventory-II) were increased in both clusters C and E.



Clustergram of the Hierarchical Clustering analysis applied to factor-transformed renormalized data. Colors under the dendogram (left) divide the data in different clusters.

Conclusion: Our data shows that the individuals with persistent symptoms after mild COVID present a heterogeneous neuropsychological profile with subgroups showing impairments in different cognitive domains.

Disclosure: Nothing to disclose.

EPO-258 | Assessing the potential neurological impact of COVID-19 vaccines: An in-depth examination of reported complications

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Background and Aims: During the COVID-19 pandemic, several types of vaccines were developed, which successfully passed all stages of clinical trials and were used into practice. Like other types of vaccines, COVID-19 vaccines have their own local and systemic side effects, as well as other systemic complications, including neurological ones.
Methods: The medical records of people were examined, who received a full course of vaccination between April 2021 and March 2023 in the Tashkent city. Adverse reactions and neurological complications were identified by retrospective analysis, spontaneous reporting, and stimulated reporting.
Results: A total of 1,585,014 people have been completed the full course of vaccination (minimum age 18 years, maximum 85 years) and 6,796,188 doses of vaccines have been used (Oxford/AstraZeneca 240,144 doses, ZF2001 3,411,125 doses, Sputnik V 257,593 doses, Moderna 1,132 121 doses, Pfizer/BioNTech 1,441,627 doses, Sinovac 251,146 doses, Sputnik Light 51,141 doses, Johnson&Johnson 11,291 doses). Among the neurological complications after vaccination were identified: ischemic stroke (12 cases, 0.00075%), cavernous sinus thrombosis (1 case, 0.00006%), acute disseminated encephalomyelitis (1 case, 0.00006%), meningoencephalitis (3 cases, 0.00019%), sensorineural hearing loss (4 cases, 0.00025%), Guillain-Barré syndrome (4 cases, 0.00025%), Bell's palsy (2 cases, 0.000125%), multisystem inflammatory syndrome (1 case, 0.00006%). No deaths have been reported following vaccination. Neurological complications occurred within 28 days after vaccination.
Conclusion: Given the risk of neurological complications is extremely rare (0.001%), vaccination is the only way to protect against COVID-19. At a time when the COVID-19 infection has enormous complications not only in the nervous system, but also in other systems, even death.
Disclosure: Agree.

EPO-259 | Analysis of IgG antibodies against S1-RBD of SARS-CoV2 in patients with MS treated with DMT in North-Eastern Poland

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Background and Aims: The coronavirus disease 2019 (COVID-19) course and serological statuses of patients with relapsing-remitting multiple sclerosis (RRMS) treated with disease-modifying therapies (DMTs) is similar to the general population. Over the pandemic course a notable increase in the number of RRMS patients who received vaccination against severe acute respiratory coronavirus 2 (SARS-CoV-2) and those who had COVID-19 was reported. This virus and/or vaccination likely influenced DMT-treated RRMS patients' serological statuses.
Methods: This investigation assessed the presence and levels of the antibody directed against the S1 protein receptor binding domain (S1RBD) of SARS-CoV-2 in 38 DMT-treated RRMS patients. The antibodies were assessed twice: between March-June 2021 (visit 1) and March-June 2023 (visit 2).
Results: Statistical analysis showed that percentages of IgGS1-RBD results between vaccinated and unvaccinated patients with RRMS were not statistically significant (visit 1: $p = 0.089$; visit 2 $p = 0.501$). However, at visit 1, the number of positives was higher in the vaccinated group than in the unvaccinated group, which was significant at the trend level. Moreover, vaccination had a statistically significant effect on anti-S1RBD antibody levels at visit 1 ($p < 0.001$) and visit 2 ($p = 0.038$).
Conclusion: Study group are immunocompetent in terms of the production of neutralizing antibodies. Our research shows that vaccinated group of patients have statistically significantly higher levels of neutralizing antibodies compared to unvaccinated. It was observed over the course of two years of the pandemic. Levels of neutralizing antibodies seem to better reflect the level of protection against the SARS-CoV-2 virus than their presence alone, but this requires further research.
Disclosure: No disclosure.

EPO-260 | Radiological markers of neurological manifestations of post-acute sequelae of SARS-CoV-2 infection: A mini-review

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Background and Aims: The neurological impact of COVID-19 infection is concerning, as patients continue to experience various cognitive and psychiatric symptoms for more than 12 weeks post-infection—a condition known as neurological post-acute sequelae of COVID-19 (Neuro-PASC). Considering significant challenges exist in evaluating its impact, this mini-review aims to provide up-to-date information on the optimal usage, limitations, and benefits of neuroimaging techniques for Neuro-PASC.

Methods: Our search on PubMed and Google Scholar databases used specific equations for each imaging, such as structural MRI (magnetic resonance imaging), functional MRI, diffusion MRI, SWI (susceptibility-weighted imaging), SPECT (single-photon emission computed tomography) imaging, OR PET (positron emission tomography) imaging AND COVID-19. Articles were then selected with 2 independent reviewers.

Results: 18F-FDG-PET/CT and functional MRI demonstrated hypometabolism in cerebral regions directly linked to patient symptoms. Structural MRI studies revealed different findings, such as infarcts, white matter atrophy, and gray matter volume changes. One SPECT imaging study noted frontal lobe hypometabolism, while diffusion MRI showed increased diffusivity in limbic and olfactory cortical systems. The SWI sequence showed abnormalities in white matter near the gray-white matter junction. A study on 18F-amyloid PET/CT found amyloid lesions in frontal and anterior cingulate cortex areas, and a study on arterial spin labeling (ASL) found hypoperfusion in the frontal lobe.

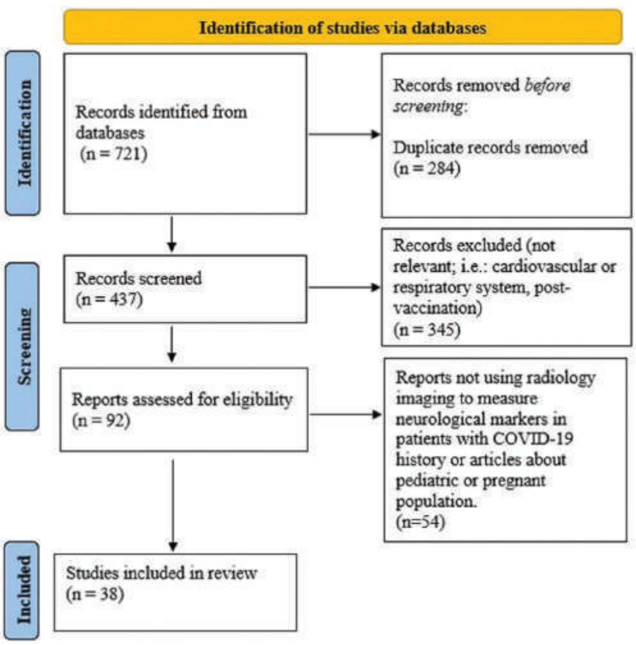

FIGURE 1 Prisma Flowchart

TABLE 1 Summary of the characteristics and findings of the imaging studies included in this review

Authors	Journal	Study design	Number of subjects	Number of controls	Gender distribution male/female	Age (years)	Time since COVID-19 infection	Type of imaging	Main findings in patients
Sollini et al. [illegible]	Springer Nature	Prospective case-control study	13	26	8/5	[illegible]	131 ± 31 days	^{18}F-FDG PET/CT	^{18}F-FDG uptake in "target" and "non-target" tissues. Relative hypometabolism in the right parahippocampus and thalamus. Specific region(s) of hypometabolism in patients with persistent anosmia/ageusia, fatigue, and vascular uptake.
Karimi-Galougahi et al. [illegible]	Academic Radiology	Case study	1	N/A	0/1	27	6 weeks	^{18}F-FDG PET/CT	Hypometabolism in the orbitofrontal cortex.
Donegani et al. [illegible]	Biomedicines	Longitudinal cross-sectional cohort study	22	41	12/10	[illegible]	>1 month	^{18}F-FDG-PET/CT	Relative hypometabolism shown in bilateral parahippocampus and fusiform gyri and in left insula.
Hosp et al. [illegible]	Oxford University Press	Prospective cohort study	29	45	18/11	65.2 ± 14.4	1 month average	3T sMRI and ^{18}F-FDG PET/CT	MRI showed subacute infarcts. ^{18}F-FDG PET/CT showed predominant frontoparietal hypometabolism.
Guedj et al. [illegible]	Springer Nature	Retrospective case control study	35	44	20/15	55.06 ± 11.22	≥3 weeks	^{18}F-FDG PET/CT	Hypometabolism in olfactory gyrus and connected paralimbic/limbic regions, extended to the cerebellum and brainstem.
Dressing et al. [illegible]	The Journal of Nuclear Medicine	Prospective cohort study	14	45	5/9	[illegible] ± 7.2	198.8 ± 63.5 days	^{18}F-FDG PET/CT	No pathological findings found on imaging.
Debs et al. [illegible]	American Journal of Neuroradiology	Retrospective single-center study	45	52	24/21	58 (18–87)	6.57 ± 4.85 months	^{18}F-FDG-PET/CT	Focal hypometabolism peak in cerebellum and in bilateral frontal, parietal, occipital, and posterior temporal lobes, during the first 2 months, nearly resolved at 6 months and disappeared at 12 months. Hypermetabolism in brainstem, cerebellum, limbic structures, frontal cortex, and periventricular white matter shown 2–6 months post-infection.
[illegible] et al. [illegible]	Viruses	Mixed method, cohort study (Action research)	55 (35 for imaging)	N/A	15/40	42.4 (12–79)	13.1 ± 8.9 (recovered mild and severe) 18.3 ± 5.9 (still ill, very severe)	SPECT-CT	SPECT-CT showed cerebral hypoperfusion lesions consistent with the severity of the condition.
Ferrucci et al. [illegible]	Springer Nature	Retrospective case study	7	N/A	4/3	[illegible]	>12 months	^{18}F-FDG PET/CT and ^{18}F-amyloid PET/CT	^{18}F-FDG PET/CT showed various hypometabolism in the left temporal mesial, pontine, and bilateral prefrontal and parietal regions. ^{18}F-amyloid PET/CT done for the patient with the greatest extent of hypometabolism showed significant Aβ deposition in the superior and middle frontal cortex, in the posterior cingulate, and mildly in the rostral and caudal anterior cingulate regions.
Thapaliya et al. [illegible]	Frontiers in Neuroscience	Cross-sectional study	8	10	3/5	43.2 ± 18.7	≤3 months	7T sMRI	Strong negative relationship between midbrain volume and "breathing difficulty". Greater pons and whole brainstem volumes in patients.
Cecchetti et al. [illegible]	Springer Nature	Longitudinal quasi-experimental study	[illegible]	[illegible]	25/11	[illegible]	[illegible]	3T sMRI	No significant differences in total brain, gray, or white matter volumes were found between patients and controls. Greater total of right frontal and right parieto-occipital white matter hyperintensity volumes. Interrelated cognitive, EEG and MRI alterations were observed after two months of COVID-19 resolution.
Douaud et al. [illegible]	Nature	Longitudinal quasi-experimental cohort study	401	384	172/229	62.1 ± 6.7	141 ± 79 days	sMRI, fMRI, dMRI	Reduced total brain size, gray matter thickness and tissue contrast in orbitofrontal cortex and parahippocampal gyrus. Greater changes in patients regarding diffusion measures in areas functionally connected to the primary olfactory cortex.
Kandemirli et al. [illegible]	Academic Radiology	Prospective case study	23	N/A	9/14	[illegible]	1–4 months	Paranasal sinus CT and 3T MRI dedicated to olfactory nerves	CT showed opacification in olfactory cleft. MRI showed olfactory bulb degeneration and changes in shape. MRI also showed diffused increase in signal intensity from the olfactory bulb, scattered hyperintense foci, and microhemorrhages.
Besteher et al. [illegible]	Psychiatry Research	Cross-sectional study	30	20	13/17	[illegible]	8.63 (2–14) months	3T sMRI	Multiple clusters of significant bilateral gray matter volume enlargement in fronto-temporal regions, insula, hippocampus, amygdala, basal ganglia and thalamus.
Hellgren et al. [illegible]	BMJ Open	Ambidirectional observational cohort study	[illegible]	N/A	28/7	[illegible]	7 months	3T SWI, DWI, and sMRI	Multiple findings of white matter lesions near gray-white matter junction in frontal and parietal lobes.
Campabadal et al. [illegible]	Annals of Clinical and Translational Neurology	Prospective cohort study	48	N/A	18/30	[illegible] (normal olfaction) 51.90 ± 7.92 (olfactory dysfunction)	[illegible] months	3T sMRI and DWI	Reduced gray matter volume and increased mean diffusivity in olfactory-related areas explaining persistent olfactory deficits in patients. Greater radial diffusivity in the anterior corona radiata, the genu of the corpus callosum, and uncinate fasciculus in patients with deficits compared to those without.
Yus et al. [illegible]	Acta Neurologica Scandinavica	Cross-sectional study	[illegible]	N/A	24/58	[illegible]	[illegible] months	ASL, sMRI, and DTI	Olfactory dysfunction associated with lower tissue perfusion in orbital and medial frontal areas. Absence of statistically significant findings in brain volumes and diffusion tensor imaging.
Kiatkittikul et al. [illegible]	Nuclear Medicine and Molecular Imaging	Retrospective case study	13	N/A	6/7	[illegible]	>28 days	^{18}F-FDG PET/CT and 3T PET/rsfMRI	^{18}F-FDG PET/CT showed uptake in many organs. ^{18}F-FDG PET showed many areas of hypometabolism in the thalamus, and in parietal, temporal, frontal, and occipital lobes. rsfMRI results showed abnormal brain connectivity which is coherent with ^{18}F-FDG PET findings.
Churchill et al. [illegible]	Frontiers in Neurology	Cross-sectional study	51	15	17/34	41 ± 12	4–5 months average	3T sMRI and fMRI	Lower connections to the thalamus and decreased temporal subcortical functional connectivity in patients.
Ajčević et al. [illegible]	Nature Portfolio	Prospective cohort study	24	22	9/15	[illegible]	≥4 weeks	ASL MRI	Hypoperfusion predominantly in frontal, parietal, and temporal cortex.
[illegible] et al. [illegible]	medRxiv pre-print, not peer reviewed	Prospective cohort group-level study	[illegible]	30	[illegible]	[illegible]	<6 months	3T SWI and sMRI	Higher susceptibility imaging values in the frontal lobe and brainstem in patients. Observed cluster in midbrain and bilateral clusters in white matter near the orbitofrontal gyri and the gray-white matter junctions. Significant clusters negatively correlated with fatigue scores found in frontal lobe, anterior cingulate cortex, and brainstem.

^{18}F-FDG PET/CT, Positron emission tomography with 18 fluoro-D-glucose integrated with computed tomography; SPECT-CT, Single Photon Emission Tomography-Computed Tomography; sMRI, structural MRI; dMRI, diffusion MRI; SWI, susceptibility-weighted imaging; DWI, diffusion weighted imaging; DTI, diffusion tensor imaging; ASL, arterial spin labeling.

Conclusion: While accessibility and cost limit the widespread use of 18F-FDG-PET/CT scans and functional MRI, they appeared to be the most promising techniques. SPECT, SWI sequence, and 18F-amyloid PET/CT required further investigation. Nevertheless, imaging remains a reliable tool for diagnosing Neuro-PASC and monitoring recovery.

Disclosure: Nothing to disclose.

EPO-261 | Functional and cognitive outcomes and trajectories three years after hospitalization for COVID-19

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Background and Aims: Little is known about long-term outcomes and trajectories of recovery after hospitalization for COVID-19.

Methods: We conducted a prospective, longitudinal cohort study of patients hospitalized for COVID-19 between 3/2020 and 5/2020. Healthy control patients with no history of COVID-19 and negative SARS-COV-2 nucleocapsid IgG antibodies were also enrolled. Cognitive and functional outcomes as well as post-COVID symptoms were assessed at 6 and 36 months. Outcomes and symptoms were compared between cases and controls using Mann-Whitney U-test and multivariable logistic regression analyses were performed to evaluate the impact of COVID-19 on 3-year outcomes. Non-parametric paired samples Sign test was performed to evaluate changes in metrics over time.

Results: Of 83 subjects, $N=61$ COVID-19 cases (median age 62, 57% female), and $N=22$ non-COVID-19 controls (median age 75, 23% female) were enrolled. At 3-years, t-MoCA was abnormal in 36% of COVID-19 patients compared to 23% of controls. Multiple neuropsychiatric symptoms occurred at higher frequencies in COVID-19 patients compared to controls ($p<0.001$). eGOS scores were significantly lower in COVID patients compared to controls after adjusting for age and sex (aOR 0.05, 95% CI 0.006–0.440, $p=0.007$). Among $N=24$ patients that completed 6 and 36-month follow-up, mRS scores significantly improved over time ($p=0.003$), while no changes were observed in t-MoCA scores.

Conclusion: At 3 years post-hospitalization for COVID-19, neuropsychiatric symptoms were significantly more prevalent and functional outcomes (eGOS) were significantly worse than in controls, even after adjusting for age and sex, despite improvements in mRS from 6 to 36 months.

Disclosure: Thomas Wisniewski has NIH/NIA R01 grant. Yulin Ge has NIH/NIA R01 grant. Jennifer Frontera has NIH R01 grant and NIH/NINDS funding for COVID research. Melanie Li, Zariya Alvarez, Nadir Bilici, Leomaris Caba Caceres, Natasha De La Cruz, Celia Engelson, Julia Greenberg, Salma Hammam, Jessica Hunter, Sohail Karimi, Jon Links, Miguel Rodriguez, Floyd Silva, Alok Vedvyas, Amin Yakubov, have nothing to disclose.

EPO-262 | Innovative in vitro model of human blood-brain barrier mimicry to study neurological effects of SARS-CoV-2

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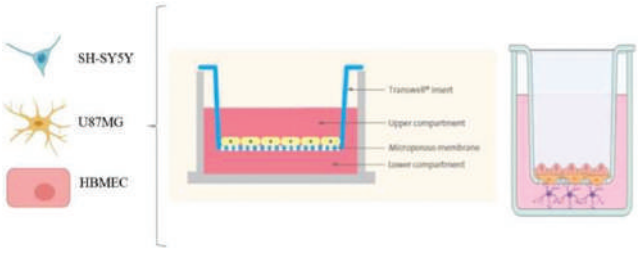
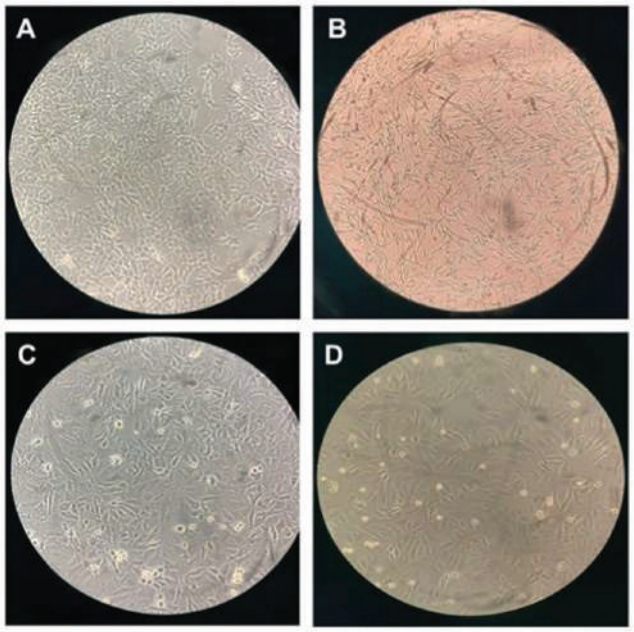
Background and Aims: SARS-CoV-2 is implicated in cerebral manifestations, like meningoencephalitis and stroke. Clinical findings and animal models suggest direct and indirect effects of SARS-CoV-2 on the cerebral microvascular bed. Few studies have applied in vitro models of human BBB to examine interactions between SARS-CoV-2 and the brain. This study aims to validate a novel human BBB model for experiments on molecular and cellular effects of SARS-CoV-2.

Methods: Designed as a triple monolayer membrane, this 2D model includes human cerebral microvascular endothelial cells (hCMEC/D3), human neurons (SH-Sy5y) and human glial cells (U-87MG). Each cell lineage was cultured alongside Vero cells E6 and CCL81, at 37°C and 5% CO2, in flasks with respective medium: 199 (hCMEC); MEM/F-12 (SH-Sy5y); MEM (U-87MG); DMEM-HG (Vero). Each 48–72 h, cells' morphology was checked with an inverted light microscope. Once ≥80% confluency was reached, the cells were expanded by transferring to more flasks, until a maximum of 60 transfers. Eventually, a monolayer of each cell was placed into plates' wells with a semipermeable membrane (Figure 1).

Results: We reached a cell storage (Figure 2) required to plaque 80,000 endothelial cells/mm3 and 150.000 neuronal and glial cells/mm3 per well (concentrations from pilot experiments), and perform all planned experiments: in vitro SARS-CoV-2 exposition, in situ cytokines and chemokines measurements, ex vivo observation of white blood cells from patients.



The transwell plates of 96 wells plus inserts with an 8 µm porous membrane (Corning Life Science, USA); a monolayer of endothelial cells in the top chamber (BBB luminal side), and neural and glial cells in the bottom chamber (BBB parenchymal side).



A. Human Neurons (SH-Sy5y); B. Human Glial Cells (U-87MG); C. Human Cerebral Microvascular Endothelial Cells (hCMEC/D3); D. Vero Cells CCL81.

Conclusion: This is the first in vitro endothelial-neural-glial triple layer model validated to study the interaction between SARS-CoV-2, the neurovascular unit and the immunocytes of patients with cerebrovascular or neuroinflammatory syndromes.
Disclosure: Nothing to disclose.

EPO-263 | Small fiber neuropathy following COVID-19 vaccination: A case series

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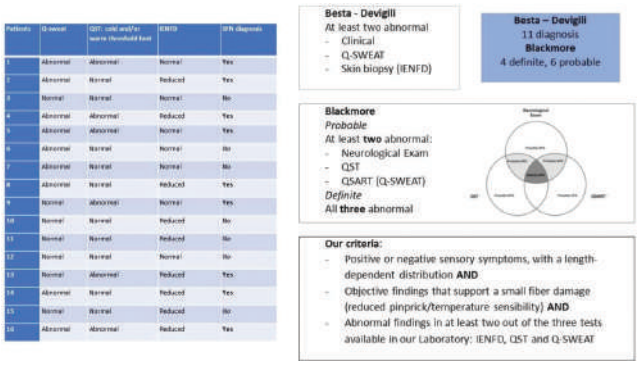
Background and Aims: In several vaccination contexts, different peripheral neuropathies have been described as possible adverse effects. Small fiber neuropathy (SFN) is no exception. Therefore, we investigated the relation between SFN and COVID-19 vaccination.
Methods: We present a case series of 16 patients (F = 14; M = 2) with age 27–64 (50.1 ± 12.1) referred to our Department of Clinical Neurophysiology, Rigshospitalet, Copenhagen, Denmark, with the suspicion of a SFN related to COVID-19 vaccination, with symptoms 'debut within the first month after vaccination. Patients were vaccinated towards COVID-19 with different vaccines and different doses.
Results: All patients underwent nerve conduction studies to exclude a large fiber polyneuropathy, and the following small fiber tests: quantitative sensory testing (QST), quantitative sudomotor axon reflex test (QSART), cutaneous biopsy for intraepidermal fiber density count (IEFND). Following actual criteria, 9 patients were diagnosed with SFN.

Patients	Gender	Age	Time to onset (days)	Vaccination (Type, dose)	Comorbidities
1	M	64	1	Pfizer, 2nd	**Seronegative Rheumatoid Arthritis**, Spinal stenosis
2	F	49	7	Astra Zeneca, 1st	/
3	F	64	0	Pfizer, 1st	Osteoporosis, Chronic Pyelonephritis
4	F	64	1	Pfizer, 1st	Dystonia
5	F	60	0	Pfizer, 2nd	Depression
6	F	51	15	Pfizer, 2nd	**Lung sarcoidosis**
7	F	61	30	Pfizer, 2nd	/
8	F	37	0	Pfizer, 2nd	ADHD, Tourette, Asthma, Fibromyalgia, Hypothyroidism
9	F	45	7	Pfizer, 2nd	Chronic pain after car accident
10	F	48	7	Pfizer, 1st	/
11	F	28	2	Moderna, 2nd	Sinusitis treated with Bioclavid at the same time of vaccination.
12	F	59	7	Pfizer, 1st	Hypothyroidism, interstitial cystitis.
13	M	43	5	Pfizer, 2nd	Horton's headache
14	F	57	9	Pfizer, 2nd	Constipation, borderline personality with anxiety
15	F	52	5	Pfizer, 2nd	K colon
16	F	27	2	Pfizer, 3rd	/

Demographics and general information of patients. In bold most relevant comorbidities.

Clinical findings: neurological symptoms and signs.



Small Fiber Tests and Small Fiber Neuropathy diagnosis with comparison of different sets of criteria. (Q-sweat, quantitative sweat test; QST: quantitative sensory test; IENFD: intraepidermal nerve fiber density).

Conclusion: Assessing the causality between a vaccination and a supposed adverse effect is very difficult. However, a wealth of evidence supports our hypothesis. Firstly, other single cases with similar findings are described, both in association with COVID and other vaccines. Secondly, other neurological complications are described in association with vaccination, pointing to a common pathogenesis. Lastly, same neurological symptoms/affections are described with COVID-19 infection itself. We therefore underline the importance of post-authorization surveillance to assess adverse effects of vaccines.
Disclosure: Nothing to disclose.

EPO-264 | Patients with neurological or psychiatric complications of COVID-19 have worse long term functional outcomes: COVID-CNS

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Background and Aims: Patients hospitalised with COVID-19 often have ongoing morbidity affecting activities of daily living (ADLs), employment, and mental health. However, functional outcomes in patients with COVID-19 neurological or psychiatric complications are poorly understood. We aimed to assess post-discharge functional outcomes of these patients relative to those with isolated respiratory COVID-19.

Methods: We conducted a UK multicentre case-control study of patients hospitalised with COVID-19 (controls) and those with acute neurological or psychiatric complications (cases). Data were collected from clinical records and participants followed-up at 13–16 months for assessment of ADLs, employment, anxiety, and depression.

Results: Between March 2020-July 2022, for 651 patients (362 [56%] cases and 289 [44%] controls), where data were available, a higher proportion of cases than controls had impairment in ADLs (199 [68.9%] vs 101 [51.8%], OR [95% CI] 2.01 [1.40–2.98]) and reported symptoms impacting employment (159 [58.2%] vs 69 [35.6%], OR 2.53 [1.72–3.71]). There was no significant difference in depression or anxiety between overall. For cases, impairment of ADLs was associated with increased risk in females, age >50 years and hypertension (OR 5.43 [1.79–16.96], 3.11 [1.17–8.26], and 3.67 [1.06–12.68]). Those receiving either statins or angiotensin converting enzyme inhibitors had a lower risk (OR 0.09 [0.03–0.37], and 0.17 [0.03–0.84]; AUROC 0.794 [0.71–0.88]).

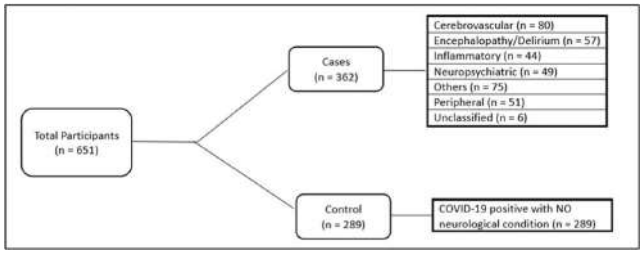

FIGURE 1 Recruitment flowchart

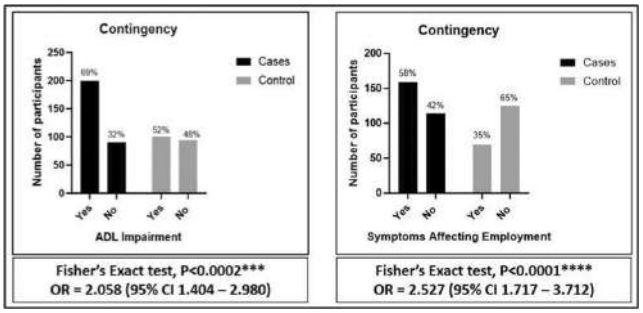

FIGURE 2 Cases vs controls, ADL and Employment. OR: Odds Ratio, CI: Confidence interval

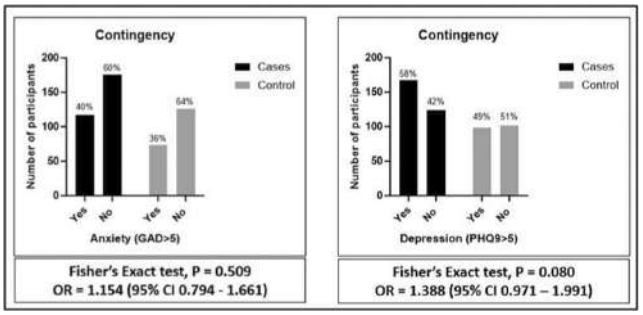

FIGURE 3 Cases vs Controls, anxiety, and depression. OR: Odds Ratio, CI: Confidence Intervals

Conclusion: Patients with neurological or psychiatric complications of COVID-19 had worse functional outcomes than those with respiratory COVID-19 alone in terms of ADLs and employment. Female sex, age >50 years, and hypertension were associated with worse outcomes, and statins or ACE inhibitors with better outcomes.

Disclosure: RS, GK and YH are funded by the UK National Institute for Health Research (NIHR) as NIHR academic clinical fellows and ME as NIHR academic clinical lecturers. YH, TS, ME and BM are funded by the NIHR Health Protection Research Unit (HPRU) in Emerging and Zoonotic Infections at University of Liverpool. BM is supported to conduct COVID-19 neuroscience research by the UKRI/ MRC (MR/V03605X/1). BM is also supported for additional neurological inflammation research due to viral infection by grants from the NIHR (award CO-CIN-01), the Medical Research Council (MC_PC_19059) and by the NIHR Health Protection Research Unit (HPRU) in Emerging and Zoonotic Infections at University of Liverpool in partnership with Public Health England (PHE), in collaboration with Liverpool School of Tropical Medicine and the University of Oxford (award 200907), NIHR HPRU in Respiratory Infections at Imperial College London with PHE (award 200927), the MRC/UKRI (MR/V007181/1), MRC (MR/T028750/1), and Wellcome (ISSF201902/3).

EPO-265 | Longitudinal analysis of 92 subjects reveals structural brain alterations after 1 year of COVID-19

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Background and Aims: Although Neuroimaging studies have demonstrated structural alterations (most subacute and chronic changes) in individuals after COVID-19 infection, few studies have assessed brain changes longitudinally. Here, we present a longitudinal analysis of post-infected individuals, comparing individuals after 3 and 12 months and controls.

Methods: we acquired two longitudinal T1-structural 3T-MRI images of 92 post-infected participants (median interval for the first MRI (T1) = 102 days and second MRI (T2) = 388 days; median age = 42 years; 62 women); and an image of 142 controls (median age = 39.5 years; 99 women). We performed a Voxel-Based Morphometry analysis with CAT12 longitudinal tools (http://www.neuro.uni-jena.de/cat/;/SPM12/MATLAB2019b). T-tests were performed (control group [CG], T1-patients and T2-patients) between the different groups (paired t-test T2P–T1P, t-test CG–T1P, t-test CG–T2P). All results were FDR-corrected for multiple comparisons, and we used total intracranial volume, sex and age as covariates (only for independent t-tests).

Results: The CG-T1 analysis showed a trend of atrophy in the left supramarginal atrophy (did not survive FDR correction). The paired comparison (T2P–T1P) revealed atrophy of the right caudate nucleus and hypertrophy of the cerebellum. The CG-T2 comparison exhibited atrophy of the left supramarginal and left postcentral gyri in the post-infected subjects.

Conclusion: Our results suggest persistent left supramarginal gyrus atrophy after one year of infection and signs of progressive right caudate atrophy and cerebellum hypertrophy. Further analysis of larger groups (stratified for severity and symptomology) with longitudinal controls is necessary to confirm persistent and dynamic brain changes over time.

Disclosure: Nothing to disclose.

Neuroimmunology 2

EPO-266 | EEG findings in autoimmune encephalitis-associated epilepsy compared with structural temporal lobe epilepsy

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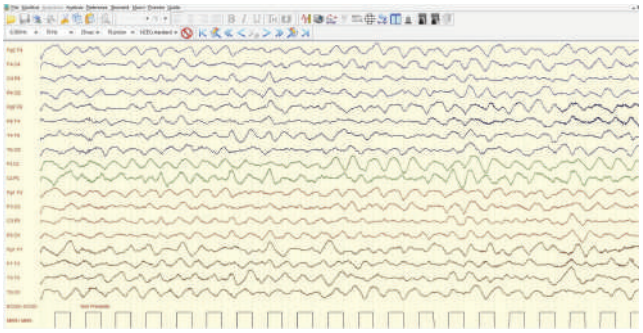
[1]Epilepsy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran; [2]Clinical Neurology, Department of Medicine (DMED), University of Udine, Udine, Italy; [3]Neurology Unit, Department of Head-Neck and Neuroscience, Azienda Sanitaria Universitaria Friuli Centrale (ASU FC), Udine, Italy; [4]Department of Neurology, Jefferson Comprehensive Epilepsy Center, Thomas Jefferson University, Philadelphia, PA, USA; [5]Clinical Pathology, Department of Laboratory Medicine, Azienda Sanitaria Universitaria Friuli Centrale (ASU FC), Udine, Italy; [6]Neurophysiopathology Unit, Department of Head-Neck and Neuroscience, Azienda Sanitaria Universitaria Friuli Centrale (ASU FC), Udine, Italy

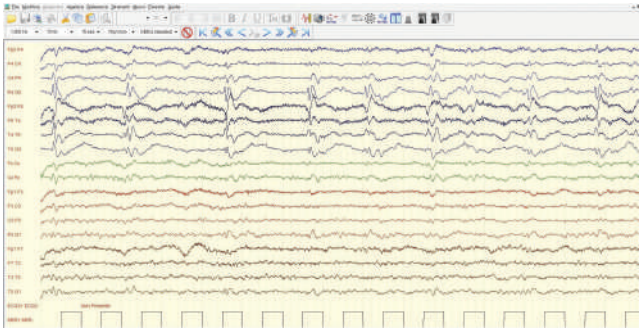
Background and Aims: Autoimmune encephalitis (AE) is a rare yet relevant cause of seizures that requires early treatment to reduce the risk of neurological sequelae and to improve long-term epilepsy outcome. Clinical scores and diagnostic criteria are useful to suspect AE as the aetiology of seizures, but still fail to identify some patients. An extensive description of electroencephalogram (EEG) specificities in AE patients may facilitate an early diagnosis, using an inexpensive and non-invasive test.

Methods: We retrospectively reviewed clinical, neuroradiological, laboratory, and EEG data from 19 patients with AE-associated epilepsy who were treated at Udine University Hospital, Italy. We compared them with a group of 19 consecutive patients with temporal lobe epilepsy (TLE) of structural, non-immune-mediated aetiology. EEG findings were classified according to the American Clinical Neurophysiology Society (ACNS) guidelines.

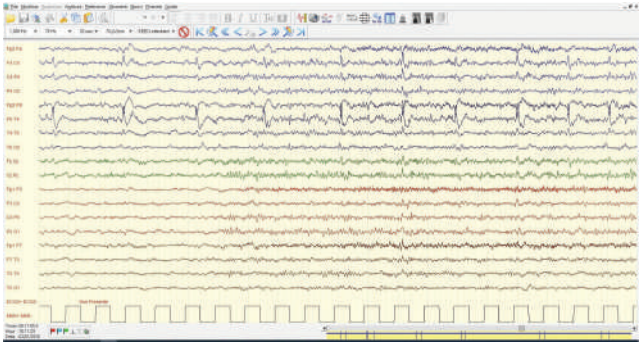
Results: Patients with immune-mediated seizures had a later age at epilepsy onset ($p = 0.024$), likely due to the inclusion of paraneoplastic cases, and had more frequent status epilepticus ($p < 0.001$). Rhythmic and periodic EEG patterns were significantly more frequent in patients with immune-mediated seizures ($p = 0.001$; Figure 1: generalized rhythmic delta activity; Figure 2a and b: lateralized periodic discharges), while the presence of focal polymorphic delta activity was higher in the other group ($p = 0.004$). Seizure outcome was comparable among the two groups: 12/19 seizure-free AE patients and 10/19 TLE patients at their last follow-up ($p = 0.847$).



Generalized rhythmic delta activity in a patient with autoimmune encephalitis-associated epilepsy.



Lateralized periodic discharges in a patient with autoimmune encephalitis-associated epilepsy.



Lateralized periodic discharges in a patient with autoimmune encephalitis-associated epilepsy.

Conclusion: We highlight some EEG features that may help the clinician to suspect AE and might be integrated into future clinical scores and diagnostic criteria to suspect an immune-mediated aetiology for focal seizures.

Disclosure: None.

EPO-267 | Clinicoradiological spectrum of primary CNS vasculitis/primary angitis of CNS (PACNS): A case series

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Background and Aims: PACNS is a rare and devastating inflammatory disorder affecting the CNS. Although headache, cognitive decline and focal neurologic deficits are the clinical hallmarks of PACNS, the disease can have a heterogeneous presentation, leading to diagnostic dilemma. While brain biopsy is confirmatory, it is invasive and patients often opt out of this procedure. In such cases, clinical profiling with imaging (MR studies and DSA) are paramount for prompt diagnosis and treatment. We present 6 atypical cases of probable PACNS, diagnosed clinicoradiologically, to highlight the clinical heterogeneity of the disease and underscore the importance of brain imaging/angiography in establishing earlier diagnosis, when biopsy is not feasible.

Methods: Number of patients: 6 Period: 2022-2023 Symptomatology: Heterogeneous, suspicious of PACNS (illustrated in attached images) Investigations: Infectious and immune profile, Ophthalmoscopy, MRI (Brain/Cord), MR Vessel Wall, DSA, CSF Study

Results: In MRI, all patients had diffuse white matter lesions with enhancing lesions in 2, ring lesions in 1. Parenchymal and sulcal bleeds were present in 5 patients. 3 patients had evidence of myelopathy, and 2 patients patient had optic neuropathy. All patients showed concentric vessel wall enhancement in MRI with classic beading pattern in DSA. Atherosclerosis and secondary immune causes were excluded in all.

Table 1

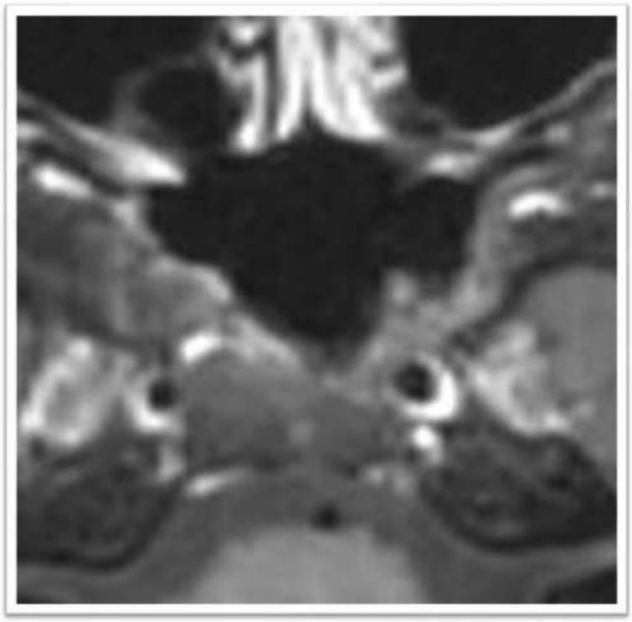
	CASE 1	CASE 2	CASE 3
CLINICAL PRESENTATION	43 year/Male Headache Recurrent Left Facial palsy Spastic paraparesis	47 year/Male Recurrent seizure Cognitive impairment Spastic paraparesis	22 year/Male Headache of 1 year Left sided dimness of vision
CSF	Protein: 66 Glucose 54 Cell: 5, mononuclear	Protein: 46 Glucose 46 Cell: 5, mononuclear	Protein: 146 Glucose 62 Cell: 3, mononuclear
MRI BRAIN/SPINE	Multiple white matter hyper-intensity with GRE blooming in Brain, myelitis	Multiple white matter hyper-intensity, infarct, GRE blooming in Brain, myelitis	Diffuse white matter hyper-intensity with contrast enhancement in Brain, optic neuritis
MR VESSEL WALL	Concentric contrast enhancement	Concentric contrast enhancement	Concentric contrast enhancement
MENINGEAL BIOPSY	Consent not given	Consent not given	Consent not given
SECONDARY IMMUNE TITRES	Negative	Negative	Negative
PREVIOUSLY TREATED AS	Bell's Palsy, Migraine, ADEM, TBM	Epileptic encephalopathy , Seronegative LETM	TTH
TREATMENT GIVEN	Steroid+ Cyclophosphamide	Steroid+ Cyclophosphamide	Steroid+ Cyclophosphamide
CLINICAL STATUS	Improvement	Improvement	Improvement

Clinicoradiological profile of patients (table 1).

Table 2

	CASE 4	CASE 5	CASE 6
PRESENTATION	23 year/Male, Encephalitis, Spastic Paraparesis	34 year/Male, previous hemiparesis, Headache, Optic Neuritis	23/M, hemicranial headache, Right 3rd, LMN 7th, 6th cranial nerve involvement
CSF	Protein: 58 Glucose 43 Cell: 5, mononuclear	Protein: 38 Glucose 56 Cell : 5, mononuclear	Protein : 117 Glucose: 42 Cell: 4, mononuclear
MRI BRAIN/SPINE	Multiple white matter hyper intensity with contrast enhancement, GRE blooming in Brain, myelitis	Multiple white matter lesions, ring enhancing lesions, GRE blooming in Brain	Multiple white matter hyper intensity, GRE Blooming in Brain
MR VESSEL WALL	Concentric contrast enhancement	Concentric contrast enhancement	Concentric contrast enhancement
MENINGEAL BIOPSY	Consent not given	Consent not given	Consent not given
SECONDARY IMMUNE TITRES	Negative	Negative	Negative
PREVIOUSLY TREATED AS	ADEM	Previous hypertensive ICH, with ADEM	Migraine
TREATMENT GIVEN	Steroids plus Cyclophosphamide	Steroids plus cyclophosphamide	Steroids plus Cyclophosphamide
CLINICAL STATUS	Improvement	Improvement	Improvement

Clinicoradiological profile of patients (table 2).



Vessel wall MRI showing contrast enhancement in bilateral internal carotid arteries.

Conclusion: The cases highlight the importance of imaging findings of parenchymal/sulcal microbleeds, underscoring the role of vessel wall MRI and angiographic findings in suspected cases of PACNS as virtual biopsy, where histopathology is missing. Further, isolated myelitis and optic neuropathy can be the first or sole presentation of PACNS, as elucidated.

Disclosure: Nothing to disclose.

EPO-268 | Exploring the role of EBV in MS pathogenesis starting from EBV interactome

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Background and Aims: Epstein-Barr virus (EBV) has been described as one of the main risk factors for developing multiple sclerosis (MS). The molecular mechanisms of this association are complex and may involve different immunological routes; however, the ultimate role of EBV in the pathogenesis of MS is still missing. To identify MS associated genes overlapping with EBV interactome and their expression in immune cell subtypes.

Methods: We obtained EBV interactome from p-HIPSTER, the MS associated genes from NHGRI-EBI and the single cell gene expression from B and T-cells, astrocytes, macrophages, granulocytes, monocytes, microglia, dendritic and natural killer cells from the Human Protein Atlas. We overlapped the lists thus obtained by using the geneOverlap R package.

Results: We identified a "core" group of 15 genes resulting from the overlap between EBV interactome and MS associated genes and expressed in all immune cell type selected ($p < 0.001$). We selected transcriptomic studies from GEO that analyze gene expression at glial cell's level.

Conclusion: The present findings suggest a broad range immune system involvement in mediating EBV effect on MS pathogenesis. We find a statistically significant up regulation compared to healthy controls for MINK1 in glial cells, MEF2C for astrocytes and MAPK3 for microglia.

Disclosure: Nothing to disclose.

EPO-269 | Real-world evidence for ofatumumab in multiple sclerosis: A sicilian multicenter experience

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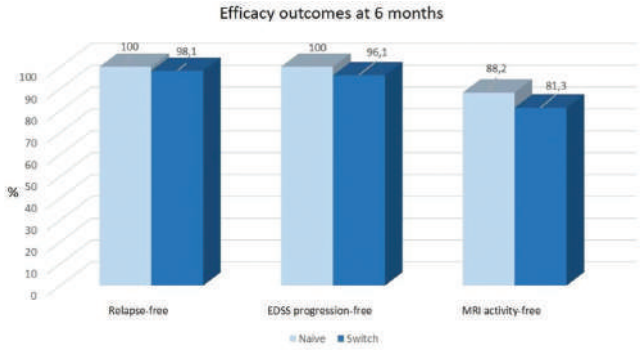
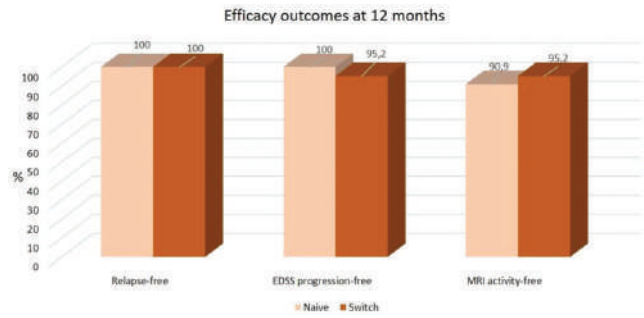
Background and Aims: Ofatumumab (OFA), a human recombinant IgG1 CD20 next-generation monoclonal antibody, was investigated in two phase III trials, showing significant reductions of the relapse-rate and of confirmed disability compared to teriflunomide. However, to date, real world data about the effectiveness of OFA are still scarce. We aimed to evaluate efficacy and safety of OFA in a real-world setting.

Methods: this prospective real-world study consecutively screened all relapsing-remitting Multiple Sclerosis (RRMS) patients from seven Italian MS centers, who were treated with OFA in the period between August 2022 and January 2024. Data about Expanded Disability Status Scale (EDSS), relapses, previous treatments, adverse events (AEs) and magnetic resonance imaging (MRI) were collected.

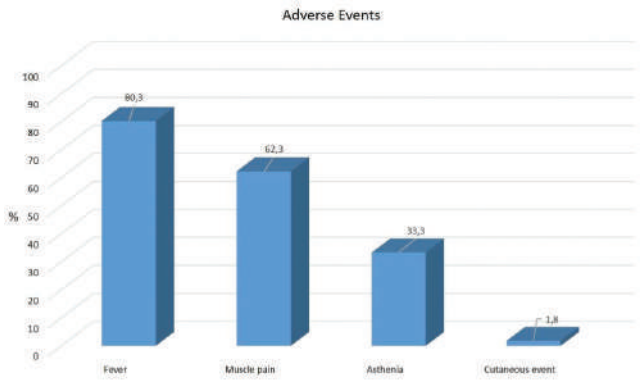
Results: A total of 223 patients (136 [61%] women, mean age of 39.8±10 years), were enrolled. Of these, 68 (30.5%) were naïve to treatment and 155 (69.5%) switched from another DMTs. After 6 months from OFA initiation, 206 (92.4%) of patients were EDSS progression free, 220 (98.7%) were relapse-free and 188 (84.3%) were MRI activity-free. Among 64 (28.7%) who continued treated for 12 months, 62 (96.9%) were EDSS progression free, 64 (100%) were relapse-free and 60 (93.8%) were MRI activity-free. No significant differences were found between naive and switch groups.



Efficacy outcomes after 6 months of treatment with Ofatumumab in naive and switch groups.



Efficacy outcomes after 12 months of treatment with Ofatumumab in naive and switch groups.



Percentage of patients reporting adverse events.

No serious AEs were reported. Particularly, fever at the first administration was the most frequent AE reported in 179 (80.3%) patients.

Conclusion: We confirmed that OFA is effective in reducing risk of progression and disease progression in a real-world cohort of RRMS patients, also demonstrating a favorable safety profile.

Disclosure: Francesco Patti has received honoraria for speaking activities by Almirall, Bayer Schering, Biogen, Merck Serono, Novartis, Roche, Sanofi Genzyme, and TEVA; he also served as advisory board member the following companies: Bayer Schering, Biogen Idec, Merck Serono, Novartis, Roche, Sanofi Genzyme, and TEVA; he was also funded by Pfizer and FISM for epidemiological studies; he received grants for congress participation from Almirall, Bayer Shering, Biogen Idec, Merck Serono, Novartis, Roche, Sanofi Genzyme, and TEVA. Other authors have nothing to disclose.

EPO-270 | Rituximab as first-line or escalation immunotherapy in aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder

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Background and Aims: Aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG+ NMOSD) primarily manifests with attacks of optic neuritis or myelitis. Rituximab is highly efficient in reducing the likelihood of NMOSD attacks. However, not all patients receive rituximab as first-line therapy. Here, we compared the treatment efficacy between rituximab as first-line and escalation immunotherapy.

Methods: We analyzed retrospective clinical data from AQP4-IgG+ NMOSD patients from neuroimmunology outpatient clinics in the United Kingdom (Liverpool) and Germany (Duesseldorf, Hannover, Munich).

Results: AQP4-IgG+ NMOSD patients received rituximab as first-line ($n=58$) or escalation ($n=96$) immunotherapy. Administered as first-line immunotherapy, rituximab was associated with a higher probability of an attack-free disease course (beta [95%-CI]=-0.92 [-1.52;-0.33], $p<0.005$, Cox proportional hazards regression coefficient, H0: beta=0). Younger age at diagnosis and being male was associated with a higher probability of an attack-free disease course. Eleven patients showed a significant annualized expanded disability status scale (EDSS) progression (AEP) during rituximab immunotherapy. Higher annualized attack rates (AAR) during rituximab immunotherapy predicted a significant AEP. In contrast, AAR before rituximab immunotherapy, age at diagnosis and whether rituximab was administered first-line or as escalation immunotherapy showed no effect on AEP. Patients who showed significant AEP during rituximab had competing risk factors for attacks such as severe comorbidities, anti-rituximab antibodies or deviations from their treatment protocol (e. g. due to pregnancy).

Conclusion: Early use of highly effective immunotherapies in AQP4-IgG+ NMOSD such as rituximab can reduce further disease activity and thereby potentially prevent disability progression.

Disclosure: DE received speaker honoraria from Alexion and Horizon. CR is currently a clinical and research training fellow funded by ECTRIMS. JH reports a grant for OCT research from the Friedrich-Baur-Stiftung and Merck, personal fees and nonfinancial support from Merck, Alexion, Novartis, Roche, Celgene, Biogen, Bayer and Horizon and nonfinancial support of the Sumaira-Foundation and Guthy-Jackson Charitable Foundation, all outside the submitted work. AB receives funding from the Innovationsausschuss of the German Federal Joint Committee (G-BA; grant 01VSF23040) and from the German Federal Ministry of Education and Research (BMBF; grant 01ZZ2102B). He has received consulting and/or speaker fees from Alexion, Argenx, Biogen, Horizon, Merck, Novartis, Roche and Sandoz/Hexal, and his institution has received compensation for clinical trials from Alexion, Biogen, Merck, Novartis, Roche, and Sanofi Genzyme; all outside the present work. MWH received research support from Myelitis e. V., speaker honoraria from selpers og, Horizon and Alexion, and reimbursement of travel expenses and compensation for serving on an advisory board from Alexion. TK has received speaker honoraria and/or personal fees for advisory boards from Novartis Pharma, Roche Pharma, Alexion/AstraZeneca and Biogen. All other authors have nothing to disclose in relation to this project.

EPO-271 | Cerebral thrombi analysis in cancer-related stroke

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Background and Aims: Stroke is a frequent complication in neoplastic patients. Lung, gastrointestinal, gynecologic tumors have a higher incidence of cerebral thrombosis. The mechanism undergoing the stroke presentation in active cancer patients is unclear; primary and secondary prevention therapy need further studies.

Methods: We analyzed 20 patients with a diagnosis of active cancer (AC) with large vessel occlusion stroke treated with mechanical endovascular thrombectomy (EMT). Active cancer was defined as a tumor diagnosis <6 months and/or undergoing an active treatment over the past 6 months and/or metastatic cancers. 7 patients had lung tumor, 5 gynecologic neoplasm (breast and ovary), 6 gastrointestinal (pancreatic, gastric, colorectal) and 2 urinary tract cancer. We evaluated the histological composition of AC thrombi compared to 20 matched controls (for sex, age and pre-stroke therapy) with an history of inactive tumor.

Results: The median baseline NIHSS was higher (21) in lung tumor patients (p 0.03). D-dimer values had a higher trend in gastrointestinal tumors, with a major risk of coagulopathy (p 0.04). AC thrombi displayed lower neutrophil (MPO+) counts (p 0.03) and higher platelets (CD61+) counts (p 0.04) compared to controls. No differences were found in term of neutrophil extracellular traps (CITH3+). A statistically significant correlation between acute blood fibrinogen value and the platelets thrombus content (p value 0.01).

Conclusion: Thrombus composition and blood biomarkers could be important tools to understand pathophysiological mechanism and possible secondary prevention therapy in cancer related stroke patients.

Disclosure: Nothing to disclose.

EPO-272 | Comparison of serum NFL values in multiple sclerosis using SIMOA and lumipulse platforms: A real-world study in Greece

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Background and Aims: Serum neurofilament light chain (sNfL) as a biomarker of neuronal axonal loss has an emerging value in monitoring disease activity and progression in Multiple Sclerosis (MS). SIMOA™ and Lumipulse™ are two platforms for sNfL measurement. Our aim was to compare sNfL measurements by both methodologies in MS patients investigating for discrepancies in the comparative results.

To compare serum neurofilament light chain (sNFL) measurements by SIMOA and Lumipulse in Multiple Sclerosis (MS) patients.

Methods: sNfL concentrations from 44 patients (57 samples) with Relapsing Remitting (RRMS) and Progressive MS (PMS) from an MS center were measured by SIMOA and Lumipulse. Results were stratified by z-scores in 4 groups: a) low, z-score≤0.84, b) medium, 0.84 < z-score≤1.5, c) high, 1.5 < z-score≤ 2, d) very high, z-score >2.

Results: 33 RRMS and 11 PMS (5 Secondary Progressive, 6 Primary Progressive) were included; median age 36.97 and 47.42 years respectively. In the RRMS-group (46 samples), 31 had sNfL z-scores in agreement between both methods (67.39% agreement): 16 with low, 5 with medium, 4 with high, 6 with very high z-scores. In 15/46 RRMS samples there was disagreement between SIMOA and Lumipulse z-scores; in 10 samples, differences were by one step (low-vs-medium, medium-vs-high, high-vs-very high), in 5 differences were by two steps. In the PMS-group, sNfL-z-scores in 8/11 (72.73%) samples

were in agreement between platforms, whereas in 3 samples there was disagreement by one step.

sNfL z-scores from 33 Relapsing Remitting (RRMS) and 11 Progressive MS (PMS) patients showed a percentage of agreement between both methods 67.39% for the RRMS-group and 72.73% for the PMS-group.

Conclusion: SIMOA- and Lumipulse-measured sNfL z-scores were similar in the ~70% of MS patients (in both PMS and RRMS groups). Our next goal is to elaborate on the sera with different z-scores between methods to compare their clinical value.

SIMOA- and Lumipulse-measured sNfL z-scores were similar in the ~70% of MS patients (in both PMS and RRMS groups).

Disclosure: ST has shares in the company Tzartos NeuroDiagnostics. DT, CS, JK, EMD, AA, GP, SG, GT, JT: Nothing to disclose.

EPO-273 | Autoimmune screening panel in patients with multiple sclerosis – A Vienna MS database study

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Background and Aims: Autoimmune screening panel (ASP) is routinely ordered as a part of diagnostic work-up in people with suspected multiple sclerosis (MS). However, data on prevalence and significance of ASP seropositivity in MS is scarce.

Methods: We retrospectively investigated patients from the Vienna MS database (VMSD) who were diagnosed with MS between 2014 and 2023 according to current McDonald criteria and had blood samples drawn for ASP. Autoantibody titers were defined as either negative, or mildly (≤1:160), moderately (1:320-1:640) and strongly (≥1:1280) positive.

Results: We analyzed 212 patients (median age 29 [IQR 25–36] years, 67.0% female). Ten (4.7%) patients had red flags for presence of systemic autoimmune disease (joint pain [$n=4$], dermatitis [$n=3$], sicca syndrome [$n=2$], bronchial asthma/rheumatic fever in childhood [each $n=1$]). Complement levels (C3c and C4) were below the lower reference level in 26/134 (19.4%) and 3/134 (2.2%), respectively, and C4 levels were above the upper reference level in 3/134 (2.2%). Antinuclear antibodies (ANA) were positive in 24/210 (11.4%) with 18 (8.6%), 5 (2.4%), and 1 (0.5%) having mildly, moderately, and strongly positive ANA titers, respectively. Positive autoantibodies were found as follows: anti-Ro (5/211; 2.4%), IgM against cardiolipin (4/205; 2.0%), anti-centromere B (2/211; 0.9%), anti-dsDNA (1/208; 0.5%) and anti-La (1/211; 0.5%). Further evaluation following positive results led to diagnosis of rheumatoid arthritis ($n=2$) and Sjögren's syndrome ($n=1$). (ASP positive predictive value 9.1%, negative predictive value 97.2%)

Conclusion: Rate of ASP seropositivity in MS is low, aligning with the general population. Performance of ASP without clinical suspicion of systemic autoimmune disease appears unwarranted.

Disclosure: Nothing to disclose.

EPO-274 | Retinal neuroaxonal loss and disease progression in multiple sclerosis

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Background and Aims: Progression Independent of Relapse Activity (PIRA) is the main driver of disability in multiple sclerosis (MS). Retinal neuroaxonal loss measured by optical coherence tomography (OCT) is associated with cortical thinning and neurodegeneration. We aimed to evaluate the association between OCT markers and PIRA in patients with MS.

Methods: We included patients from the Swiss MS Cohort Study with ≥1 OCT. Peripapillary retinal nerve fiber layer (pRNFL) thickness, ganglion cell inner plexiform layer (GCIPL)-, and inner nuclear layer (INL) volumes were assessed. Eyes with prior optic neuritis were excluded. Neurological examination was performed every 6-12 months including the Expanded Disability Status Scale. PIRA events were defined as previously described (Table 1). Annualized PIRA rate was the number of PIRA events divided by years of follow-up, during a period of ≥4 years before the OCT (Table 1). We examined the association of OCT markers with annualized PIRA rate in linear regression models adjusted for disease duration, age at disease onset, sex, body mass index, and treatment.

Results: Baseline characteristics at time of OCT are shown in Table 2. The adjusted models estimated that mean pRNFL thickness and GCIPL volume decrease by 28.4 μm respectively 0.53 mm3 with each additional PIRA event per year (Table 3). No association was found for INL.

Table 1: Definitions of PIRA events and annualized PIRA rate

PIRA events	
If baseline EDSS Score:	**EDSS worsening***
0 →	≥ 1.5 points
1.0-5.5 →	≥ 1 point(s)
>5.5→	≥ 0.5 point (s)

*confirmed after 6 months, without relapse in between

Annualized PIRA rate (per patient)

$$\frac{\text{number of PIRA events}}{\text{f—up time in years}}$$

*before OCT, during a period of at least 4 years

EDSS: Expanded Disability Status Scale, f-up: follow-up, OCT: Optical Coherence Tomography, PIRA: Progression Independent of Relapse Activity

Table 2: Baseline clinical characteristics at time of OCT

Parameter	n = 172
Age, years: median [IQR]	51.0 [42.2, 59.7]
Sex, female	64 %
Disease duration, years: median [IQR]	15.9 [10.5, 23.1]
EDSS: median [IQR]	2.5 [1.5, 4.0]
RRMS	87.2 %
Patients on DMT	84.9 %
Patients with PIRA events before OCT	36.6 %

DMT: Disease Modifying Treatment, EDSS: Expanded Disability Status Scale, IQR= interquartile range, OCT: Optical Coherence Tomography, PIRA: Progression Independent of Relapse Activity, RRMS: Relapsing-Remitting Multiple Sclerosis

Table 3: Associations of OCT markers with annualized PIRA rate in unadjusted (upper table) and adjusted models (lower part)

OCT marker	β	95% CI	R^2	p-value
pRNFL, mcm	-20.65	-41.55, 0.24	0.016	0.0527
GCIPL, mm^3	-0.50	-0.87, -0.13	0.036	**0.0079**
INL, mm^3	-0.02	-0.14, 0.10	-0.005	0.6971
Unadjusted models, each with one OCT-marker				
OCT marker	**β**	**95% CI**	**R^2**	**p-value**
pRNFL, mcm	-28.40	-48.90, -7.89	0.197	**0.0069**
GCIPL, mm^3	-0.53	-0.90, -0.17	0.183	**0.0045**
INL, mm^3	-0.01	-0.13, 0.11	0.04	0.8252
Models adjusted for disease duration, age at disease onset, sex, body mass index and treatment *				

β: estimate (beta), CI: confidence interval, GCIPL: ganglion cell inner plexiform layer; INL: inner nuclear layer; OCT: Optical Coherence Tomography; PIRA: Progression Independent of Relapse Activity; pRNFL: Peripapillary retinal nerve fiber layer. *Note that the covariate "treatment" had four categories: untreated, platform, oral, and monoclonal antibodies

Conclusion: Our findings show an association between rate of PIRA and retinal neuroaxonal integrity. pRNFL and GCIPL may represent a sensitive measure of disease progression in MS.

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EPO-275 | Safety of inebilizumab in participants over 50 and 65 years of age with neuromyelitis optica spectrum disorder (NMOSD)

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Background and Aims: Inebilizumab is approved for aquaporin-4 seropositive (AQP4-IgG+) NMOSD. Here we evaluate the safety of inebilizumab in AQP4-IgG+ NMOSD participants ≥50 and ≥65 years of age.

Methods: N-Momentum (NCT02200770) was a phase 2/3 trial (randomized 3:1, inebilizumab 300 mg: placebo) with an open-label-extension-period (OLP) ≥2 years. Post hoc analyses were conducted to analyze outcomes in AQP4-IgG+ participants <50, ≥50, and ≥65 years of age.

Results: Of 213 AQP4-IgG+ NMOSD participants, 65 (30.5%) were ≥50 years, 10 (4.9%) were ≥65 years. In the RCP, among inebilizumab participants ≥50 years, 31.3% (15/48) reported ≥1 investigational product related treatment emergent AE (IP-TEAE) versus 35.3% (6/17) in placebo. Among participants <50 years IP-TEAEs were 22.1%(25/113) in the inebilizumab group and 20.0% (7/35) in the placebo group. For patients ≥65 years in the RCP, 66.7% (4/6) inebilizumab and 25% (1/4) placebo patients had IP-TEAEs. Infections were reported in 66.7% (4/6) of inebilizumab and 100% (4/4) of placebo patients ≥65 years. The most frequent AE was urinary tract infection in 50% (3/6) of inebilizumab and 75% (3/4) of placebo participants ≥65 years. No IP-related serious AEs or deaths occurred in the participants ≥50 years in either treatment group of the RCP. The NMOSD related annualized hospitalization rate (95% CI) in the OLP for participants ≥50 years, ≥65 years, and <50 years were 0.16 (0.06 – 0.42, $n=65$), 0.19 (0.04-1.01, $n=10$), and 0.13 (0.08– 0.22, $n=148$) respectively.

Conclusion: This data supports the safety of inebilizumab in AQP4-IgG+ NMOSD participants ≥50 and ≥65 years of age although evaluation of larger populations is needed to confirm these results.

Disclosure: F Paul: Bayer, Biogen Idec, Merck Serono, Novartis, Sanofi Genzyme, Teva, DFG Exc 257, GCNMS, Guthy-Jackson Charitable Foundation, Novartis. Y Mao-Draayer: Acorda, Bayer, Biogen, Bristol Myers Squibb-Celgene, Chugai, EMD Serono, Genentech-Roche, Janssen, TG Therapeutics, Horizon, Novartis, Sanofi-Genzyme, Teva Pharmaceuticals, Chugai, Genentech-Roche, NIAID Autoimmune Center of Excellence, NIH NINDS, Novartis, PCORI, Sanofi-Genzyme. D Wingerchuk: Genentech, Horizon, Novartis, Reistone Biopharma, Bristol Meyer Squib, Imcyse, Merck, Roche, UCB Pharma, Alexion, and UCB Pharma. J Graves: Horizon, TG Therapeutics, and Novartis. A Kunchok: Genentech, Horizon, and EMD Serono. EA Lackey: EMD Serono, Sanofi, and Doximity. K Fujihara: AbbVie, Alexion, Asahi Kasei Kuraray Medical Co., Biogen, Chugai/Roche, Eisai, Japan Tobacco, MedImmune/Viela Bio, Merck, Merck Biopharma, Mitsubishi-Tanabe, Novartis, Teijin, Takeda, UCB, and Ministry of HWL of Japan. DK Sato: CNPq, FAPERGS, Teva, Merck, Biogen, Merck, Roche, Horizon, and Alexion. Z Wang, D Cimbora and KR Patterson: Amgen Inc. BAC Cree: Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Hexal/Sandoz, Horizon, Immunic AG, Kyverna, Neuron23, Novartis, Sanofi, Siemens, TG Therapeutics and Genentech.

EPO-276 | Clinical and pathophysiological implications of intrathecal MOG-IgG synthesis for cerebrospinal fluid MOG-IgG detection

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Background and Aims: Diagnosis of MOG antibody-associated disease (MOGAD) relies on the detection of serum MOG-IgG with cell-based assays (CBA). Clinical and diagnostic relevance of CSF MOG-IgG needs further assessment.

Methods: we retrospectively studied consecutive patients with paired serum and CSF samples screened for MOG-IgG using a live CBA. Antigen-specific Antibody Index (AIMOG-IgG) was calculated to assess intrathecal MOG-IgG synthesis (MOG-IgG ITS). An aggregated analysis of literature data on CSF MOG-IgG and findings from another centre were used for comparison with our results.

Results: MOG-IgG were found in 55/960 patients. Serum/CSF MOG-IgG titres showed a significant correlation in patients without ITS (rho = 0.47, $p<0.001$), but not in those with ITS (rho = 0.14, $p=0.65$). There were no clinical-paraclinical differences between MOG-IgG CSF+ vs CSF- patients. Conversely, patients with MOG-IgG ITS showed more frequent pyramidal symptoms (73% vs 32%, $p=0.03$), spinal cord involvement (82% vs 39%, $p=0.02$), and severe outcome at follow up (36% vs 5%, $p=0.02$) than those without MOG-IgG ITS. MOG-IgG ITS was the only predictor of a poor

outcome in the multivariate logistic regression model (OR: 9.87 [CI: 1.22–86.88], $p=0.039$). In cohorts with consecutive patients ($n=3148$), positive predictive value (PPV) was higher for MOG-IgG seropositivity (99.43% [CI: 97.76%–99.86%]), than for CSF-restricted MOG-IgG positivity (83.9% [CI: 72.07% - 91.36%]).

Conclusion: Consistently with physiopathology, our data suggest that the implementation of ITS calculation could enhance clinical, prognostic, and therapeutic purposes of CSF MOG-IgG testing, making a case for its introduction in clinical practice.

Disclosure: Nothing to disclose.

EPO-277 | Evaluating the role of MOG antibodies in pseudotumor cerebri presentations: A clinical perspective

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Background and Aims: Pseudotumor cerebri (PTC), characterized by symptoms and signs of increased intracranial pressure without an occupying lesion, can overlap clinically with Optic Neuritis (ON) and may co-occur in patients. This study examines the relationship between Myelin Oligodendrocyte Glycoprotein (MOG) antibodies, which can be observed in ON, and PTC in patients presenting with symptoms indicative of increased intracranial pressure.

Methods: The study included 42 patients who were evaluated with a preliminary diagnosis of PTC. Anti-MOG antibodies were assessed using flow cytometry and live cell-based assays.

Results: Findings revealed MOG IgG positivity in 9 female patients, with significantly high titers in two patients. Notably, one patient was initially diagnosed with PTC, but was later identified as having ON and was diagnosed with MOGAD. A significant portion of MOG+ patients met the Dandy criteria for 'Definite PTC', whereas MOG positivity was more prevalent in patients classified as 'Probable' or 'Possible PTC' according to the Friedman criteria but did not meet the Dandy criteria. Common symptoms in both MOG positive and negative groups included transient visual loss and headache, with the former significantly associated with positivity.

Conclusion: This study emphasizes including MOG-AD in PTC differential diagnosis, noting the need for thorough evaluation and exploring MOG antibodies' role in Pseudotumor Cerebri etiology.

Disclosure: Nothing to disclosure.

EPO-278 | Real-world experience of efgartigimod treatment for autoimmune encephalitis

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Background and Aims: Efgartigimod, approved in China for AChR Ab+gMG in September 2023, mechanism of action involves binding to FcRn and competitively blocking endogenous IgG binding to FcRn, leading to IgG degradation at lysosomes and subsequent acceleration of IgG clearance in vivo. However, limited evidence in other IgG-mediated disorders like autoimmune encephalitis (AE). This study aims to describe the treatment outcomes of autoimmune encephalitis patients treated with efgartigimod.

Methods: 12 AE patients treated in Neurological Care Unit (NICU) in 2023 were included and categorized into traditional treatment group and add-on efgartigimod treatment group. The latter received efgartigimod at 20mg/kg at weekly intervals. The evaluation relied on electronic medical records, focusing on Modified Rankin Scale (mRS) scores and post-immunotherapy hospitalization duration.

Results: Among the 12 AE patients (median age 23.19 years; 11 with anti-NMDA receptor, 1 with GFAP antibody), baseline treatment averaged 2.16 immunomodulatory therapies (including steroids, IVIG, and plasma exchange). The efgartigimod group demonstrated IgG reduction (average decrease 13.69±5.71 mg/ml) and more mRS score improvement from baseline (mean reduction 21.67% vs 13.33%) compared to the traditional treatment group. Additionally, the efgartigimod group experienced shorter hospital stays (20.83±12.3 days vs. 31.67±8.48 days).

Conclusion: The study is the first to suggest that the addition of efgartigimod to immunosuppression therapy in patients with autoimmune encephalitis may result in a shorter hospital stay and accelerate recovery (evidenced by lower mRS scores). Despite the small sample size, these findings warrant further investigation.

Disclosure: Nothing to disclose.

EPO-279 | Use of rituximab in primary angiitis of the central nervous system: Observational study in a tertiary center

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Background and Aims: There is paucity of data on treatment for primary angiitis of the central nervous system (PACNS), especially regarding rituximab. We aim to characterize the cohort of patients diagnosed with PACNS in our center, evaluating radiological and clinical response, comparing rituximab to other treatments.

Methods: Observational retrospective study of patients diagnosed with PACNS (Birnbaum criteria) in a tertiary hospital. Clinical information was obtained from electronic health records. Patients were grouped according to use of rituximab at any time-point. A favorable outcome was defined as a modified Rankin scale (mRS) score ≤2 at

last follow-up. Clinical and radiological response was defined as absence of relapse during treatment.

Results: 23 patients were included (women 65.2%). All patients received several lines of immunotherapy (21 included cyclophosphamide). Median age at onset was 38 years (IQR: 29.9–60.1), 28.0 in the group treated with rituximab ($n=9$, IQR: 21.7-36.8) and 52.8 in the non-rituximab group ($n=14$, IQR: 37.1-65.9, $p=0.019$). mRS at peak was 4 (IQR: 1-5) in rituximab patients and 3 (IQR: 2-4) in non-rituximab ($p=0.369$). At last follow-up, median mRS for rituximab was 1 (IQR: 1-4) and 2 for non-rituximab (1-4) ($p=0.439$). Throughout the duration of treatment, rituximab patients presented a similar clinical and radiological response to the 21 patients receiving cyclophosphamide (77.7% and 45.5% vs. 71.4% and 57.1% respectively).

Conclusion: In our cohort, rituximab and cyclophosphamide presented similar rates of clinical and radiological response. Recognizing age difference between groups, this study suggests rituximab could be a non-inferior alternative to treat PACNS, especially more severe cases.

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology 2

EPO-280 | Spontaneous speech alterations and evolution in primary progressive aphasia variants

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Background and Aims: To identify: which features of speech, standard language and gray matter (GM) parameters most effectively distinguish primary progressive aphasia (PPA) variants from each other; how speech evolves over time, and the best combination of features predicting speech evolution.

Methods: 95 PPA patients underwent the "Picnic Scene" test and structural MRI. 34 patients underwent a follow-up. Stepwise-regression-models were used to identify speech, standard-language tests and GM parameters that best distinguished groups. In each PPA group, linear-mixed-effect models were performed for defining speech changes over time, and the prediction analysis was conducted using variables from the best stepwise-models.

Results: The best models to differentiate PPA variants included: left temporal and frontal volumes, and syntax production features when comparing nfvPPA vs svPPA ($R^2=0.89$); lexical contents, syntax complexity, left temporal and insular volumes in nfvPPA vs lvPPA ($R^2=0.81$); left temporal volumes and speech production rates in svPPA vs lvPPA ($R^2=0.86$). Over time, nfvPPA patients showed more phonological errors, which were predicted by syntax production features at baseline. SvPPA and lvPPA showed reduced naming and reduced number of words in sentences, respectively, which were predicted by left temporal volumes.

Conclusion: The speech, standard-language and GM variables that we identified as the most affected at baseline and over time by each PPA variant, may be used in the clinical practice for increasing knowledge on disease progression, patients' prognosis and for planning speech language therapy interventions. Funding. ERC (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease. Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

Disclosure: V Castelnovo, L Lumaca, S Santicioli, E Gatti, A Lamanuzzi, E Spinelli, F Caso, G Magnani, P Caroppo, S Prioni, C Villa, SF Cappa have nothing to disclose. E Canu receives research support from Italian Ministry of Health (IHM). S Basaia receives research support from IHM. G Cecchetti received speaker honoraria from Neopharmed Gentili. M Filippi consulting or speaking activities or advisory boards for Alexion, Almirall, Biogen, Bayer, Bristol-Myers Squibb, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM. F Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from IMH, Italian Ministry of University and Research, ARiSLA, ERC, EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease.

EPO-281 | Cognitive deficits in asymptomatic carotid stenosis: A FMRI study

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Background and Aims: Asymptomatic carotid stenosis may cause cognitive loss in patients. In our study, cognitive status and functional connectivity changes and cognitive functions in patients with asymptomatic carotid stenosis (CS group) were evaluated compared to healthy controls.
Methods: Thirty-five individuals (21 male/ 14 female) were enrolled in the study. Nineteen of the participants had carotid stenosis and 16 were healthy controls. CS group and control groups' carotid stenosis evaluations were done and confirmed by radiologists. Participants' brain morphology alterations were evaluated with non-contrast brain MRI, using Schelten's score. Montreal Cognitive Assessment test (MOCA) and Mini Mental State Examination (MMSE) test were used to evaluate cognitive state. Structural and resting-state fMRI scans were conducted with specific parameters.
Results: The two groups had similar demographic characteristics in terms of age ($p=0.051$), education level ($p=0.786$) and gender ($p=0.557$). In addition, there was no difference between the Schelten scores of the carotid stenosis group and the control group ($p=0.362$). Finally, our analysis revealed that there was a significantly lower MOCA scores in carotid stenosis group compared to control group ($p=0.030$). Our whole-group partial correlation analysis showed a significant correlation between rostral prefrontal cortex prominence. Our findings showed that the CS group exhibited significantly lower MOCA scores and showed a significant correlation with salience networks compared to the control group, suggesting that carotid stenosis leads to consequential cognitive decline.

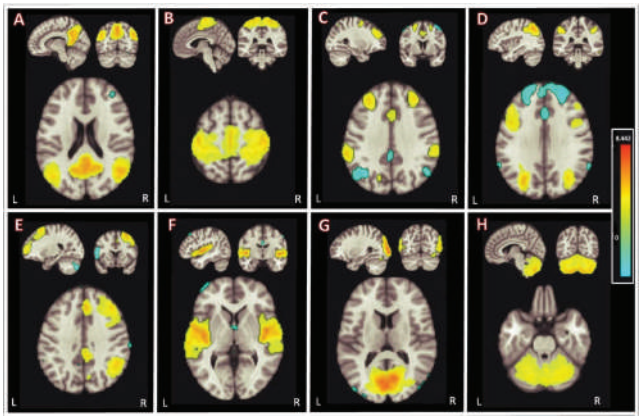

FIGURE 1 Resting-state networks identified via independent component analysis (ICA) A) DMN, B) Sensorimotor, C) Salience, D) Dorsal attention, E) Frontal-parietal, F) Language, G) Visual, H) Cerebellar.

Conclusion: Our study revealed that individuals with asymptomatic carotid artery stenosis had significantly worse cognitive functions which correlated with frontoparietal, and sensorimotor networks.
Disclosure: Nothing to disclose.

EPO-282 | Investigation of functional brain dynamics in Alzheimer's disease with short-term TMS stimulation on the DLPFC and EEG

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Background and Aims: Transcranial magnetic stimulation (TMS) and electroencephalography (EEG) are combined and used to investigate the brain network dynamics of neuropsychiatric diseases. Objectives: Our study aims to investigate the changes caused by short-term repetitive TMS stimulation applied to the left DLPFC region in Alzheimer's Disease (AD) on the brain's resting-state electrophysiological activity (Resting-State EEG).
Methods: 26 early/mid-stage AD patients, including active ($n=13$) and sham ($n=13$), were included in the study. 150 pulses of 20 Hz rTMS (two stimulations consisting of 75 pulses; pulse duration = 3.5 sec; time between pulses = 45 sec) were applied to the left DLPFC. Resting-state EEG was recorded at baseline and immediately after TMS to assess the effects of TMS on the functional brain network.
Results: There was no statistically significant difference between the active and sham groups in demographic, clinical, and cognitive characteristics. In the active group, a significant increase in beta activity was observed in the occipital regions after TMS application ($p<0.05$).
Conclusion: Increased beta activity may indicate the neuroplastic effects of TMS stimulation of DLPFC in AD. Monitoring the changes caused by short-term stimulation in resting EEG may play an important role in understanding the nature of brain network dynamics resulting from TMS stimulation in AD and in planning individualized treatments in the future.
Disclosure: This study was supported by TÜBİTAK.

EPO-283 | Vocabulary knowledge as a reliable proxy of cognitive reserve in multiple sclerosis: A validation study

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Background and Aims: Cognitive reserve (CR) operationalization is often limited to the educational/occupational attainment, but the lifetime intellectual enrichment represents a crucial source of CR, estimated by objective measures such as Vocabulary knowledge (VOC) test [2]. Thus, this study aimed to explore the suitability of the VOC as an accurate and reliable proxy of CR by evaluating its psychometric properties and discrimination accuracy compared to other CR measures in Multiple Sclerosis (MS).

Methods: Sixty-eight consecutive people with MS (pwMS) completed a clinical evaluation and a neuropsychological assessment including: VOC, Brief Repeatable Battery of Neuropsychological Tests, Cognitive Reserve Index questionnaire (CRIq), and questionnaires on neuropsychiatric aspects. Reliability, convergent and divergent validity, and discrimination accuracy of the VOC using educational level as reference standard were assessed. The possible effect of sociodemographic and clinical factors on the VOC and its role in predicting the global cognitive status were also explored.

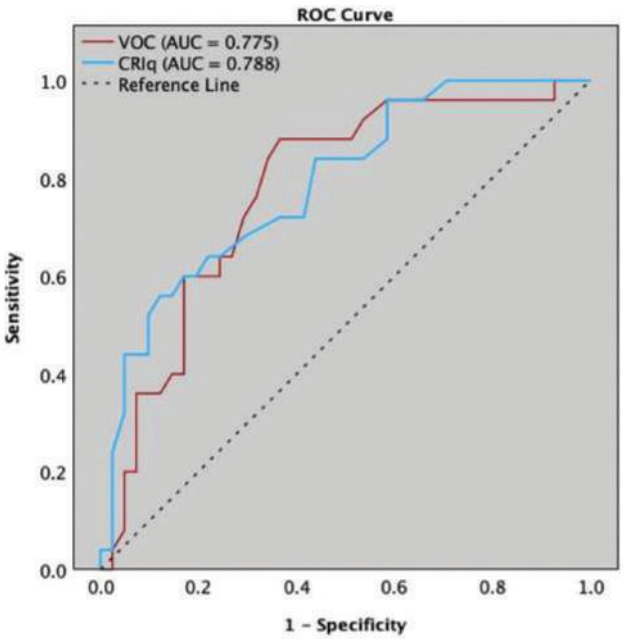

FIGURE 1 ROC of the Vocabulary Knowledge (VOC) and Cognitive Reserve Index questionnaire (CRIq) when discriminating people with Multiple Sclerosis (pwMS) with high and low cognitive reserve measured using educational level as reference standard.

Results: The VOC demonstrated good internal consistency (Cronbach's alpha = 0.894) and an adequate construct validity. It showed a level of discrimination of pwMS with high and low CR comparable to the CRIq score (Figure 1). VOC scores were independent of MS features and predicted, together with MS-related disability, the global cognitive status.

Conclusion: CR should be measured by fixed objective measures independent of brain pathology and clinical features such as the VOC found to be a reliable and valid instrument for CR estimation in pwMS. Early CR estimation may help clinicians in identifying pwMS at higher risk of cognitive decline to plan a strict neuropsychological monitoring and cognitive interventions.

Disclosure: Nothing to disclose.

EPO-284 | Psychophysiological markers of creative thinking: Preliminary findings from an experimental study

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Background and Aims: According to the Neurovisceral Integration Model, brain regions involved in self-regulation are implicated in cardiac autonomic activity through the vagus nerve. Previous literature showed that greater parasympathetic activity at rest predicts better cognitive performances, but its association with creative thinking processes is still under-investigated. Moreover, both cognitive control mechanisms and creative thinking appear to be modulated by specific psychological traits. Thus, the aim of this study is to explore the relationship between Heart Rate Variability (HRV) at rest, specific psychological traits, and creative thinking.

Methods: A preliminary sample of 44 participants (age: 25.24 ± 3.74; education: 16.02 ± 2.04) filled out an online survey investigating psychological dimensions; then underwent an experimental procedure that included a baseline, two creative thinking tasks (figural and verbal) and a recovery condition. An electrocardiogram (ECG) was recorded during the procedure and two HRV indices of parasympathetic activity (i.e., Mean HR and RMSSD) were computed. We performed non-parametric correlations between HRV indices at rest, creative thinking scores and psychological traits.

Results: We found a significant, positive correlation between parasympathetic activity and a verbal creative index (i.e. flexibility) associated with executive functioning. Conversely, we found a significant negative correlation between perfectionistic traits and parasympathetic activity.

Conclusion: Results showed a relation between HRV and cognitive performance during a creative thinking task; the more executive component of verbal creative thinking was associated with vagal activity. Additionally, perfectionistic tendencies were associated with a vagal withdrawal at rest, suggesting a possible greater effort expenditure in cognitive control mechanisms in those individuals.

Disclosure: The present work has not been financed, in whole or in part, by any company with economic interests in the products, equipment or similar mentioned in it.

EPO-285 | Vertigoheel promotes rodent cognitive performance in multiple memory tests

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Background and Aims: Cognitive deficits associated with old age or various pathological conditions influence up to 3% of the general population. Repurposing drugs that had been safely used for other indications may be a promising approach to reverse or slow down cognitive impairment. Vertigoheel (VH-04) is a multicomponent medication made of Ambra grisea, Anamirta cocculus L., Conium maculatum and Petroleum rectificatum that has been successfully and safely used for several decades in the treatment of vertigo. Here, we explored its potential as a cognitive enhancer.
Methods: We have examined the effects of single and repeated administrations of VH-04 on the performance of mice and rats in several standard behavioral tests assessing different types of memory.
Results: We found that VH-04 positively influenced visual recognition memory in the novel object recognition test and alleviated impairments in spatial working memory and olfactory memory caused by the muscarinic antagonist scopolamine in the spontaneous alternation and social transmission of food preference tests. In addition, VH-04 improved retention of the spatial orientation memory of old rats in the Morris water maze. In contrast, VH-04 did not significantly modify scopolamine-induced impairments in tests of fear-aggravated memory or rewarded alternation. Experiments in vitro showed that incubation with VH-04 stimulated neurite growth of mouse primary hippocampal neurons and possibly reversed the decrease in synaptophysin mRNA expression in the hippocampus of aged rats, which implies that VH-04 may preserve synaptic integrity in the aging brain.
Conclusion: Our findings allow a cautious conclusion that VH-04 may improve cognitive performance in individuals with memory deficits.
Disclosure: This study received funding from Heel GmbH, an international pharmaceutical company that specializes in developing and manufacturing medicines made from natural ingredients. Charles River Discovery Services Finland Oy and Neurofit are contract research organizations. At the time of the study, KW, KO, YB, and BS were employed by Heel GmbH. TH, KL, KP, JP, and RP were employed by Charles River Discovery Services Finland Oy. EA, BH, and SW were employed by Neurofit. CS, AW, BE, and CA were employed by the Ulm University.

EPO-286 | Vocabulary knowledge as predictor of cognitive decline in multiple sclerosis: A long-term follow-up study

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Background and Aims: Few studies longitudinally evaluated the effect of Cognitive Reserve (CR) on cognition in people with Multiple Sclerosis (pwMS) [1,2] reporting mixed results. This study assessed changes in CR - evaluated with an objective measure of lifetime enrichment, the Vocabulary subtest (VOC) of WAIS - and cognition after more than 6 years.
Methods: Eighty pwMS (35% males) were evaluated at baseline and after a follow-up of 6.39 (1.84) years. A global cognition score (COG) was computed by meaning all scores of BRB-N and Stroop test. Repeated measures and mixed-design ANOVAs, regression and receiver operating characteristics (ROC) analyses evaluated: 1) changes in VOC over time, 2) demographic/clinical predictors of changes of VOC and COG over time, 3) accuracy of VOC compared to baseline COG in predicting cognitive decline.
Results: We found that higher VOC scores at follow-up evaluation and this change was independent of demographic/clinical aspects. VOC was the only predictor of COG changes. pwMS with high CR reported higher COG scores at both baseline and follow-up; moreover, COG scores improved at follow-up only in pwMS with high CR. ROC analysis (with presence of cognitive decline as gold standard) indicated that VOC predicted future cognitive decline, better than educational level and slightly lower than baseline COG.

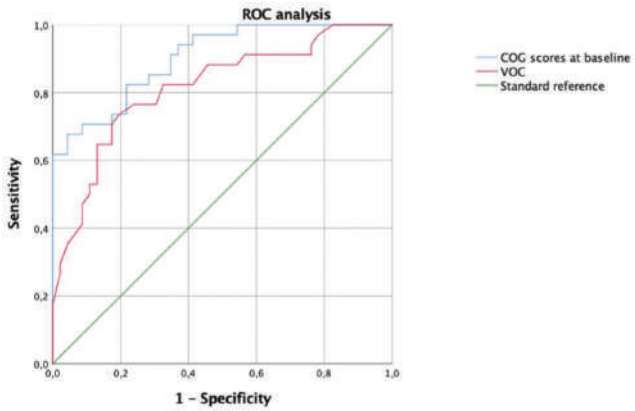

FIGURE 1 ROC analysis of Vocabulary Knowledge and overall cognition score at baseline evaluation as predictors of cognitive decline at follow up evaluation.

Conclusion: The results revealed that CR can be increased over time independently from the effect of disease, and that the measurement

of CR can be useful after MS diagnosis to identify people at risk of future cognitive decline.

Disclosure: Antonio Gallo reports a relationship with Biogen, Merck Serono, Mylan, Novartis, Roche, Teva, Sanofi Genzyme that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement. Alvino Bisecco reports a relationship with Biogen, Merck&Co Inc, Celgene Corp, Sanofi Genzy that includes: consulting or advisory and speaking and lecture fees. Rosaria Sacco received compensation for consulting fees and speaking activities from Biogen Idec, Merck, Novartis, Sanofi, and Roche.

EPO-287 | Advancing neurological assessment: The importance of social cognition screening

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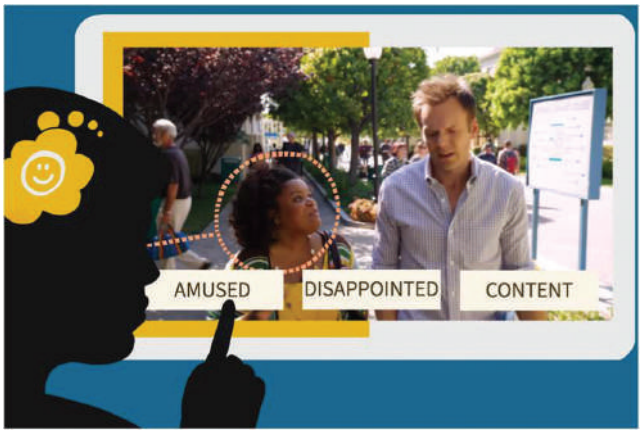
Swiss Epilepsy Centre, Zurich, Switzerland

Background and Aims: Social cognition, the capacity to recognize, understand, and predict emotional and mental states in oneself and others, has gained prominence in the last decade. Acknowledging its impact, the DSM-V includes social cognition as a core neurocognitive domain. However, there is a shortage of screening tools for assessing social cognition in neurological disorders. To bridge this gap, we created the Cognition of Social Interaction in Movies (COSIMO) screening tool – a brief, video-based, ecologically valid, freely accessible, browser-based test providing immediate results (https://cosimo-project.com).



Example of a COSIMO item.

Methods: 1) To explore potential applications in neurology, we conducted a systematic second-order literature review to identify and characterise the nature and extent of social cognitive dysfunction in different neurological conditions. 2) Preliminary data analyses examined COSIMO test scores in healthy controls ($N=900$) and in neurological populations with epilepsy ($N=50$) and multiple sclerosis ($N=100$).

Results: Our systematic second-order review reveals the presence of significant social cognitive deficits in several neurological disorders. Analyses of COSIMO showed satisfactory psychometric properties, with particularly high sensitivity in detecting deficits in patients with temporal lobe epilepsy ($N=25$, $g=1.02$, $p=0.006$).

Conclusion: Neurological disorders can be associated with social cognitive dysfunction, highlighting the urgent need for concise and reliable screening tools for clinical use. COSIMO shows promising potential for the efficient identification of such deficits. We are actively collecting normative data and validating COSIMO across a range of neurological and psychiatric conditions.

Disclosure: Nothing to disclose.

EPO-288 | Longitudinal assessment of cognitive function in non-relapsing MOG-IgG associated disease: A case series

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Background and Aims: MOGAD is an inflammatory antibody-mediated disease, affecting both white and grey matter of CNS. It is more frequent in children and young adults. The clinical course can be either monophasic or relapsing, often with complete recovery. To date, only few studies explored cognitive function in patients with MOGAD. Patients with relapsing MOGAD have been reported to have impaired reasoning skills and overall response time, compared to healthy controls. To assess longitudinal change in cognitive function in a cohort of six patients with non-relapsing MOGAD.

Methods: we assessed cognitive function with the Rao's Brief Repeatable Battery and the Stroop test after ≥12 months from recovery and after 1-year. Patients who failed ≥2 subtests (Z-scores < -1.5 SD) were defined cognitively impaired (CI). Results were adjusted for age, sex, and education.

Results: as disease onset, 3 had ADEM, 1 had cortical encephalitis, and 2 had optic neuritis. Complete clinical recovery occurred for all patients. Only one received Rituximab due to severity of initial attack. Basal cognitive evaluation revealed a mild multidomain impairment only in the two pediatric-onset patients of the cohort, without worsening over 1-year. Annualized brain atrophy rate was normal for all patients.

Conclusion: differently from patients with relapsing MOGAD, we found no CI subjects within our cohort of non-relapsing adult patients, while the two with pediatric-onset showed a mild cognitive impairment. Interestingly, no patients had worsening in cognitive function and brain atrophy rate over 1-year follow-up. These data suggest that the relapsing course and pediatric onset could be risk factors for cognitive impairment in MOGAD.

Disclosure: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this work.

EPO-289 | Spontaneous intracranial hypotension presenting as frontotemporal dementia: Two case reports and literature review

M. Del Chicca[1]; D. Viola[1]; E. Bergamin[1]; L. Tommasini[1]; L. Giampietri[1]; E. Del Prete[2]; V. Nicoletti[2]; G. Tognoni[2]; R. Ceravolo[1]; G. Siciliano[1]; F. Baldacci[1]

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Background and Aims: Spontaneous intracranial hypotension (SIH) can present with cognitive and behavioral changes resembling behavioral variant-frontotemporal dementia (bvFTD). This study reports two cases of SIH manifesting with behavioral alterations and reviews the existing literature on other reported cases.

Methods: Two male patients experienced subacute orthostatic headache, behavioral changes (disinhibition, apathy) and impaired executive and attentional functions on neuropsychological tests. Brain Magnetic Resonance Imaging (MRI) revealed brain sagging and dural contrast enhancement, leading to an SIH diagnosis. Despite unsuccessful blood patching in one case, subsequent exploration identified a cerebrospinal fluid (CSF)-venous fistula and embolization resolved SIH, improving cognition. In addition the study compares clinical and radiological features, as well as treatment options, of these cases, with existing literature to consolidate our understanding of clinical features, diagnosis and management of this condition.

Results: Radiological and clinical data, in our cases, support a diagnosis of Brain Sagging Dementia (BSD). Literature review identified well-documented cases of BSD, highlighting its rarity and potential reversibility with identified SIH causes and proper treatment.

Conclusion: SIH presenting as bvFTD may result from frontotemporal cortex stretching and/or from venous stagnation at the confluence of the straight sinus and Galenic vein. Given its treatable nature, when symptoms typical of bvFTD coexist with brain sagging without clear cerebral atrophy on MRI, it is crucial to consider BSD. Further investigations are recommended to identify CSF hypotension causes and implement appropriate treatments. Considering the potential reversibility of BSD, such interventions frequently result in the improvement of cognitive disorders.

Disclosure: Nothing to disclose.

EPO-290 | Exploring cognitive function in subarachnoid hemorrhage patients: A mini-mental state examination analysis

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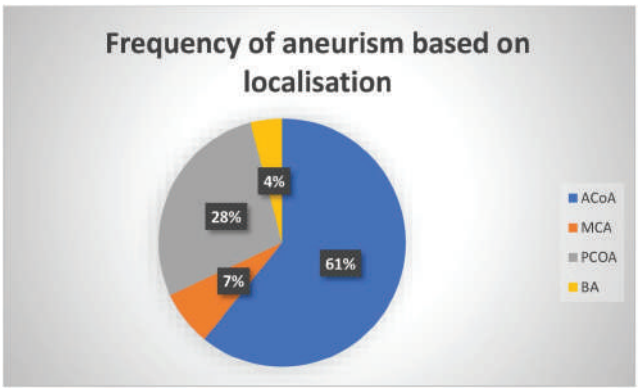
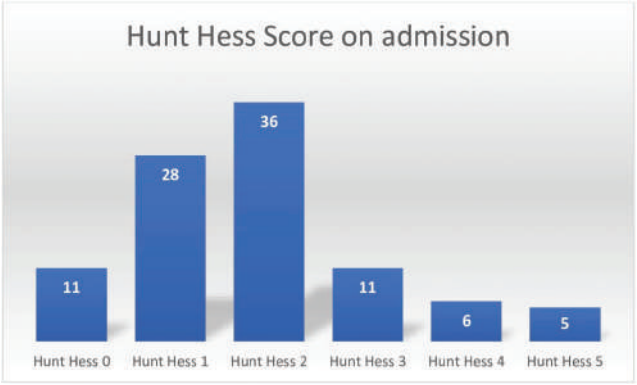
Background and Aims: This study examines the cognitive status of individuals recovering from subarachnoid hemorrhage (SAH) using the Mini-Mental State Examination (MMSE). The findings elucidate the extent of cognitive impairment post-SAH and highlight specific areas of vulnerability

Methods: A prospective study utilizing Mini-Mental State Examination (MMSE) to assess cognitive function in 97 patients diagnosed with subarachnoid hemorrhage (SAH) patients from June 2022-December 2023 in American Hospital in Tirana, Albania. Standardized MMSE protocols applied at discharge and 6 months follow up, with data analyzed for correlations with SAH severity and outcome.

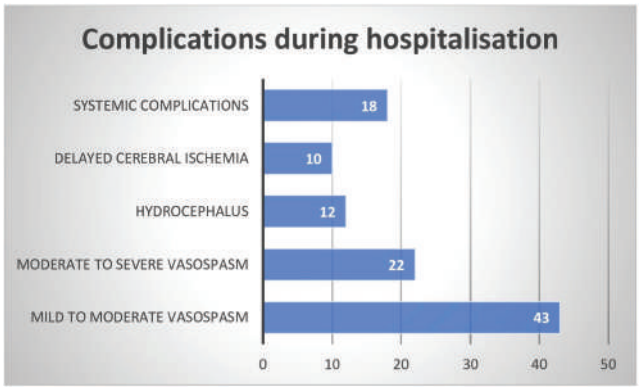
Results: 97 patients diagnosed with SAH from a ruptured brain aneurism, mean age 39.27 (SD17.21), with a female predominance (60.82% female vs 39.18% male). 59 (60.82%) aneurism ACoA, 7 (7.22) aneurism MCA, 27 (27.85) aneurism ACoP, 4 (4.12%) aneurism BA. In patients admitted with Hunt-Hess scores of 0-2, MMSE yielded 3-4 points higher compared to those with Hunt-Hess scores of 3-5.($p < 0.05$). Statistical analysis revealed no significant changes in MMSE scores upon reevaluation after 6 months ($p > 0.01$).



Frequency of aneurism based on localisation.



Hunt Hess score on admission.



Complications during hospitalisation.

Conclusion: MMSE in SAH patients provides valuable insights into cognitive function. While initial scores may correlate with Hunt-Hess severity, long-term stability suggests the need for continuous monitoring and tailored interventions for optimal cognitive outcomes. Study limitations: MMSE may not fully capture subtle cognitive changes, emphasizing the importance of supplementary assessments for a comprehensive understanding of cognitive function in this population

Disclosure: Nothing to disclose.

EPO-291 | Executive functioning training to reduce cognitive intra-individual variability in HIV adults: A case comparison study

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Background and Aims: As people with HIV (PWH) age, they experience increased risk of developing cognitive impairments. To mitigate these challenges, healthcare professionals must create intervention strategies. An emerging concept in the realm of cognitive vulnerabilities is cognitive intra-individual variability (IIV). Cognitive IIV pertains to the variations observed in cognitive performance, offering predictive insights beyond conventional mean-based cognitive assessments. In the context of HIV, cognitive IIV has shown associations with the prediction of cognitive decline, cortical atrophy, and mortality. Based on the Executive Dysfunction Hypothesis, improvement in executive functioning could reduce cognitive IIV.

Methods: In our feasibility study, a two-group pre/posttest randomized controlled trial involving 120 PWH, participants are randomized into either the executive functioning training group or a no-contact control group. The training group undergoes 20 hours of computerized exercises aimed at enhancing executive function. To characterize this study, an interim case comparison was performed, focusing on the initial two participants who completed the training and two demographically matched control participants.

Results: Utilizing the Connor's Continuous Performance Test 3rd Edition, a computerized assessment of reaction time and cognitive IIV, the findings indicated significant enhancements in reaction time (i.e., Hit RT) and cognitive variability (i.e., HRT SD, Variability) within the training group when compared to the no-contact control group.

Conclusion: While preliminary, these initial promising findings imply that delving deeper into cognitive IIV could offer insights into enhancing cognition in aging PWH. This provides a new avenue for cognitive interventions, specifically targeting the reduction of cognitive IIV.

Disclosure: Nothing to disclose.

EPO-292 | Accelerated TMS for Alzheimer's disease; bilateral DLPFC stimulation twice daily for 5 days: Randomized controlled trial

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[1]Department of Neurology, İstanbul Medipol Mega University Hospital, Istanbul, Turkey; [2]Department of Neuroscience PhD Program, Institute of Health Sciences, Istanbul Medipol University, Istanbul, Turkey; [3]School of Medicine, Istanbul Medipol University, Istanbul, Turkey; [4]Center for Psychiatric Neuroscience, Feinstein Institute for Medical Research, Manhasset, New York, USA; [5]Department of Neurology, Istanbul Medipol University, Istanbul, Turkey

Background and Aims: Different protocols have been developed to affect mood, anxiety, cognition, memory, executive functions, and behavioral and motor symptoms in Alzheimer's patients. Our aim with this study is to investigate the changes of short-term intensified rTMS on cognitive, behavioral and daily living activities in AD patients.

Methods: 31 early and mid-term AHD were included in the rTMS Group ($n = 19$) and the control group ($n = 12$). Before and after rTMS; Mini Mental State Test and Alzheimer's Disease Assessment Scale, Geriatric Depression Scale, Activities of Daily Living Scale and

neuropsychometric inventory were used. In the rTMS group, 20 Hz rTMS was applied to bilateral DLPFC.

Results: The average age of the rTMS group is 72.36 ± 3.81; the control group is 68.50 ± 7.72. The average education year of the rTMS group is 8.36 ± 5.15. The average education year of the control group is 10.25 ± 4.88. Intra-group and intergroup analyzes of rTMS and control groups are shown in Tables 1&2 and 2 and Table 3.

Table 1: rTMS GROUP ANALYSIS

rTMS Group	Pre-evaluation (Mean ± SD)	Post-evaluation (Mean ± SD)	p Value
MMSE	19,57 ± 5,12	19,84 ± 5,10	0,69
GDS	5,05 ± 3,90	3,73 ± 3,29	0,12
ADAS-COG	22,64 ± 10,72	22,71 ± 12,83	0,96
ADCS-ADL	56,94 ± 14,08	62,89 ± 9,99	0,004*
NPQ	8,73 ± 7,68	4,05 ± 5,63	0,013*
NPQ - Severity	5,36 ± 4,99	2,36 ± 3,51	0,000*

MMSE: Mini-Mental State Examination; GDS: Geriatric Depression Scale; -COG: The Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL: Alzheimer's Disease Cooperative Study–Activities of Daily Living; NIQ: Neuropsychiatric Inventory Questionnaire; ADAS. SD: Standart Deviation (p <0.05)

Table 2: CONTROL GROUP ANALYSIS

Control Group	Pre-evaluation (Mean ± SD)	Post-evaluation (Mean ± SD)	p Value
MMSE	19,00 ± 6,82	19,08 ± 7,15	0,93
GDS	5,00 ± 4,61	4,58 ± 3,62	0,66
ADAS-COG	26,30 ± 10,82	23,64 ± 13,83	0,14
ADCS-ADL	58,00 ± 10,74	56,91 ± 12,03	0,60
NPQ	7,91 ± 7,52	12,66 ± 16,98	0,17
NPQ - Severity	5,41 ± 6,14	8,16 ± 8,99	0,15

MMSE: Mini-Mental State Examination; GDS: Geriatric Depression Scale; -COG: The Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL: Alzheimer's Disease Cooperative Study–Activities of Daily Living; NIQ: Neuropsychiatric Inventory Questionnaire; ADAS. SD: Standart Deviation (p <0.05)

Table 3: *ANOVA (group × time)*

	rTMS Group		Control Group			
	Pre-evaluation (Mean ± SD)	Post-evaluation (Mean ± SD)	Pre-evaluation (Mean ± SD)	Post-evaluation (Mean ± SD)	p Value	f
MMSE	19,57 ± 5,12	19,84 ± 5,10	19,00 ± 6,82	19,08 ± 7,15	0,755	0,099
GDS	5,05 ± 3,90	3,73 ± 3,29	5,00 ± 4,61	4,58 ± 3,62	0,18	1,877
ADAS-COG	22,64 ± 10,72	22,71 ± 12,83	26,30 ± 10,82	23,64 ± 13,83	0,33	0,976
ADCS-ADL	56,94 ± 14,08	62,89 ± 9,99	58,00 ± 10,74	56,91 ± 12,03	0,095	2,97
NPQ	8,73 ± 7,68	4,05 ± 5,63	7,91 ± 7,52	12,66 ± 16,98	0,98	0,000
NPQ - Severity	5,36 ± 4,99	2,36 ± 3,51	5,41 ± 6,14	8,16 ± 8,99	0,88	0,023

MMSE: Mini-Mental State Examination; GDS: Geriatric Depression Scale; -COG: The Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL: Alzheimer's Disease Cooperative Study–Activities of Daily Living; NIQ: Neuropsychiatric Inventory Questionnaire; ADAS. SD: Standart Deviation (p <0.05)

Conclusion: After the rTMS, there were positive changes in the behavioral and daily living activities of individuals with AD. The main goal is to slow or stop the progression of the disease as a result of TMS stimulation. Although magnetic stimulation does not compensate for the loss of cell number resulting from atrophy, it is thought that TMS increases the synaptic connectivity between neurons and thus plays a role in slowing down the progression.

Disclosure: This study was supported by TÜBİTAK.

EPO-293 | Late-onset vs adult-onset multiple sclerosis: Comparison of clinical and cognitive features and sex-related differences

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Background and Aims: The proportion of patients with multiple sclerosis (MS) experiencing disease onset after 45 years (late-onset [LO] MS) is increasing. Although previous studies suggested different clinical features between LOMS and adult-onset (AO) MS patients, a comprehensive evaluation including cognitive profiles and sex influence has not been investigated yet. This study compares clinical and cognitive characteristics between LOMS and AOMS patients and explores sex-related differences.

Methods: Sixty-one LOMS patients (females=31) and 122 sex-matched AOMS patients (females=62) underwent neurological and neuropsychological assessments. Differences in clinical (onset type, disability status, 9-hole Peg Test, Timed 25-Foot Walk [T25FWT]) and neuropsychological features (performance and frequency of impairment of global cognitive function and specific domains, presence and severity of fatigue and depression) were evaluated, also considering sex differences.

Results: Compared to AOMS, LOMS patients exhibited higher motor onset prevalence, worse T25FWT and visual memory performance ($p \leq 0.036$). LOMS males had more frequent motor onset, worse T25FWT, higher prevalence of depression and cognitive impairment compared to AOMS males ($p \leq 0.030$). LOMS females performed worse in visual memory ($p \leq 0.006$) and had lower fatigue compared to AOMS females ($p \leq 0.005$). Compared to AOMS females, males showed worse performance in global cognitive function, attention, and verbal memory with higher prevalence of impairment in the latter ($p \leq 0.011$). Compared to LOMS females, males showed higher prevalence of depression and impairment in attention ($p \leq 0.035$).

Conclusion: LOMS patients exhibited worse clinical and cognitive features compared to AOMS patients, regardless from sex. Male patients showed more severe clinical and cognitive impairment in both AOMS and LOMS.

Disclosure: N Tedone, D Mistri, M Azzimonti have nothing to disclose. P. Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He has received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo

Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPO-294 | The development of a multimodal AI-assisted Thai mini-mental state examination (MMSE-T) framework for Thai population

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[1]Faculty of Medicine, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand; [2]College of Advanced Manufacturing Innovation, King Mongkut's Institute of Technology Ladkrabang, Bangkok, Thailand

Background and aims: With approximately 50 million people affected globally, dementia prevalence is expected to triple by 2050. Early detection, traditionally reliant on manual, paper-based cognitive screening, is shifting towards digitized, artificial intelligence (AI)-assisted methods. This study aims to develop a multimodal AI-assisted neurocognitive assessment framework, using the MMSE-T 2002 as a model, and compare its effectiveness with the traditional version.

Methods: MMSE-T was completed by 233 individuals who visited the medical center of King Mongkut Institute of Technology, Ladkrabang (KMITL). Data were captured via videos and images. AI models for 11 MMSE-T test batteries were developed using 150 dataset. Speech-based and handwritten answers were converted to digital text using Microsoft Azure's speech-to-text (STT) and Google Cloud AI's optical character recognition (OCR), respectively, and scored by the ChatGPT. The deep learning (DL) algorithms-based object detection were trained to detect drawing and action-based answers. The primary outcome of the correlation between the scoring of MMSE-T by traditional paper-based and digital AI-assisted versions was analyzed using the intraclass correlation coefficient (ICC).

Results: Of 83 records analyzed, a high correlation between traditional and digital AI-assisted versions was observed ($r=0.85$; $p<0.001$). Among 11 test batteries, the eye-action test battery has the highest correlation of $r=1$ ($p<0.001$). The AI-assisted version demonstrated sensitivity, specificity, positive (PPV) and negative predictive values (NPV) of 68.7%, 89.6%, 61.1%, and 92.3%, respectively, compared to human grading.

Conclusion: The study indicates a high correlation between traditional paper-based and digital AI-assisted MMSE-T, suggesting the effectiveness of AI integration in cognitive screening for dementia.

Disclosure: Nothing to disclose.

Neurogenetics 2

EPO-295 | REKLAIM, a novel Phase Ib clinical trial of intravenous FBX-101 (AAVrh10.GALC) after UCBT for infantile Krabbe disease

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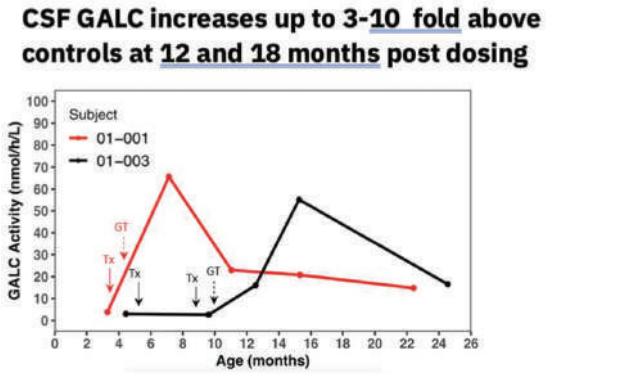
Background and Aims: REKLAIM is a novel intravenous AAVrh10.GALC gene therapy administered after umbilical cord blood transplantation (UCBT) for Krabbe disease. We report on the first 5 subjects treated. Infantile Krabbe is a neurodegenerative disorder due to galactocerebrosidase (GALC) deficiency that results in psychosine toxicity to myelinating cells and death by 2 years. UCBT in pre-symptomatic neonates halts brain disease, but motor function declines due to progressive peripheral neuropathy. We hypothesized that FBX-101 administered during myeloablation for UCBT will override the antibody response to the vector's capsid and transgene and increase GALC.

Methods: REKLAIM is a Phase 1b dose-escalating intravenous gene therapy of FBX-101 given >21 days after UCBT during myeloablation or immune suppression approved by an independent committee. It includes a protocol using Rituximab, Serolimus and Prednisolone adjusted to subject needs.

Results: Five subjects with IKD treated with FBX-101 low dose (1.6 x1013 gc/kg). FBX-101 was well tolerated, with no treatment-related serious adverse events or development of antibodies to the transgene after follow up of 4 to 24 months. In the 2 subjects treated during myeloablation, there were no AAV antibodies, plasma and CSF GALC significantly increased, psychosine dropped below detection and subjects achieved normal gross motor skills. The three subjects treated during immune suppression developed total antibodies to AAV with no humoral or cellular toxicity and improved gross motor skills.



CSF GALC activity post-FBX-101 administration. The red and black lines depict the longitudinal measure of CSF GALC activity in each subject. Normal range ~6 nmol/hr/L (n=1). Arrows indicate time of transplant (Tx) and gene therapy (GT) administration.

CSF GALC

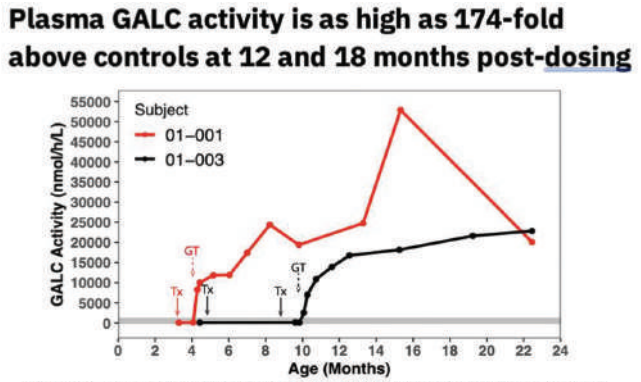


Figure 4. The red and black lines depict the longitudinal measure of plasma GALC activity in each subject. Grey line represents the GALC activity levels in the normal range ~300 nmol/hr/L (n=4). Arrows indicate time of transplant (Tx) and gene therapy (GT) administration.

Plasma GALC activity

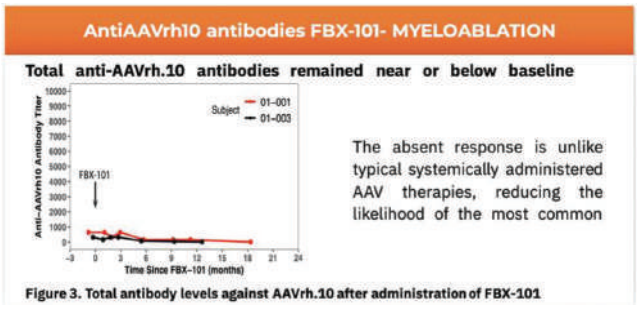


Figure 3. Total antibody levels against AAVrh.10 after administration of FBX-101

Anti AAVrh antibodies

Conclusion: FBX-101 leverages the myeloablation and immune suppression after UCBT, resulting in efficient AAV transduction and increased GALC enzyme supporting brain myelination and gross motor development

Disclosure: M. Escolar is an inventor on the patent application describing FBX-101 (WO2018/136710), licensed by Forge Biologics from the University of Pittsburgh. Dr. Escolar receives salary from Forge Biologics. Adjunct Professor of Pediatrics, University of Pittsburgh.

EPO-296 | Case report: DYNC1H1 mutation as a rare mimic of spinal muscular atrophy (SMA) type 3

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Background and Aims: Our patient developed weakness of the legs at the age of 6y, being slowly progressive over decades. Since childhood, he was diagnosed of suffering from spinal muscular atrophy (SMA) type 3 (never genetically confirmed). At the age of 48y, he was admitted to us. He reported, that his mother, sister and niece have similar symptoms (onset ~5-7 years).

Methods: Neurological examination, ENMG, genetics

Results: Clinically he presented with proximally pronounced pareses of both legs with areflexia. Interestingly, atrophy was distally pronounced. There were no sensory or cognitive deficits. Nerve conduction studies were normal, but EMG detected severe chronic denervation with partial reinnervation. Genetically, there was no deletion of the SMN1 gene. Finally, we found a heterozygous mutation in the DYNC1H1 gene, classified as probably pathogenic (ACMG guidelines). It's a c.1793G>T missense mutation leading to an amino acid exchange p.(Arg598Leu). The same mutation was also found in his niece. This mutation was described first in 2015 (Scoto et al.), who found it in 4 patients (2 families) with symptom onset at birth or in childhood. Since then, there are no further reports about that mutation in the literature, to our knowledge.

Conclusion: The clinical picture of SMA3 is similar to that of DYNC1H1 mutation associated lower extremity predominant SMA. The autosomal-dominant inheritance (versus autosomal-recessive in SMA3) is an important clinical hint. Describing the clinical follow up of patients with such rare mutations is essential, to gather information about their prognosis, avoid false diagnosis/treatment and to collect patients for future therapeutic studies.

Disclosure: Nothing to disclose.

EPO-297 | Frequency of LRRK2 p.L1795F variant in Parkinson's disease patients from Central Europe within the CEGEMOD consortium

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Background and Aims: Pathogenic variants in LRRK2 are one of the most common high-risk genetic factors for Parkinson's disease (PD). Recently, the lesser-known LRRK2 p.L1795F variant was proposed as a strong genetic risk factor for PD [1], with a functional effect via stimulating the LRRK2 kinase activity [2]. However, further families are currently lacking in the literature.

Methods: A multicentre early-onset and familial PD cohort from 9 movement disorder centres across Central Europe within the CEGEMOD consortium [3] was screened for rare LRRK2 variants using whole exome sequencing data ($n = 219$).

Results: We identified 3 PD cases with heterozygous LRRK2 p.L1795F variant and 1 PD case was additionally identified through standard genetic testing. All 4 patients were from a region close to Slovak-Hungarian borders. The age of onset was 25, 45, 55 and 69 respectively and 3 cases had positive family history with several family members affected. All 4 cases were characterized by early onset of severe motor fluctuations, with 2 of them receiving LCIG therapy and 2 implanted with STN DBS; 3/4 of these cases showed unsatisfactory effect on motor fluctuations.

Conclusion: Our data suggest that the p.L1795F may represent the most common currently known pathogenic LRRK2 variant in Central Europe (AF = 0.0091) compared to more studied p.G2019S (AF = 0.00164), which is lower than in North-West Europe as reported previously [4]. Together with the ongoing clinical trials for LRRK2 inhibitors, this finding emphasizes the urgent need for more ethnic diversity in PD genetic research.

Disclosure: This study was funded by the Slovak Grant and Development Agency under contracts APVV-22-0279 and by the Slovak Scientific Grant Agency under contract VEGA 1/0712/22.

EPO-298 | First description of c.3478 A>G DYNC1H1, a potentially pathogenic variant in a SMALED sibship

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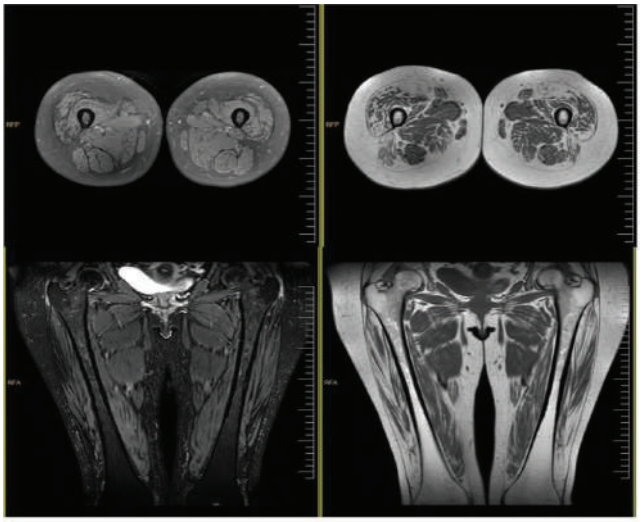
Background and Aims: Pathogenic variants of the DYNC1H1 gene were first identified in 2012 as the cause of a group of autosomal dominant spinal atrophy affecting the lower limbs (SMALED). We describe a previously unreported variant of unknown significance (VUS) with features to suggest a pathogenic loss of function.

Methods: 3 members of the same sibship were assessed in our centre: a female (p1) with a prior diagnosis of SMA type 4 displaying a full SMALED phenotype, another female (p2) with a milder SMALED phenotype and no previous diagnosis and a male (p3) with CNS features of DYNC1H1 dysfunction since childhood (Intellectual disability, seizures, behavioural disturbance). EMG showed features of dHMN in p1 and p2 while MRI of the lower limbs demonstrated a pattern of muscular atrophy typical for SMALED. Brain MRI for p3 showed focal cortical thickening on the left precentral gyrus; however, those were not diagnostic for a neuronal migration disorder.

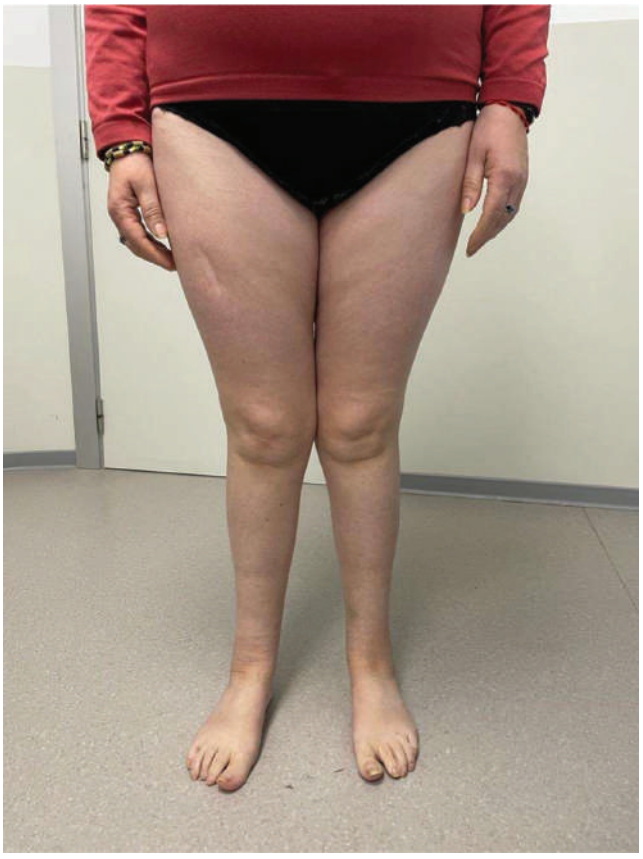
EMG											
			Act. espontánea					PUMs			Reclutamiento
Músculo	Nervio	Raíces	Ins	Fib	Pos	H.F.	Fasc	Amp	Dur	Polif	Patrón
L. Gastrocnemius (Medial head)	Tibial	S1-S2	No	No	No	No	No	1+	N	N	Reduced
R. Gastrocnemius (Medial head)	Tibial	S1-S2	No	No	No	No	No	1+	N	N	Reduced
L. Gastrocnemius (Lateral head)	Tibial	S1-S2	No	No	No	No	No	N	N	N	N
R. Gastrocnemius (Lateral head)	Tibial	S1-S2	No	No	No	No	No	1+	N	N	Reduced
L. Tibialis anterior	Peroneal	L4-L5	No	No	No	No	No	1+	N	N	Reduced
R. Tibialis anterior	Peroneal	L4-L5	No	No	No	No	No	1+	N	N	Reduced
L. Peroneus longus	Peroneal	L5-S1	No	No	No	No	No	1+	N	N	Discrete
R. Peroneus longus	Peroneal	L5-S1	No	No	No	No	No	1+	N	N	Reduced
L. Vastus lateralis	Femoral	L2-L4	No	No	No	No	No	Giant	N	N	Simple
R. Vastus lateralis	Femoral	L2-L4	No	No	No	No	No	2+	N	N	Discrete
L. Adductor longus	Obturator	L2-L4	No	No	No	No	No	1+	N	N	Discrete
R. Adductor longus	Obturator	L2-L4	No	No	No	No	No	2+	N	N	Discrete
L. Iliopsoas	Femoral	L2-L3	No	No	No	No	No	N	N	N	Reduced
R. Iliopsoas	Femoral	L2-L3	No	No	No	No	No	1-	N	1+	Reduced

EMG findings for p1, demonstrating chronic longstanding denervation. NCS and H reflex were normal.

Results: Genetic testing identified a c.3478 A>G DYNC1H1 VUS in all probands, a single nucleotide polymorphism (SNP) leading to a Thr1163Ala substitution, not currently present in any of the available databases. Protein function modelling using the PolyPhen-2 tool predicted a potentially damaging effect with high confidence.



Thigh MRI images from p2: widespread asymmetrical atrophy and fatty infiltration, sparing the Gracilis and Semitendinosus muscles.



Proband p1 has prominent Genu valgo and pes planovalgus, with significant calf atrophy.

Conclusion: Although the lack of an animal model and limited in-silico modelling does not allow to establish definite pathogenicity according to current ACGM/ACGS scoring, the familiar aggregation, clinical presentation and paraclinical findings would endorse its inclusion on databases at least as a high risk VUS.

Disclosure: Dr Boix Codony has received honoraria (<500€) for contributing to the MAVEN-4 study (MS700568_073), promoted by Merck Serono. The other Authors declare no relevant disclosures.

EPO-299 | Autosomal dominant optic neuropathy without polyneuropathy due to novel c.1988G>A MFN2 mutation

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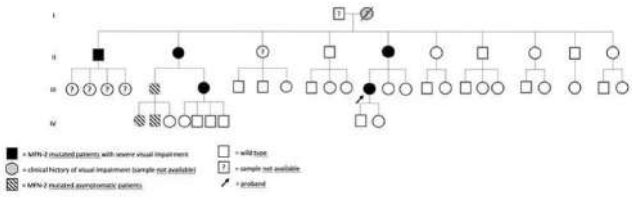
Background and Aims: The mitofusin-2 (MFN2) gene (1p36.22) encodes GTPase proteins involved in the fusion of mitochondrial membranes. Numerous MFN-2 mutations have been associated with the axonal form of Charcot–Marie-Tooth (CMT) disease type 2A and hereditary optic atrophies [1, 2]. Here we describe a Southern Italian family with a novel missense c.1988G>A MFN2 variant presenting with painless progressive visual impairment without peripheral motor or sensitive manifestations.
Methods: Twenty-three subjects across three generations underwent serum DNA analysis screening tests with next-generation sequencing (NGS). All MFN2-mutated carriers performed an ophthalmological evaluation with optical coherence tomography (OCT), instrumental evaluation with visual evoked potentials (VEP) and electroneurography (ENG).
Results: Serum DNA analysis revealed the MFN2 c.1988G>A variant in 8 out of 23 (5F, median age: 41.5 years, IQR: 20.5-65) patients (see pedigree chart, figure 1). In silico analysis by PolyPhen-2, Mutation Taster and Align-GVGD predicted this variant as pathogenic. Neurological evaluation revealed decreased visual acuity in 5 subjects (2M, 3F mean age: 49 ± 24.1 years), while no abnormalities resulted in three asymptomatic younger carriers (2M, 1F mean age 32 ± 15.1 years). VEP was bilaterally delayed in all five symptomatic patients. One also showed a bilaterally reduced radial nerve fibre layer thickness on OCT. Motor and sensory nerve conductions on ENG were normal in all mutated subjects.



Pedigree of family with MFN-2 c.1988G>A variant, demonstrating an autosomal dominant inheritance.

Conclusion: Our study illustrated a distinctive clinical presentation marked by adult-onset isolated optic neuropathy without peripheral neuropathy, associated with a newly identified c.1988G>A MFN-2 variant exhibiting autosomal dominant inheritance.
Disclosure: Nothing to disclose.

EPO-300 | Clustering analysis of a cohort of primary mitochondrial diseases patients: Novel associations from the GENOMIT registry

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Background and Aims: Primary mitochondrial diseases (PMDs), characterized by a complex genotype-phenotype interplay, demand innovative approaches for comprehension. This study leverages artificial intelligence (AI), specifically clustering techniques, on a polycentric dataset to reveal genotype-phenotype subgroupings, offering valuable insights to enhance clinical decision-making in the intricate landscape of PMDs.
Methods: The dataset includes 770 PMD patients (female: 54%; age of onset: ≤16 yo 21%, >16yo 79%) from 3 Italian centres, extracted from the GENOMIT international clinical registry (https://genomit.eu/). Pre-processing reduced variables to 71 from 802 using clinical knowledge's discriminative capabilities. Principal Component Analysis (PCA) further condensed them to 44 components. Subsequently, K-means clustering was performed, determining optimal clusters via silhouette score, which ensured homogeneity within clusters while maximizing inter-cluster separation.
Results: The optimal cluster count was three. Distinctive genotype patterns include a prevalence of nuclear DNA (44.4%) and mitochondrial DNA single large-scale deletions (24.1%) in cluster 3, which showed the youngest age of onset (53.4% <16 yo), and SURF1 gene mutations prevalence. Regarding phenotypes, apparently similar clinical diagnosis distribution was found, with multisystem involvement more prevalent in cluster 1 and 3 and more diverse systems involved in cluster 2.
Conclusion: This study used clustering analysis for exploring genotype and phenotype distributions in PMDs. Employing unsupervised clustering on a comprehensive dataset identified distinct PMDs patient subgroups but still heterogenous distribution which needs further interpretation. These preliminary findings hold promise for personalized medicine, marking a significant step in unravelling the complexities of these rare diseases through innovative AI-driven approaches.
Disclosure: The authors have no conflicts of interest to declare.

EPO-301 | Ataxia-neuropathy due to a novel mtDNA mutation affecting processing of MT-ATP6 and MT-CO3, subunits of complex 4 and 5

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Background and Aims: The ataxia-neuropathy spectrum covers a large variety of diseases and also includes hereditary mitochondrial disorders. In mitochondrial disease, the ataxia typically occurs in combination with other central nervous system features, including epilepsy and cognitive decline, or optic atrophy. The nuclear-encoded mutations in mitochondrial polymerase-gamma (POLG) have been recognized as the commonest cause of mitochondrial disease leading to ataxia-neuropathy, but a considerable proportion of patients harbor mtDNA mutations.
Methods: A 41-year old patient developed progressive gait ataxia, sensory neuropathy, bilateral deafness and mild visual impairment. There was a strong family history of an ataxia-neuropathy-deafness syndrome in 1st degree relatives. After exclusion of POLG-mutations, workup of the clinical presentation and sequencing of the entire mitochondrial DNA were performed in the patient and her affected relatives.
Results: The patient, her mother and all affected sibs were found to carry a novel, homoplasmic mutation in MT-ATP6 (m.9198delC). One sib also fulfilled the Barkhof MRI-criteria for Multiple Sclerosis.
Conclusion: We identified a family with a late-onset ataxia-neuropathy-deafness syndrome caused by a unique mtDNA mutation. The mutation leads to the loss of the Stop Codon in MT-ATP6, and thus can also affect the processing of the polycistronic mRNA transcript, consisting of the MT-ATP6 and the MT-CO3 mRNAs. This scenario is expected to reduce the synthesis of both MT-ATP6 and MT-CO3, a subunit of mitochondrial complex 4.
Disclosure: Nothing to disclose.

EPO-302 | Novel homozygous KCNJ10 mutation in sisters with clinical picture of complex hereditary spastic paraparesis

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Background and Aims: Mutations in KCNJ10 gene encoding the inwardly rectifying potassium channel Kir4.1 cause a complex syndrome characterized by seizures, sensorineural deafness, ataxia, intellectual disability, and electrolyte imbalance known as SeSAME/EAST syndrome. One patient with non-syndromic early-onset cerebellar ataxia was described. Until now, hereditary spastic paraparesis has not been considered as part of the clinical spectrum of this channelopathy.
Methods: Genetic and clinical investigations were performed in two sisters (S1 and S2) with early-onset progressive spastic paraparesis (combined with focal dystonia in S2) and their asymptomatic father, referred to the Center of Hereditary Ataxia, Motol University Hospital. Clinical data, medical history, neurological examination, laboratory tests, MRI of the brain, and results of other electrophysiological methods and clinical examinations, were collected.
Results: Targeted next-generation sequencing identified previously described homozygous c. 179T>C, p.(Ile60Thr) variant in the KCNJ10 gene (NM_002241.5) in both sisters (S1,S2), with the same heterozygous mutation in the father. In both patients, the clinical picture was dominated by spastic paraparesis, ataxia and suspected cognitive deficit. Sister S1 suffered from the epilepsy from the age of 6 months with gait disturbances appearing in the first decade. Sister S2 observed first difficulties with running at the age of 11. Audiometry and neuropsychological examination confirmed perceptual hearing loss and cognitive deficit in both siblings. Electrolyte imbalance/tubulopathy was absent.
Conclusion: Our findings broaden the clinical and mutational spectrum of KCNJ10-related disorders and suggest that screening for this gene should be performed in patients suspected of having complex hereditary spastic paraparesis.
Disclosure: No disclosure.

EPO-303 | Spatial perspective taking is impaired in spinocerebellar ataxias

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Background and Aims: Perspective taking, the ability to imagine the environment from a different viewpoint, is an essential component of spatial navigation. Animal and functional neuroimaging studies have shown that the cerebellum is important for spatial navigation, but studies in patients with cerebellar disorders, including those with hereditary ataxias, are lacking. The current study aimed to investigate perspective taking in patients with spinocerebellar ataxias (SCA) and Friedreich's ataxia (FRDA).
Methods: We recruited 23 SCA patients 19 FRDA patients from the Centre of Hereditary Ataxias, and 34 age-matched healthy controls (HC). All participants underwent the Perspective Taking/Spatial Orientation Test (PTSOT), an established paper-and-pencil test of perspective taking. Participants were asked to imagine standing at one object and facing another. Their task was to indicate the direction to a third object in a circular diagram.
Results: The SCA group performed significantly worse than the HC group. Specifically, the mean angular error was 63.02° compared to 26.01° ($p < 0.001$), and the mean percentage of responses lying in the correct quadrant of the circular diagram was 46.1% compared to 82.8% ($p < 0.001$), respectively. The FRDA group did not differ significantly from the HC group.
Conclusion: Perspective taking is impaired in SCA but not in FRDA patients. This may be due to more pronounced cerebellar grey matter atrophy in patients with SCA. More research is needed on spatial navigation in patients with cerebellar diseases, as navigation impairment may have a negative impact on patients' mobility and independence.
Disclosure: Supported by Charles University Grant Agency (GAUK) projects No. 224522, 309121, and 226423, and project National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107). The authors are members of the European Reference Network for Rare Neurological Diseases (ERN-RND).

EPO-304 | The role of serotonergic gene polymorphisms in functional motor disorder: A case-control association study

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Background and Aims: Understanding the genetic factors contributing to functional motor disorders (FMD) remains limited. A previous study in a small FMD group ($n=69$) found a link between the T allele variant of the tryptophan hydroxylase 2 gene (TPH2) polymorphism c.-703G>T and an earlier onset of FMD symptoms.1 In our case-control study, we aimed to investigate the association between single-nucleotide polymorphisms (SNPs) within the TPH2 and 5-hydroxytryptamine receptor 2A (HTR2A) genes, both involved in serotonin regulation, and FMD, as well as their impact on the age of symptom onset.
Methods: We genotyped 357 FMD patients and 243 healthy controls for 5 SNPs including rs4570625, rs10784941 for TPH2 gene, and rs6311, rs6313, rs6314 for HTRA2 gene using TaqMan Assays. We performed standard association tests, including allelic, genotypic, dominant, and recessive models, as well as the Cochran–Armitage test for trend using the PLINK statistical package v1.9.2 Linear regression and quantitative association tests assessed the influence of selected SNPs on the age of FMD onset.
Results: We found significant associations between rs4570625 (recessive model, $p=0.007$; nominal) and rs6311 (dominant model, $p=0.0030$; nominal) SNPs with FMD. There was no observed link between these genetic variants and an earlier onset of FMD.
Conclusion: These preliminary findings suggest possible involvement of the serotonergic pathway in FMD, but its link to earlier symptom onset was not confirmed. Results emphasize the need for further research in a broader cohort, considering potential confounding factors such as psychiatric comorbidities.
Disclosure: Supported by NU20-04-00332, NW24-04-00456 and Cooperation by Charles University.

EPO-305 | The first clinical and genetic characterization of patients with cerebrotendinous xanthomatosis in Hungary

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Background and Aims: Cerebrotendinous xanthomatosis (CTX) is a rare lipid storage disorder caused by mutations in CYP27A1 gene which leads to reduced production of chenodeoxycholic acid (CDCA) and excess of cholestanol, causing a wide spectrum of neurological and non-neurological symptoms.
Methods: We aimed to characterize the patients diagnosed with CTX in Hungary and follow the efficacy of the treatment with CDCA.
Results: We present 9 patients from 6 families (two females and seven males (mean age=44.7±8, range=29-52). Mean age at onset was 24.7±12 years. In 3-3 cases the c.1184+1G>A. and c.819delT rare variants of the CYP27A1 caused the disease. The most common clinical manifestations were cerebellar ataxia, polyneuropathy, cognitive impairment and juvenile cataract. Xanthomas were present only in 22.2%. Of the cases, diverse non-neurological findings (diarrhea, severe atherosclerosis) were observed in five patients. Brain MRI detected T2, FLAIR hyperintensity in the dentate nuclei in all patients. ENG and nerve ultrasound revealed neuropathy in all cases, and suspected intraneural cholesterol accumulation in two. Elevated cholesterol and oxysterols were detected in all cases, but the levels didn't correlate with the severity of the disorder. Six patients are on CDCA supplementation for an average of 38±25 months which resulted in the normalization of the cholesterol level and the stagnation of the ataxia score and polyneuropathy.
Conclusion: CDCA supplementation may reverse the pathophysiological process in patients with CTX, especially if treatment is initiated early in the disease process. Therefore, early diagnosis and treatment are crucial in preventing clinical deterioration.
Disclosure: Nothing to disclose.

EPO-306 | Abstract withdrawn

EPO-307 | SCA27B – New ataxia with late onset and response to 4-aminopyridine – First 14 cases diagnosed in the Czechia

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Background and Aims: SCA27B is a newly described autosomal dominantly inherited late-onset ataxia caused by the expansion of GAA repeats in the first intron of the FGF14 (Fibroblast growth factor 14) gene. Recently, an excellent response to 4-aminopyridine has been published.
Methods: 28 patients followed at the Center of Hereditary Ataxia, Motol University Hospital with chronic degenerative ataxia of

unknown origin with adult-onset were molecular-genetically examined for the presence of the FGF14 GAA repeat expansion.

Results: The expansion in the FGF14 gene within the pathological range (GAA≥300) was found in 11 (39%) patients, and 3 patients (11%) had a borderline repeat length (GAA250-299) with presumed incomplete penetrance. Eight patients had a positive family history of ataxia in a parent or sibling, and 6 cases were sporadic. The mean age of onset was 52 years. All patients had progressive cerebellar syndrome. Four patients (37%) presented with a parkinsonian syndrome. Significant fluctuations of symptoms during the day were present in 9 patients. Treatment with 4-aminopyridine was initiated in 5 patients, with an excellent effect in 4 of them.

Conclusion: SCA27B is a newly described common cause of hereditary late-onset ataxia in the Czechia. Based on the estimated frequency in the Czech population, we have included targeted molecular genetic testing for SCA27B as a standard investigation in patients with adult-onset chronic ataxia. This step is important not only for accurate diagnosis but also because of the significant therapeutic benefit observed with 4-aminopyridine treatment in SCA27B cases.

Disclosure: Supported by project No. LX22NPO5107 (Ministry of Education and Science).

EPO-308 | Abstract withdrawn

Epilepsy 2

EPO-309 | Therapeutic drug monitoring of antiseizure medications through quantitative dried blood spot

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Background and Aims: Therapeutic drug monitoring (TDM) of antiseizure medications (ASMs) is an essential tool for persons with epilepsy (PWE). Traditional venipuncture for TDM requires high-volume blood and physically mandates patients at hospital1,2. Microsampling requires lower-blood volume through less painful and invasive fingerprick offering a sampling methodology potentially performed at-home. This study aimed to validate the extraction method of ASMs from a quantitative Dried-Blood-Spot microsampling (qDBS)2.

Methods: Carbamazepine (CBZ), lacosamide (LCS), levetiracetam (LEV) lamotrigine (LTG) and valproic acid (VPA) were considered. The quantification of ASMs from 10µl qDBS-device by UHPLC-Mass spectrometry (UHPLC-MS/MS) was performed through an extraction technical validation, according to EMA guidelines3. Bland-Altman analysis and Passing-Bablok regression were performed to compare ASMS concentrations in qDBS collected with leftover venous blood and plasma samples.

Results: The method was proven accurate and precise using the chosen extraction procedure. Indeed, intra and inter-assay reproducibility analyses showed accuracy and precision ≤15% across the calibration range (0.4-15µg/ml CBZ; 0.5-10µg/ml LCS; 0.5-20µg/ml LTG; 1-80µg/ml LEV; 10-120 µg/ml VPA). Recovery was found >85 % and matrix effect <10% for most of the ASMs considered. Stability was tested at 7, 15, 30 days of storage, showing mutual robustness at 7-days room-temperature. Preliminary statistics via Bland-Altman analysis and Passing-Bablok regression indicated a linear correlation for most of the ASMs.

Conclusion: A UHPLC-MS/MS assay was developed and validated according to EMA guidelines for quantifying ASMs-qDBS3. Advantage of this validation allows the potential for utilizing the new microsampling qDBS devices, providing a patient-friendly approach to blood sampling even at-home in PWE.

Disclosure: Nothing to disclose.

EPO-310 | Repetitive transcranial magnetic stimulation in refractory and super-refractory status epilepticus: A systematic review

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Background and Aims: Currently, there are no guidelines available on the treatment of refractory status epilepticus (RSE) and super-refractory status epilepticus (SRSE). Therefore, off-label treatments are often used. We performed a systematic review regarding the efficacy of repetitive transcranial magnetic stimulation (rTMS) as a treatment in RSE/SRSE.

Methods: We systematically searched EMBASE, PubMed, Opengre.eu, CENTRAL and conference abstracts from AES and EAN meetings (2005-2023) to identify trials investigating the use of rTMS in RSE and/or SRSE. The following parameters were collected: RSE/SRSE etiology, RSE/SRSE classification, RSE/SRSE abortion, latency to abortion, duration of RSE/SRSE before rTMS.

Results: We identified 32 patients, whereof 15 with epilepsia partialis continua (EPC). 19/32 were classified as focal motor SE, 7/32 as non-convulsive SE and 3/32 as convulsive SE. Cortical malformations were the most frequent cause (10/32), followed by stroke (5/32) and genetic mutations (5/32). NORSE accounted for eight cases. For three and four patients respectively, data were lacking regarding classification and etiology. In 81.25% (26/32) of patients rTMS resulted in cessation of RSE/SRSE. After rTMS, two deaths (6.25%) were reported but considered unrelated to rTMS and attributed to the underlying disease. Median duration of acute/subacute RSE/SRSE and RSE/SRSE in EPC patients before rTMS was 44 days

(range: 0-140 days) and 128 days (range: 28-7300 days) respectively. After rTMS, the latency to abortion ranged from 0-4 days.
Conclusion: rTMS interrupts RSE and SRSE in 81.25% of patients. Data originates from studies graded as level IV with a high risk of reporting bias, warranting further studies.
Disclosure: Nothing to disclose.

EPO-311 | Deep learning-based automated detection of focal interictal epileptiform discharges on electroencephalogram

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Background and Aims: The lack of specialists in the field, combined with technical and scientific progress, is stimulating interest in developing new methods for diagnosing, classifying, and treating focal epilepsy. In this study, we focus on the use of deep learning neural networks (DLNN) for epileptic discharges detection on electroencephalography during the interictal phase.
Methods: The dataset used in this research comprises interictal electroencephalographic (EEG) recordings from thirteen patients with a diagnosis of focal epilepsy, provided by the Institute of Emergency Medicine, Republic of Moldova. Data preprocessing techniques were applied to EEG signals stored in European Data Format files. This study employed convolutional neural networks (CNNs) and long short-term memory (LSTM) networks, which are most commonly used in the field of EEG processing. The focal discharges on EEG were split randomly into training, validation, and test sets. The accuracy, precision, and F1-score were evaluated on the training, validation, and test sets.
Results: The study had an average accuracy of 95.7%, precision of 0.997 and an average F1 score of 0.94 on the training, validation and test sets.
Conclusion: This study substantiates the potential of DLNN in accurately identifying epileptic seizures through EEG analysis. Nonetheless, it underscores the necessity for the compilation of an extensive learning database for the algorithm, potentially introducing an additional layer of complexity to the deployment process.
Disclosure: Nothing to disclose.

EPO-312 | Stereoencephalography-guided thermocoagulation: Experience in our center

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Background and Aims: Stereoelectroencephalography-guided thermocoagulation (SEEG-guided TC) stands as an advanced therapeutic modality in the management of refractory focal epilepsy, boasting a 25% estimated seizure freedom rate, and a >50% seizure reduction rate in 58% at one year of follow-up in some series. We conducted a retrospective analysis of outcomes in our centre.
Methods: We retrospectively analyzed patients undergoing SEEG-guided TC at Hospital Universitario y Politécnico La Fe, Valencia, Spain´s Refractory Epilepsy Unit, spanning from January 2019 to January 2023. Patients with at least one year of follow-up were only included. Clinical data were systematically extracted using a standardized collection form from an electronic database.
Results: The study included 41 patients (20 males, 48.8%) with a median age of 34 (9-63). The mean follow-up duration was 16.42 months (12-36). At the last follow-up, 19 patients (46.64%) remained seizure-free, and the responder rates at 75% and 90% were 65.85% and 60.9%, respectively. In 10 out of 13 patients (76.9%) with follow-ups exceeding two years, a seizure reduction rate of >90% was maintained. Medication was modified for only one patient, with adjustments made in two others, while the remainder maintained their existing therapeutic schedules. Postoperative permanent complications were observed in 1 patient as hemianopsia (2.4%).
Conclusion: In appropriately selected patients, SEEG-guided TC emerges as a promising intervention, demonstrating the potential for sustained outcomes, especially when combined with pharmacological therapy.
Disclosure: Nothing to disclose.

EPO-313 | First experience with cenobamate in the treatment of paediatric patients with epilepsy: A single-centre study

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Background and Aims: Cenobamate is a new anti-seizure drug currently indicated for the adjunctive treatment of focal seizures with or without secondary generalization in adult patients with epilepsy without adequate control despite prior treatment with at least 2 antiepileptic drugs.

Methods: Retrospective evaluation of paediatric patients treated at the Department of Paediatric Neurology, Faculty of Medicine, Masaryk University and University Hospital Brno, Czechia starting CNB between 4/2023 and 12/2023. We evaluated dosing and efficacy on seizures in relation to the type of epilepsy.

Results: A total of 16 patients with a mean age of 13.7 years (min 7 years; max 17 years), 8 boys and 8 girls, were included in the study. 6 patients were diagnosed with focal epilepsy, 4 patients with multifocal epilepsy, and 6 patients with LGS. Before CNB deployment, patients tried an average of 2.5 ASMs (min 1, max 4). Patients older than 12 years were dosed at 150-200mg/day, younger patients were titrated to 100mg/day. Seizure reduction of more than 75% was achieved in 5 of 16 patients (31.2%), and seizure reduction of more than 50% was achieved in 8 of 16 patients (50.0%). Interestingly, 4 of the 6 LGS patients were included in the responder group, one of whom experienced a transient 3-month seizure-free period.

Conclusion: The results of our cohort are promising and show that even pharmacoresistant patients with DEE can benefit from CNB medication. Further data regarding pediatric patients and longer follow-up will definitely be beneficial.

Disclosure: Nothing to disclose.

EPO-314 | Epilepsy and co-morbid depression in Northern Rwanda

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Background and Aims: In persons living with epilepsy (PwE), depression is the most frequent co-morbidity. The prevalence of epilepsy in Rwanda ranges between 2.9-7.6%. In a tertiary hospital, depression is observed in more than 22% of PwE. This prospective interventional study determined the prevalence and incidence of depression in PwE in three rural villages in Northern Rwanda.

Methods: PwE enrolled between June 2018 and December 2018. At each study visit, PwE were screened for depression with Patient Health Questionnaire-9 (PHQ-9). If positive, the Hamilton Depression Rating Scale (HDRS) was administered to confirm diagnosis of depression. PwE with moderate to severe depression (MSD), were followed for one year and started on anti-depressant treatment. We report depression prevalence and incidence, baseline characteristics of PwE, and clinical outcomes of PwE with and without depression.

Results: Of 304 PwE enrolled, 25 (8.2%) were diagnosed with MSD during the study. At baseline visit, prevalence of any depression and MSD was 27% and 4.3% respectively. Incidence of any depression or MSD was 245 and 48/1000 patient-years. Improvement in seizure frequency was observed in both PwE with and without depression. There was a significant reduction in HDRS score for PwE with depression from 22.8 at baseline to 7.9 after 12 months, resulting in 94.7% of PwE having no or mild depression.

Conclusion: The Kinyarwanda versions of PHQ-9 and HDRS were successful in screening and diagnosing depression in PwE. Treatment of epilepsy and co-morbid depression resulted in improved outcomes, implementation of depression screening in daily neurology practice in Rwanda is warranted.

Disclosure: Peter Dedeken received consultancy fees from UCB Pharma, Merck, Pfizer, and Novartis. Dirk E Teuwen received consultancy fees from UCB Pharma. Paul AMJ Boon received speaker and consultancy fees from UCB Pharma, LivaNova, and Medtronic, as well as research grants through his institution. Ieme Garrez and Fidèle Sebera received research grants through his institution.

EPO-315 | Effects on memory of chronic hippocampal stimulation in patients with refractory mesial temporal epilepsy

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Background and Aims: Chronic, continuous, bilateral, hippocampal stimulation (CHS) is a novel treatment for refractory epilepsy in patients with bilateral independent hippocampal seizure onset unsuitable for resective surgery. This report will present a review of the current use of hippocampal stimulation (Hip-DBS) in clinical practice and the effects of CHS on the memory of two patients with an average of 10 focal impaired awareness seizures per month (pre-CHS).

Methods: Two patients (K1 and K2) were implanted with depth electrodes in both hippocampi for CHS in 2016 and 2017 at King's College Hospital (KCH). Both had continuous bilateral hippocampal stimulation (amplitude 1-1.5mA, pulse duration 300-360 microseconds, frequency 130 Hz) for more than seven years. Neuropsychological assessment was performed pre-CHS: patient K1 had a full-scale IQ (FSIQ) of 96 and patient K2 of 98. We also conducted a review of the use of Hip-DBS and noted outcomes on seizure frequency and memory.

Results: At the follow up at 67 and 84 months, both patients had a marked (>90%) decrease in seizure frequency post CHS. Neuropsychometry found mildly less efficient memory in the context of low mood for patient K1 (FSIQ = 99) and potential improvement in verbal memory for patient K2 with other parameters stable (FSIQ = 103). This is in general agreement with other studies.

Conclusion: Chronic, continuous, bilateral, hippocampal stimulation has not shown clear adverse effects on memory in the literature and

in the two patients implanted at KCH. The reduction of seizures and interictal activity by CHS may instead lead to an improvement in memory.

Disclosure: Nothing to disclose.

EPO-316 | Translation and validation of an epilepsy screening instrument for use in resource-poor settings

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Background and Aims: The prevalence of epilepsy in sub-Saharan Africa varies considerably and there is little data from peri-urban areas. More community-based studies are required to understand the true burden of epilepsy in these areas and access to Healthcare.

Methods: We developed a 17-item epilepsy screening instrument by modifying validated English language questionnaires. We included questions on convulsive and non-convulsive seizures. Language experts translated and back-translated the survey instrument to two languages spoken in this region: Asante Twi and Dangme. Cases were persons with epilepsy attending healthcare facilities where these languages are spoken. Controls were unaffected relatives of cases or people attending the healthcare centers for other medical conditions.

Results: A total of 100 (50 cases and 50 controls) for Twi and 140 (70 cases and 70 controls) for Ga-Dangme were recruited. The sensitivity and specificity of the questionnaire were: Stage 1; (Twi 98 % and 92%, Ga-Adangme 100% and 80% respectively) and stage 2 (Twi 96% and 94%, Ga-Adangme 98.6% and 85.7% respectively). The two versions reliably indicated epilepsy with positive predictive values of 92.5% and 83.3% for Twi and 83.8% and 87.3% for Ga-Dangme at stages 1 and 2 respectively.

Conclusion: The current data shows that our questionnaire has good validity for the two test languages and can be used for community-based epilepsy surveys in Ghana. The questionnaire can be adapted for other resource-poor settings, although there will need to be iterative in-country testing to ensure validity is maintained.

Disclosure: Nothing to disclose.

EPO-317 | The association of excessive daytime sleepiness with quality of life and mood in adults with epilepsy

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Background and Aims: Excessive daytime sleepiness (EDS) is considered common in adults with epilepsy (AWE). EDS in AWE is multifactorial, including antiseizure medication (ASM) effects, seizures, poor sleep quality and accompanying affective states. We aimed to study the interconnection of EDS with health-related quality of life (HRQOL) and mood among AWE.

Methods: AWE were examined for EDS using the Epworth Sleepiness Scale (ESS) and divided into two groups: Non-EDS - ESS score <9, EDS - ESS score ≥9. HRQOL was evaluated by SF-36 questionnaire, consisting of 8 domains (Table 1). Sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI). Validated Armenian versions were used. Hamilton scales for anxiety (HAMA) and depression (HAMD) were also used. Mann-Whitney U test was used for statistical analysis.

Results: We included 169 AWE (mean age-35.3 (18-71) years, males-52.1%), 30 (21.6%) of whom had EDS by ESS. No significant difference according to ASM status was found for EDS (ESS 5.5/4.7, $p > 0.05$). For the groups NonEDS/EDS - BMI = 23.7/25.3kg/m2 ($p > 0.05$), means for SF-36 domains for the groups are presented in Table 1. AWE with EDS had significantly lower levels of HRQOL. AWE with higher scores of the ESS had higher scores of anxiety and depression: HAMA-13.45/20.3 ($p < 0.05$), HAMD-11.5/18 ($p < 0.05$), and poorer sleep quality: PSQI-7.5/9.9 ($p < 0.05$).

SF-36 Domains	Non-EDS	EDS	*p*
D1 Physical Functioning	70.3	58.3	<0.05
D2 Role-Limitations Due to Physical Health	45.1	21.2	<0.05
D3 Role Limitations Due to Emotional Problems	46.4	24.6	<0.05
D4 Energy/Fatigue	55	39.2	<0.05
D5 Emotional Well-Being	55.6	40.5	<0.05
D6 Social Functioning	66.5	45.3	<0.05
D7 Pain	68.2	44.7	<0.05
D8 General Health	49.8	40.3	<0.05

EDS- Excessive daytime sleepiness

Health-related quality of life measured by SF-36 questionnaire in adults with epilepsy with and without EDS.

Conclusion: We found EDS in one-fifth of AWE and it seemed not associated with ASM. AWE with EDS, had more depression and anxiety, their HRQOL was significantly lower. Our study underscores the importance of considering multiple factors behind EDS' significant impact on quality of life in AWE.

Disclosure: Nothing to disclose.

EPO-318 | Status epilepticus as a complication of COVID-19 vaccination: A literature review

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Background and Aims: Status Epilepticus (SE) stands as a prominent neurological emergency, showing a mortality rate of approximately 20%. Since February 2021, a worldwide vaccination campaign has been settled to fight against the Coronavirus 19 disease (COVID-19) pandemic. Several possible vaccine-related adverse events have been identified including neurological manifestations. SE is beginning to surface in literature as an emergent condition in COVID-19-vaccinated individuals, though defined reasons accounting for this correlation are still missing.
Methods: We performed a systematic search of the literature to identify the consistency of the association between the SARS-CoV-2 vaccine and the SE onset. The following databases: are PubMed, Google Scholar, and EMBASE. Patient data, encompassing demographics, comorbidities, history of epilepsy, type, and dosage of SARS-CoV-2 vaccine, SE semiology, treatment, and prognosis were extracted.
Results: Six studies with a total of seven patients were included. Four patients showed non-convulsive SE, 3 a convulsive one. Four patients received the mRNA-1273 (Moderna) vaccine, 2 patients the BNT162b2 (Pfizer/Biotech), and 1 patient the ChAdOx1-s (AstraZeneca) vaccine. The first vaccine dose (5/7, 71.4%) emerged as the most frequently associated with SE onset which manifested at an average of 4.5 days (±3.4) post-vaccination. Five patients presented a refractory SE and needed continuous intravenous anesthetic drug administration. Resolution of SE was achieved in all cases.
Conclusion: Status Epilepticus appears to be a rare complication associated with both SARS-CoV-2 vaccines. Additional studies are needed to ascertain the potential association between the Sars-CoV-2 vaccine and status epilepticus.
Disclosure: None.

EPO-319 | Patient outcomes in KCNQ2 developmental and epileptic encephalopathy (KCNQ2-DEE): Systematic literature review

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Background and Aims: We conducted a systematic literature review to describe seizure and non-seizure outcomes in KCNQ2-DEE.
Methods: A systematic literature search was conducted, applying Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, to identify and describe seizure and non-seizure outcomes in KCNQ2-DEE patients ≤18 years of age. Case reports/series, observational studies, non-randomised and single arm trials, and surveys were eligible for inclusion. No geographical or publication time restrictions were applied.
Results: Of 92 publications identified, 74 reported individual patient data, of which 41 (55.4%) were case reports or series, from 363 patients. Most patients, where age data available, (42/137, 30.7%) were aged 2-5 years. Seizures had initial onset in the first week of life for 328 (90.4%) patients. Seizure frequency, where data were available, was "multiple daily" for most patients. Seizure freedom was reported for 202 patients with cumulative proportions seizure free of 57% and 66.7% by ages 1 and 2 years respectively. Seizures recurred in 33 of 176 (18.8%) individuals. In 19 individuals for whom data were available, time to recurrence ranged from <1 month to 5 years. Non-seizure outcomes, predominantly developmental and often other neurological and medical, were reported in 348 individuals, among whom communication issues were specified for 63 (18.1%). Other reported non-seizure issues included vision, breathing and bulbar function (typically feeding/eating difficulties), orthopaedic and sleep.
Conclusion: Although seizure control is often achieved in KCNQ-DEE in early childhood or infancy, most patients experience various ongoing challenges related to development, including communication.
Disclosure: This study was sponsored by Biohaven Pharmaceuticals, Inc. ATB has received consulting fees from Biogen, Biohaven Pharmaceuticals Inc, and Encoded Therapeutics; Speakers bureau for Biomarin Pharmaceuticals. JM has received royalties or licenses from UpToDate; received consultancy fees from Biohaven, Eisai, Neurocrine, and Xenon; received speaker honoraria from Biomarin and Greenwich; has participated in a Data Safety Monitoring Board for Praxis; and serves on the board of directors for Child Neurology Foundation (unpaid). GM, MHP, JL, VC and GL have received personal compensation for serving as an employee of Biohaven Pharmaceuticals. DP, SS and KR are employees of Parexel International who conducted the study on behalf of Biohaven Pharmaceuticals, Inc.

EPO-320 | Disability and depression in children and adolescents with epilepsy at a tertiary hospital in Rwanda

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Background and Aims: Epilepsy is one of the most common neurological diseases in children and adolescents. The disorder affects a child's development and increases mental health diseases. We assessed the impact of epilepsy on disability and depression in children and adolescents living with epilepsy (CwE) in Rwanda.

Methods: In 2018, 74 CwE aged ≤20 years were enrolled in an observational study during their monthly neurology consultation at the tertiary Ndera Neuropsychiatric Teaching Hospital. During follow-up in 2022, CwE or their caregivers were contacted to assess disability and to screen for depression using the Kinyarwanda Washington Group-Short Scale (WG-SS) and Patient Health Questionnaire-9.

Results: In 2022, only 29 CwE (39.2%) had continued routine hospital visits. Thirty CwE or caregivers (40.5%) were identified at home and 15 (20.3%) cases remained unascertained. Among 59 CwE, five had died yielding a mortality rate of 24.2/1000 person-years. Mean age of the remaining 54 (46.3% female) was 12.6 ± 5.6 years. Mean age at seizure-onset was 5.7 ± 4.8 years. Generalized-onset seizures occurred in 59.3%, with 97% motor-onset. Focal-onset seizures occurred in 37.0%, with 42.9% exhibiting focal-to-bilateral tonic-clonic seizures. WG-SS revealed a handicap in three (54%) and four domains (23%) and the cognitive domain was mostly affected (71%). Mild and moderate-to-severe depression was present in 38.1% and 14.3%, respectively.

Conclusion: This study documents prominent disability and mental health challenges in Rwandan children and adolescents with epilepsy. Improved healthcare accessibility and holistic care are required to manage disability and prevent mortality.

Disclosure: Ieme Garrez is supported by the Fund for Scientific Research Flanders (FWO). Delphine Kajeneza was supported by a grant of Fracarita Belgium. Peter Dedeken received consultancy fees from Merck, UCB Pharma and Novartis. Paul Boon received consultancy fees from UCB Pharma and grants through his institution. Dirk Teuwen received consultancy fees from UCB.

	N (%)
Sex	
Male	103 (39.6)
Female	156 (60.0)
Non-binary	1 (0.38)
Residence	
Urban	229 (93.1)
Rural	17 (6.9)
Education	
No studies	9 (3.5)
Primary	44 (16.9)
Medium	71 (27.3)
Superior	136 (52.3)
Marital status	
Single	97 (37.3)
Stable partner	130 (50.0)
Separated / divorces	29 (11.2)
Widowed	4 (1.5)
Ocupation	
Housekeeper	15 (5.8)
Worker	117 (45.0)
Student	7 (2.7)
Worker and Student	17 (6.5)
Unemployed	22 (8.5)
Pensioner	82 (31.5)
Seizures frequency	
Daily	29 (11.1)
Weekly	21 (8.1)
Monthly	34 (13.1)
Every 2-3 months	11 (4.2)
Every 6 months	15 (5.8)
Annually	25 (9.6)
Without seizures	125 (48.1)

TABLE 1 Sample descriptive ($N = 260$).

EPO-321 | Spanish validation of the Epilepsy Self-Stigma Scale

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Background and Aims: The Epilepsy Self-Stigma Scale (ESSS) has been developed in Japan for patients with epilepsy (PWE). We aimed to validate the scale into Spanish and examine its reliability.

Methods: We validated the ESSS to the Spanish version (ESSS-S). Recruitment took place in September 2023. PWE also completed the Rosenberg Self-Esteem Scale (RSES), the Hospital Anxiety and Depression Scale (HADS), and the 10-item questionnaire (QOLIE-10).

Results: 260 study questionnaires were completed. A two-factor analysis explained 61.3% of the total variance: factor 1 "perceived discrimination" Cronbach's $\alpha = 0.80$ and factor 2 "social isolation" 0.75. External validity was tested with both anxiety (Cronbach's $\alpha = 0.86$) and depression (Cronbach's $\alpha = 0.86$) sets of the HADS; stigma using the RSES (Cronbach's $\alpha = 0.92$), and quality of life with QOLIE-10 (Cronbach's $\alpha = 0.90$). Perceived discrimination scores were associated with higher anxiety/depression scores ($r = 0.53/0.54$; $p < 0.001$), lower self-esteem (-0.53; $p \leq 0.001$) and lower quality of life ($r = -0.66$; $p < 0.001$). Social isolation scores were also associated with higher anxiety/depression scores ($r = 0.41/0.33$; $p < 0.001$), lower self-esteem (-0.34; $p \leq 0.001$), and lower quality of life ($r = -0.35$; $p < 0.001$). Perceived discrimination scores were inversely correlated with age ($r = -0.12$, $p = 0.045$) and directly with epilepsy duration ($r = 0.20$, $p = 0.001$), while social isolation scores were directly associated with epilepsy duration ($r = 0.15$, $p = 0.013$). The retest was stable ($r = 0.77$) with strong internal validity (ICC = 0.87).

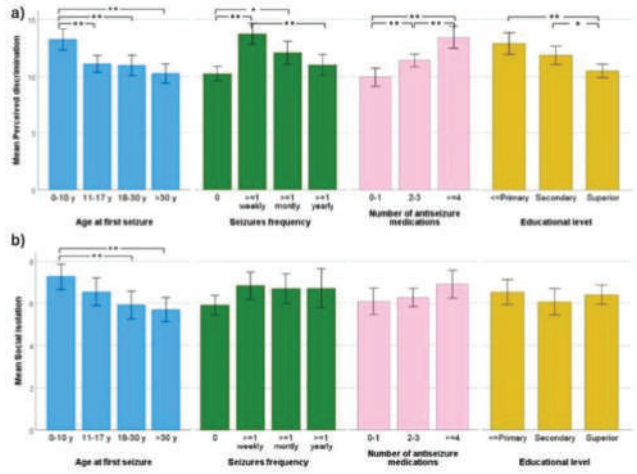

FIGURE 1 Group comparison of Perceived discrimination scores (a), and Social isolation scores (b).

Stigma factors	HADS anxiety	HADS Depression	Rosemberg self-esteem	Qolie-10 quality of life
Perceived discrimination r (p)	0.53 (<0.001)	0.54 (<0.001)	-0.53 (<0.001)	-0.66 (<0.001)
Social isolation r (p)	0.41 (<0.001)	0.33 (<0.001)	-0.34 (<0.001)	-0.35 (<0.001)
Mean (sd)	7.2 (4.4)	5.2 (4.6)	19.1 (6.7)	35.4 (9.2)

TABLE 2 Correlation of stigma factors with anxiety, depression, self-esteem and quality of life, and descriptive. HADS: Hospital anxiety and depression scale.

Conclusion: The E-ESSS is a valid and reliable tool for the assessment of self-stigma in PWE among Spanish speakers.
Disclosure: No disclosures.

EPO-322 | Family history of epilepsy and seizure disorders and age of epilepsy onset in focal cortical dysplasia

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Background and Aims: Previous studies have established the familial occurrence and early age of epilepsy onset as predictors of genetic epilepsy but have not evaluated the rate of their occurrence based on structural epilepsy etiology. Our study determines the rate of familial occurrence and age of epilepsy onset (AEO) in patients with FCD compared to patients with known acquired causes of focal epilepsy (FE).
Methods: We retrospectively analyzed 965 patients with FE evaluated in Neurology Clinic, University Clinical Center of Serbia and identified 88 patients with radiologically defined focal cortical dysplasia (FCD). 272 patients with acquired FE (AFE) constituted the control group. Data were obtained from patient records, including sociodemographic data, AEO, family history (FH) and FE lobar diagnosis. Statistical analysis was performed in SPSS version 23.
Results: FCD patients constituted 29.7% of evaluated patients. Mean age at the disease onset was 15.06±13.22 and 20.21±14.80 years in FCD and AFE group, respectively. Positive FH was present in 10 (11.4%) FCD patients and 27 (10.7%) AFE patients, without statistically significant difference ($p=0.85$) and without difference in number or degree of relatives with epilepsy (RWE) (12 RWE in FCD vs. 30 in AFE, $p=0.38$). Disease onset was significantly earlier in patients with FCD and positive FH ($p<0.001$), especially in those with two or more relatives with epilepsy ($p=0.01$) and with insular or posterior quadrant epilepsy ($p<0.001$).
Conclusion: Positive family history of epilepsy and presence of FCD are associated with earlier disease onset due to presumably higher genetic burden, which should be further evaluated by detailed genetic analysis.
Disclosure: The authors have nothing to disclose.

EPO-323 | Antiseizure medication adherence during the COVID-19 Pandemic in South Korea: National Health Insurance data analysis

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Background and Aims: Considering the decline in prescription rates for chronic conditions throughout the COVID-19 pandemic, this study was conducted to assess anti-seizure medication (ASM) adherence among epilepsy patients during the pandemic.
Methods: Prevalent groups were defined by epilepsy patients of 2018, 2019, and 2020. Chronic groups of year 2018, 2019, and 2020 were defined by prevalent patients of each year who were prescribed with ASM annually from 2002 to 2010. Acute groups of year 2018, 2019, and 2020 were defined by prevalent patients of each year who were first diagnosed with epilepsy two years ago. For each group, the proportion of days covered (PDC) was analyzed to assess ASM compliance. Patients with ASM adherence more than 0.95 of PDC was categorized as the good compliance group, and others as the poor compliance group. Multifactor analyses were conducted in the prevalent groups.
Results: In 2020, 210.314, 72.051, and 30.097 patients were included in the prevalent, chronic, and acute group respectively. When

compared to the previous year, ASM adherence of the prevalent and chronic group has increased in 2019 and 2020. However, for the acute group, ASM adherence has increased in 2019 but decreased in 2020 compared to the previous year.

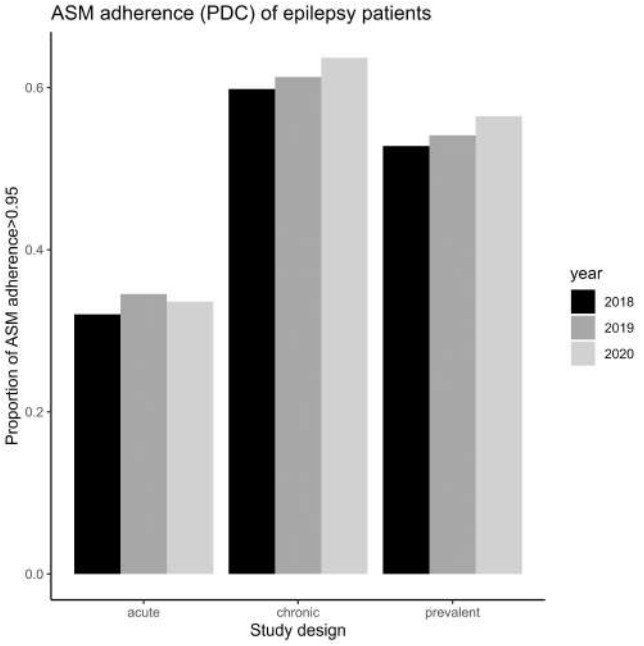
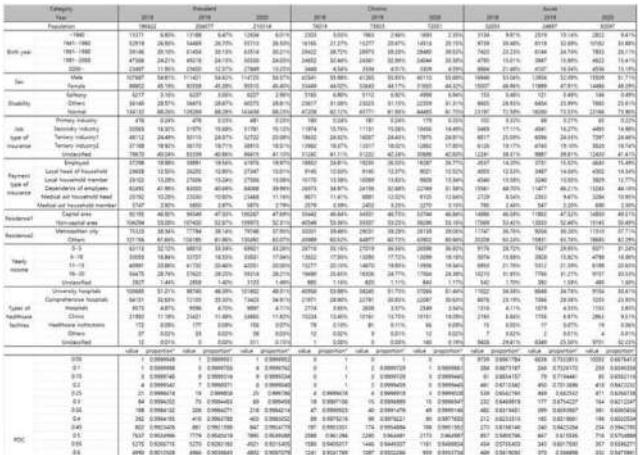


FIGURE 1 ASM adherence of epilepsy patients by year and study design.

TABLE 1 Demographic profile of prevalent, chronic, and acute groups.



Conclusion: During the COVID-19 pandemic prevailed in 2020, ASM adherence of the epilepsy patients has decreased. Further analysis of relevant subcategory will inform policy design during large-scale pandemics and evaluate factors influencing adherence in the context of remote healthcare environments.

Disclosure: This study was supported by the SNUH Research Fund (Global Excellence center), Korea Health Industry Development Institute, Republic of Korea (RS-2023-00265638) and Samjin Pharm (06-2023-2320).

Headache 2

EPO-324 | Relationship between migraine, eating attitudes, and psychiatric symptoms: A multi-center study in Turkey

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Background and Aims: Migraine and eating disorders may involve similar biochemical mechanisms. Previous research has indicated a higher prevalence of eating disorders in individuals with migraines compared to the general population. This study, conducted by the Turkey Headache Study Group, aimed to investigate the relationship between migraine severity, depression, anxiety, and irregular eating attitudes.

Methods: This multi-center, prospective, case-control study involved 20 centers across Turkey. Participants underwent assessments using the Eating Attitude Test-26 (short form), was recorded centrally. From a pool of 1200 individuals diagnosed with headaches, a sample of 531 migraine patients meeting diagnostic criteria was selected using propensity score matching. Patient data were compared with those of 531 healthy controls. The Eating Attitude Test-26, Beck Depression, and Beck Anxiety scales were administered to all migraine patients, and the results were compared with the healthy control group.

Results: Migraine patients exhibited significantly higher Eating Attitude Test-26 scores and symptoms requiring referral to a psychiatrist due to eating disorders compared to the control group ($p=0.034$, $p=0.0001$). I. No statistically significant relationship was found between pain severity, attack frequency, and eating attitudes (r: 0.09, $p=0.055$).

Conclusion: This study demonstrated statistically significant higher scores on the Eating Attitude Test-26 in migraine patients compared to a healthy control group. These findings emphasize the need to inquire about eating disorders in individuals with migraines and highlight the importance of addressing eating attitudes in migraine management.

Disclosure: Nothing to disclose.

EPO-325 | H-MR spectroscopy in vestibular and episodic migraine patients

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Background and Aims: The study aimed to evaluate the metabolite changes in thalamus in patients with vestibular and episodic migraine.
Methods: Fifteen patients with vestibular migraine and 15 patients with episodic migraine who had been diagnosed at Çukurova University Neurology Department were included in this prospective study. Magnetic resonance spectroscopy (MRS) was obtained at 3 Tesla MR 32-channel head coil. SPSS v20 was used for the statistical analysis.
Results: In cases of vestibular migraine, loss of choline in the left thalamus posterior was detected. The left thalamus posterior N-acetyl aspartate (NAA)/Choline ratio was found to increase in patients with vestibular migraine with no migraine history ($p < 0.05$).
Conclusion: Metabolite changes in thalamus in vestibular and episodic migraine patients could provide information about the pathophysiology of the disease and may help explain the different mechanisms of episodic migraine and vestibular migraine occurrence.
Disclosure: Nothing to disclose.

EPO-326 | Effectiveness and tolerability of eptinezumab: A retrospective analysis at 3 and 6 months in migraine patients

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Background and Aims: Since April 2023, Eptinezumab has been used at our hospital to treat migraine patients, including both anti-CGRP-naïve individuals and those who failed other anti-CGRP therapies. Our objective was to evaluate the response to Eptinezumab after 3 and 6 months of treatment.
Methods: Retrospective study analyzing patients treated with Eptinezumab from April to December 2023. Our analysis includes individuals with chronic and high-frequency episodic migraine. Examining demographic features, prior treatments, migraine frequency, pain intensity (Visual Analogue Scale (VAS)), and patients' global impression of change (PGIC). Additionally, we documented any treatment-related side effects.
Results: We analyzed 121 patients with Eptinezumab, mean age 48 years, 84.3% of women. They have failed 7.5 previous preventive treatments and in 57%, botulinum toxin was used concomitantly. 99 patients reached 3 months of treatment. Among them, 50 had tried 3 anti-CGRP mAbs, 22 with 2, 20 with 1, and 7 had never tried anti-CGRP. Migraine days decreased from 23.6 to 18.6, with a PGIC of 2.75. 65% experienced improvement, and 69% continued treatment after 3 months. 29 patients reached 6 months of treatment and they showed a reduction of an average of 8.6 days of migraine with an average PGIC of 2. Mild side effects occurred in 6% of patients, including two cases of mild hypersensitivity reactions.
Conclusion: Even though many patients suffer from chronic migraine and are highly refractory, a significant percentage showed benefit with eptinezumab. Therefore, we recommend prescribing eptinezumab even in cases where patients have experienced failures with other anti-CGRP agents.
Disclosure: There are no conflicts of interest in this study.

EPO-327 | Comparison of efficacy and safety of anti-CGRP monoclonal antibodies across age groups: A multicenter, real-life study

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Background and Aims: Limited data on anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs)'s safety and efficacy across age groups exists. This study investigates efficacy and safety variations among age-related groups treated with mAbs and aims to identify response predictors.
Methods: This Italian, multicentric, prospective, observational study, part of the I-GRAINE registry, categorized patients into age quartiles (1: 18 – 40 years; 2: 40 – 50; 3: 50 – 57; 4: ≥57). Data were collected at baseline (T0) and at 3 (M3), 6 (M6), and 12 (M12) months, including monthly headache (MHD) and migraine (MMD) days, acute treatment intake in terms of days (AMD) and pills (AMP) and adverse events (AEs). At T0, psychiatric comorbidities, medication-overuse headache (MOH) and migraine type (episodic or chronic) were also assessed.
Results: One thousand eight hundred ninety migraine patients participated, predominantly females (80%), median age 49 years (IQR: 18 – 80), 62% were chronic, 58% had MOH and 32% psychiatric comorbidities. All age groups showed significant clinical improvements at M3, M6, and M12 ($p < 0.001$). No significant age-related differences in AEs ($p > 0.05$) were found. Females had favorable treatment responses (OR 1.3 to 3). Psychiatric comorbidity predicted positive response (OR 1.5 to 2.5) from month 6 onward. Chronic migraine (OR 2.1 to 5.8) and MOH (OR 1.8 to 4.7) indicated good response over 12 months.
Conclusion: Our findings confirm mAbs' consistent efficacy across all ages, indicating their suitability for patients with contraindications to oral preventives. Additionally, our study emphasizes considering clinical factors to predict patients' treatment response.
Disclosure: Nothing to disclose.

EPO-328 | The presence of positive signs for functional neurological disorders is associated with migraine frequency

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Background and Aims: Positive signs (PS) are the hallmark of functional neurological disorders (FND). However, in clinical practice, migraine patients without known FND may also present PS. Our aim was to evaluate the role of PS among migraine patients.

Methods: This study recruited migraine patients without a diagnosis of FND and treated at a tertiary outpatient clinic. We performed a clinical assessment for the following validated PS: give-away, co-contraction, sternocleidomastoid sign, trapezius elevation test, head flexion test, drift without pronation, Hoover I & II, spinal injury test, arm drop test, lip pulling sign, midline splitting, splitting of vibration sign and expressive behavior sign.

Results: Among the 72 recruited patients (mean age: 37.6 ±15.1yo; 75% female), 31 (43.1%) had PS, of which 20 had only one PS. Splitting of vibration was the most common PS (28% of the whole cohort). Compared with patients without PS, patients with PS were older, had more comorbidities, more headache days per month and more headache intensity at the consultation. Even after adjusting for age and comorbidities, the association between the presence of PS and the number of headache days per month remained significant (OR: 1.058; 95% CI (1.000; 1.119); $p=0.049$) as well as between the presence of PS and the subjective headache intensity at consultation (OR 1.277; 95% CI (1.030; 1.582); $p=0.026$).

Conclusion: PS are frequent among migraine patients, mostly as isolated signs. They are associated with headache frequency and intensity. Our findings highlight the complexity of the clinical spectrum of migraine.

Disclosure: None.

EPO-329 | The effectiveness of erenumab and galcanezumab is associated with a decrease in plasma CGRP levels

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Background and Aims: It is well established that calcitonin gene-related peptide (CGRP) is involved in the pathophysiology of migraine. Monoclonal antibodies may work by blocking the CGRP receptor (erenumab) or binding to circulating CGRP (galcanezumab). However, how plasma levels of CGRP would be modified with the aforementioned monoclonal antibodies has not been formally studied. Our research group developed a study to determine the influence of treatment with erenumab or galcanezumab on plasma levels of CGRP.

Methods: Seventeen patients (2M/15F) with clinical criteria for high-frequency episodic migraine or chronic migraine (CM) were studied. Previous preventive treatments with neuromodulators (topiramate or zonisamide) and the administration of onabotulinumtoxinA were allowed. Patients were treated with erenumab ($n=9$) or galcanezumab ($n=8$) at the discretion of the neurologist responsible for each patient's care. Plasma levels of CGRP were quantified at baseline and 6 months after follow-up. Statistical analysis was performed using Student's T test for paired samples.

Results: The mean age of the patients was 47.4±7.9 years. Thirteen patients (76%) had the diagnosis of CM. All patients with CM maintained preventive treatment with onabotulinumtoxinA. A statistically significant reduction in the level of CGRP was found at 6 months post-treatment (21.15±13.55 vs 15.04±8.05; $p=0.014$). No significant differences were found between patients treated with erenumab or galcanezumab. Patients experienced a significant reduction in the HIT-6 migraine disability scale (68.9±6.2 vs 63.9±6.9; $p=0.005$).

Conclusion: Our study suggests that the effectiveness of erenumab and galcanezumab in improving the impact of migraine on quality of life is associated with a significant decrease in plasma CGRP levels.

Disclosure: Nothing to disclose.

EPO-330 | Hyperexcitability and precipitation/resolution of migraines. A study by sound induced flash illusions in migraine cycle

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Background and Aims: Sound-induced flash illusions (SIFI) that critically depend on excitability of occipital cortex are reduced in migraine according to a condition of visual cortical hyperexcitability. Here we explored SIFI across the different phases of migraine cycle (ictal, pre- and post-ictal) to assess how changes in cortical excitability can be related to precipitation and resolution of migraine attacks.

Methods: SIFI were evaluated in 78 migraine without-aura patients: 18 interictal, 20 ictal, 20 pre- and 20 post-ictal) and in 25 healthy controls with no different age and sex distribution across groups. Visual stimuli (flashes) and sounds (beeps) were given in different combinations: single flash/multiple beeps to induce "fission" illusion (perception of multiple flashes), multiple flashes/single beep to reduce the perceived flashes ("fusion" illusion).

Results: Fissions were significantly reduced in all migraineurs vs healthy controls ($p:<.001$).The highest level of reduction was

observed in the ictal-migraineurs that was significantly lower with respect to all migraine-group ($p: < .001$ vs interictal, .01 vs pre- and post-ictal); pre- and post-ictal migraineurs perceived significantly less illusions with respect to the interictal group ($p < .01$).

Conclusion: Visual cortex of migraine patients was found to be hyperexcitable interictally. Excitability increases in preparatory phase (preictal), reaches its acme during the attack and then lowers toward attack-end. This suggest a role of cortical excitability in mechanisms of migraine precipitation and ending. Moreover, they shed also light on previous paradoxical RTMS evidence by our study in migraine cycle, supporting the interpretation that the inhibitory responses are likely due homeostatic inhibitory mechanisms.

Disclosure: Nothing to disclose.

EPO-331 | Impact of erenumab treatment duration on cutaneous allodynia in patient with episodic and chronic migraine

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Background and Aims: This study aims to evaluate the efficacy of erenumab, a monoclonal antibody targeting the CGRP receptor, over a one-year period in comparison to treatment lasting beyond one year, among patients with episodic and chronic migraine

Methods: In the episodic patient cohort, 25 received treatment over a one-year period (GroupA), while 16 were treated beyond one year, up to a maximum of 21 months (GroupB). Among chronic patients, 71 and 68 were allocated to GroupA and GroupB, respectively. Clinical data were collected at baseline (T0), end of treatment (T1), after an average of 3.5 months of treatment suspension (T2), and 3-month after resuming therapy (T3). Variables encompassed monthly headache and migraine days, acute medication usage, patients' disability, migraine impact, pain intensity (NRS scores) and intra-ictal allodynia (ASC-12 scores). Intra-group variations were assessed using Wilcoxon tests whereas between-group differences of clinical variables modification among timepoints were explored through linear and cumulative effect statistical models.

Results: Both chronic and episodic migraine patients exhibited significant reductions in most clinical variables between T0 and T1, with no differences between the two treatment groups. Notably, in chronic patients, GroupB demonstrated a reduction in ASC12 scores during treatment, maintaining the effect post-discontinuation. Conversely, GroupA showed no reduction during treatment, but a delayed effect during suspension. After resuming therapy all patients showed significant improvement with no differences between groups.

Conclusion: These findings suggest that erenumab could modulate nociceptive networks, contributing to allodynia symptom. However, to achieve and maintain this effect an extended treatment duration is required

Disclosure: Authors have nothing to disclose in relation to this work.

EPO-332 | White matter lesions (WML) in migraine with aura

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Background and Aims: Several studies report the presence of WML, also potential vanishing, on brain-MRI in patients with migraine, especially with aura (MA). There is no univocal interpretation: vascular hypothesis seems to be more probable, considering MA as a risk factor for WML and ischemic stroke, but these studies are biased, and there are controversies in literature about the prevalence of WML in MA, compared with general population.

Methods: To reduce vascular co-morbidities, old age, misdiagnosis, and drugs biases, we enrolled 177, highly-selected, young, subsequent patients, afferent to our Headache Center. In 146 patients we performed Brain-MRI studies at enrollment (T0), and 12 months (T1). We compared T0-MRI with MRI of 120 matched "healthy", non-migraineurs subjects, and we evaluated clinical features, co-morbidities, cardiovascular risk factors, and thrombophilia.

Results: We found WML in 29% of the MA patients, and in 27% of the controls. There was not statistically significant difference regarding the incidence of WML, and regarding MRI-WML between T0 and T1. We found neither association between MA features and side or number of lesions.

Conclusion: Available scientific literature about increased WML in MA patients is biased, limited, and controversial. Our study, both control-compared and longitudinal, of highly selected and relatively young patients, shows that MA patients have not more WML than healthy subjects, rejecting the proposed correlation between MA, as an independent cerebro-cardio-vascular risk factor, and ischemic stroke. We are currently performing a further analysis to demonstrate whether the presence of WML is related to other co-morbidities and risk factors.

Disclosure: Nothing to disclose.

EPO-333 | A novel ATP1A2 gene variant associated with atypical phenotype of SHM identified in a 6-year-old Italian female

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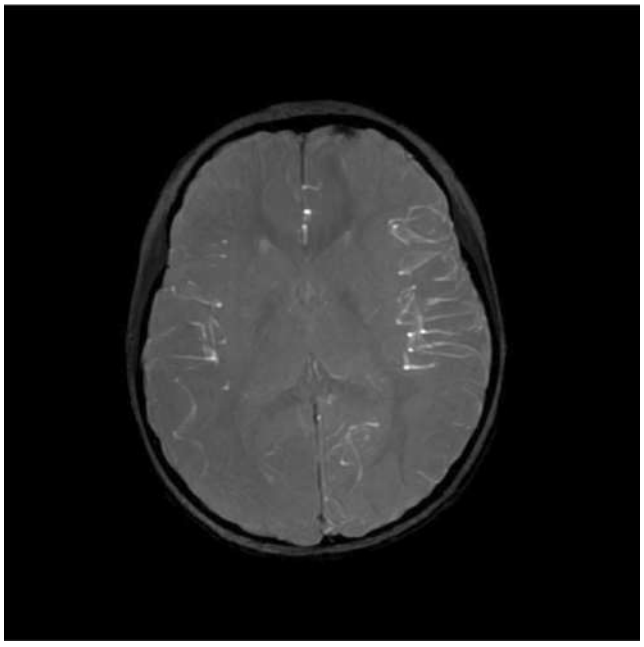
Background and Aims: Sporadic hemiplegic migraine (SHM) can be caused by a novel mutation in a gene that causes the familial form (CACNA1A,ATP1A2,SCN1A) or by inheritance of a gene mutation from a parent with "non hemiplegic" typical aura (2). Here, we describe a case of SHM, who carries a novel mutation in the ATP1A2gene.
Methods: A 6-year-old female, without family history of migraine, was admitted because she presented pulsating left-sided fronto-temporal headache, associated with photophobia, phonophobia, nausea/vomiting, right-sided weakness and paresthesia, dysarthria, ataxia, acute confusion. Two similar episodes of motor weakness without loss of consciousness and dysarthria, have occurred 3 and 6 months before that admission, with complete/spontaneous resolution after 3 days.
Results: Neurological examination showed confusion, moderate right hemiparesis and hypoesthesia. CT scan was normal; brain MRI showed a slightly prominent draining sulcal veins on the left hemisphere (Fig.1). The EEG showed alteration in the background activity with prominent involvement of the left hemisphere with continuous abnormal frontal and centro-temporal slow waves (Fig.2). SHM diagnosis was made. Sequence analysis detected a novel mutation, c.2456T>C p.(Leus819Ser), into the ATP1A2gene. Right-sided hemiparesis and hypoesthesia disappeared 6 days after the symptoms' onset, dysarthria lasted for 30 days before disappearing. Nimodipine and sodium valproate were introduced after the third attack and no further SHM episodes were recorded at 2-years follow-up.
Conclusion: Early-onset HM should be considered among the causes of focal neurological deficits. We found a novel ATP1A2 mutation, which could be responsible for the atypical phenotype, since different mutations in FHM genes partly account for clinical variability
Disclosure: Nothing to disclose.



Brain MRI swan axial sequence shows a slightly prominent draining sulcal veins on the left hemisphere.

EPO-334 | Headache in acromegaly: Not only a secondary disorder

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Background and Aims: Headache is frequently associated with pituitary disease, in which it can persist despite effective therapy. To better understand its actual secondary nature, we analyzed the headache characteristics in an acromegalic population.
Methods: 39 acromegalic patients, regularly followed for a long period, were examined to evaluate headache. Headache features were collected retrospectively through a structured interview. We carefully studied its time course and relationship with acromegaly, exploring the influence of adenoma and its treatment.
Results: Out of 39 patients, 27 (69.2%) reported headache. Twenty-one patients (53.8%) met the criteria for a primary headache: 14 had episodic migraine, 4 had chronic migraine while 3 patients presented tension-type headache. No trigeminal autonomic cephalalgia was observed. Six patients (15.4 %) fulfilled secondary headache criteria, with complete headache resolution after acromegaly treatment. Overall, a family history of headache was present in 20 cases (51.3%). Tumor size ($p=0.4$) and treatment of acromegaly ($p=0.67$) did not significantly influence the course of the disease.
Conclusion: In our population, only a small percentage (15.4%) of patients presented a picture consistent with a secondary headache that disappeared after acromegaly treatment. Interestingly, we observed a high prevalence of family history of headache and a high prevalence of migraine in acromegalic patients. A genetic predisposition to primary headache may be present: in this light, acromegaly, by favoring a pro-inflammatory state (1), might act as a trigger for migraine development. Due to the limited effect of acromegaly therapy on migraine course, headache may become disabling comorbidity, requiring careful evaluation and personalized management.
Disclosure: Nothing to disclose.

EPO-335 | 6-months-follow up of migraine patients treated with eptinezumab: Efficiency and tolerance

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Background and Aims: Since January 2023, eptinezumab, an intravenous anti-CGRP antibody, is authorized and reimbursed in France to treat severe episodic and chronic migraine patients. Our aim was to assess its efficiency and its tolerance "in real life" at 6 months, in an observational cohort in 2 hospitals (St Denis and Nimes university).
Methods: Patients with severe and chronic migraine, with failure of at least 2 preventive treatments and without cardiovascular comorbidities, were included if they had received 2 intravenous infusions of eptinezumab (every 3 months). The primary endpoint was change from baseline in monthly migraine days (MMDs) over weeks 1-24. Patients completed the following patient-reported outcomes: headache diary, intake of acute treatment for headache, 6-item Headache Impact Test (HIT-6) and the Hospital Anxiety and Depression scale (HAD). Other concomitant preventive treatments was also reported.
Results: 24 patients were included (M/F: 4/20), mean age (43.25 years old (SD 18.73), among them 16 had chronic migraine. The reduction of MMDs was 4.71 (SD 6.52). The >75% and >50% migraine responder rates were respectively 1% and 45.8%. No severe side effects were notified. The medication overuse rate decreased from 72.2% to 43.3%.
Conclusion: In this observational "real life" cohort, we highlighted that eptinezumab is efficient to prevent headaches in severe episodic and chronic migraine patients, with a reduction of medication overuse.
Disclosure: GB: advisory/Lecture for Lundbeck.

EPO-336 | Clinical presentation of occipital neuralgia in a headache unit

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Background and Aims: Occipital neuralgia is defined as a pain in one or more distributions of the occipital nerves. Case series of this entity are scarce. We aim to describe a large series of patients with occipital neuralgia.
Methods: Prospective registry of patients attended in a headache unit of a tertiary hospital. In those diagnosed with occipital neuralgia we collected demographic and clinical data.
Results: Between January-2008 and January-2024, we included 102 patients (78, 76.5% female) with occipital neuralgia out of 9388 (1.08%) attended in our unit. Age at inclusion was 58.2±16.4 years (range: 17-85) and latency from onset to diagnosis 23.7±47.5 months (1-360). In 39 cases (38.2%) pain affected right side, in 54 (52.9%) the left, and in 9 (8.8%) it was bilateral. 90 patients (88.2%) described a background pain, mostly oppressive (70 patients), and rated as 5.5±1.6 (2-10) on a verbal analogical scale (VAS). In 59 cases (57.8%) we registered exacerbations, mostly stabbing (36 patients) and rated as 8.1±1.5 (3-10) on a VAS. In 11 patients (10.8%) we recorded an event on the onset of pain (trauma in 10 cases). In 92 patients (90.2%) there was dysesthesia upon palpation of the scalp. Neuralgia affected in 18 cases (17.6%) the lesser occipital nerve. Before arriving at our unit 24 patients (23.5%) received an oral preventative with little or no effect.
Conclusion: Occipital neuralgia is a rare entity even in a headache unit. It is necessary to increase knowledge of this neuralgia to avoid diagnostic delays with the use of ineffective treatments.
Disclosure: No disclosure related to this work.

EPO-337 | Patterns of long-term response to anti-CGRP monoclonal antibodies in a 2-year prospective cohort of migraine patients

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Background and Aims: Real-world evidence on long-term response to monoclonal antibodies targeting calcitonin gene-related peptide (anti-CGRP mAbs) in migraine remains limited. Objective: To describe the long-term effectiveness and patterns of response at 2 years of anti-CGRP mAbs in a cohort of migraine patients.
Methods: Prospective unicentric observational study including high frequency episodic and chronic migraine patients treated with anti-CGRP mAbs. Demographics and efficacy variables (monthly headache days-MHD; monthly migraine days -MMD) were collected for 24 months. We defined 4 time points (6-12-18-24 months), matching to the follow-up visits. We defined sustained response (SR) as ≥50% reduction in MHD at all time points; quasi-sustained response (QSR) as a ≥50% reduction in MHD at 3 out of 4 time points; unsustained response (UR) as ≥50% reduction in MHD at 1-2 out of 4 time points; and never response (NR) as <50% at all time points.
Results: 148 patients were included (mean age 47 years [40.8-54], 82.4% (122/218) females). Median basal frequencies were 18 [14, 25.5] MHD, 13 [8, 18] MMD. After 24 months of follow-up, 31% (46/148) had SR; 26% (38/148) had QSR; 23% (34/148) had UR; and 20% (30/148) had NR. Long-term responders (SR+QSR) presented less allodynia (41.7%vs59.4%; $p < 0.04$) and higher baseline MHD

and MMD (median HDM 21 vs 15.5, $p < 0.014$; MDM 15 vs 12.5; $p < 0.016$) compared to non-long-term responders (UR+NR).

Conclusion: Over 50% of migraine patients treated with anti-CGRP mAbs exhibit a long-term response that is sustained over time. Understanding patterns of long-term response could help treatment decisions in the future.

Disclosure: LGD, RMDLV and VJG report no disclosures. EC has received honoraria from Novartis, Chiesi, Lundbeck, MedScape and his salary partially funded by Río Hortega grant Acción Estratégica en Salud 2017–2020, Instituto de Salud Carlos III (CM20/00217). He is a junior editor for Cephalalgia. AA has received honoraria from Allergan-AbbVie, Novartis, Chiesi. MTF has received honoraria from Allergan-AbbVie, Novartis, Chiesi and Teva. PPR has received, in the last three years, honoraria as a consultant and speaker for: AbbVie, Biohaven, Chiesi, Eli Lilly, Lundbeck, Medscape, Novartis, Pfizer and Teva. Her research group has received research grants from AbbVie, Novartis and Teva; also, Instituto Salud Carlos III, EraNet Neuron, European Regional Development Fund (001-P-001682) under the framework of the FEDER Operative Programme for Catalunya 2014-2020 - RIS3CAT; has received funding for RCT from AbbVie, Amgen, Biohaven, Eli Lilly, Novartis, Teva. She has been Honorary Secretary of the International Headache Society. She is in the editorial board of Revista de Neurologia. She is an associate editor for Cephalalgia, Headache, Neurologia, The Journal of Headache and Pain and Frontiers of Neurology. She is a member of the Clinical Trials Guidelines Committee of the IHS. She has edited the Guidelines for the Diagnosis and Treatment of Headache of the Spanish Neurological Society. PPR does not own stocks from any pharmaceutical company.

EPO-338 | Assessing the relative utility of a two headache "rescue rooms" and their respective treatment protocols

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Background and Aims: We compared the relative utility of two treatment algorithms in two separate outpatient clinic headache "rescue rooms" (RRs).

Methods: In two separate university-based RRs we compared clinical outcome, healthcare resource utilization (HRU), RR cost, patient satisfaction and mean RR time/visit using two different treatment algorithms. "A" involved primarily intramuscular (IM) administration of droperidol, and (B) involved an evidence-based sequence of therapies beginning with subcutaneously administered sumatriptan and proceeding as needed to intravenous ketorolac, metoclopramide, DHE/prochlorperazine, metoclopramide, magnesium, divalproex sodium and dexamethasone.

Results: 100 consecutive patients were treated according to algorithm A and 100 according to algorithm B. Clinical outcomes, RR costs, decline in ER utilization and patient satisfaction were similar in the two groups. Mean time required for an RR visit was less in group A than in the group B (47 minutes versus 127 minutes). None of the 100 group A patients treated with IM droperidol exhibited QTc prolongation.

Conclusion: An outpatient headache "rescue room" conveys a high level of clinical efficacy, decreased ER utilization, and a high degree of patient satisfaction. Droperidol IM appears to be a particularly safe, effective and efficient treatment for use in this setting.

Disclosure: Nothing to disclose.

Movement disorders 3

EPO-339 | Transcranial sonography evaluation in patients with cerebellar neurodegenerative ataxias

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Background and Aims: Cerebellar neurodegenerative ataxias are disorders affecting the cerebellum and its pathways. Transcranial sonography (TCS) is widely used for the evaluation of brain parenchymal structures in various diseases especially in neuropsychiatric and neurodegenerative diseases. The objective of this study was to investigate TCS characteristics of patients with neurodegenerative cerebellar ataxias.

Methods: We included a total of 74 patients with cerebellar degenerative ataxia, 36.5% had autosomal dominant, 20.2% with autosomal recessive pattern of inheritance, and 43.3% had sporadic onset. Standardized ultrasonographic planes were used for the identification of brain structures of interest. All patients were clinically evaluated using SARA, INAS, neuropsychological, and psychiatric scales.

Results: The brainstem raphe was discontinued in 33.8% of patients. The substantia nigra (SN) hyperechogenicity was identified in 79.7%. Third and fourth ventricle enlargement had 79.7% and 45.9% of patients, respectively. A positive and statistically significant correlation was found between SN hyperechogenicity with dystonia ($p < 0.01$), rigidity, and dyskinesia ($p < 0.05$). Higher SARA total score statistically significantly correlated with the larger diameter of III ($r = 0.373$; $p = 0.001$) and IV ventricle ($r = 0.324$; $p = 0.005$).

Conclusion: Hyperechogenicity of substantia nigra has been linked to extrapyramidal signs, while raphe discontinuity to depression. Furthermore, severity of ataxia has positively correlated with III and IV ventricle diameter indicating brain atrophy.

Disclosure: None.

EPO-340 | The genetic landscape of Parkinson's disease in an Italian cohort and the need for a standardized approach

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Background and Aims: Advances in genetics have expanded the known spectrum of Parkinson's disease (PD)-related genes, and broadened access to genetic analysis, allowing for rapid sequencing of many disease-associated genes and unraveling a high genetic variability. Our study aimed to determine the genetic characteristics in an Italian cohort of PD patients.
Methods: PD patients with family history, early-onset (≤55 years), and/or atypical phenotype underwent genetic analysis through an NGS panel containing 45 known-PD-causative genes, coupled with MLPA when needed. Variants were interpreted according to ACMG criteria, and reports were categorized as positive (≥1 variant, with definite genetic diagnosis), inconclusive (≥1 variant, insufficient for genetic diagnosis), or negative. Heterozygous pathogenic/likely-pathogenic variants in dominant genes and biallelic pathogenic/likely-pathogenic variants in recessive genes were considered positive. GBA1 variants were considered pathogenic and classified based on PD-development risk. Inconclusive reports underwent reassessment: heterozygous pathogenic variants in recessive genes and VUS with genotype-phenotype mismatch were considered negative; VUS not otherwise interpretable were clarified through family segregation studies.
Results: We recruited 197 patients. 74 (37.6%) reports revealed ≥1 variant. Of the inconclusive reports, after reinterpretation, 1 was considered positive, while 22 negative. Eventually, positive reports were 36 (18.3%), and inconclusive 16 (8.1%). The most common diagnoses were GBA1 (23, 11.7%), LRRK2 (5, 2.5%), PRKN (4, 2.0%), PINK1 (1, 0.5%) FBXO7 (1, 0.5%). The gene with the most reported variants was GBA1.
Conclusion: Our results contribute to a more in-depth understanding of PD genetic spectrum in Italian patients and underscore the importance of a standardized approach for the interpretation of genetic findings.
Disclosure: Nothing to disclose.

EPO-341 | Stigma among Tunisian patients with Parkinson's disease: The hidden side of the burden

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Background and Aims: Stigma among patients with Parkinson's disease (PD) is multilayered and a determinant of the quality of life. The social and cultural components can modulate efficiently this aspect. Thus, we aim to investigate stigma among PD patients in Tunisia in order to boost their quality of life.
Methods: We have conducted a cross-sectional study including patients with PD who presented to our clinic for regular follow-up from October to December 2023 and consent to participate. We identified general and motor characteristics using UPDRS-III score. We used MMSE for cognitive function and SCOPA-Aut questionnaire to identify dysautonomic features. Stigma was assessed based on the 8-item Stigma Scale for Chronic Illness (SSCI-8) and we used the raw summed score ranging from 8 to 40.
Results: We included 62 patients (sex-ratio = 1.4; mean disease duration of 11; 62%; illiterate). Mean UPDRS-III score was 23.6±5 with tremor-dominant PD being the most frequent (56.5%), followed by postural instability gait disorder (PIGD) phenotype (24%). Mean MMSE score was 21.4±6. Dysautonomia was noted in 66% of cases with gastrointestinal dysfunction being the most prominent (60%). Mean SSCI-8 score was 66.3 [40; 77]. SSCI score correlated positively with illiteracy ($p = 0.023$), higher UPDRS-III score ($p = 0.001$), PIGD-phenotype ($p = 0.048$), tremor-dominant phenotype ($p = 0.026$), cognitive dysfunction ($p = 0.036$) and gastrointestinal dysfunction ($p = 0.042$).
Conclusion: Stigma is frequent and severe among Tunisian patients and exceeds the rates reported from Europa and North America. It is conditioned by educational level, motor and non-motor features. Our findings highlight the necessity of a holistic approach beyond the motor aspect. Raising awareness is mandatory to pave the way for a more tolerable environment.
Disclosure: None.

EPO-342 | Suvecaltamide metabolites are CaV3 modulators and contribute to pharmacological effect

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Background and Aims: T-type calcium (CaV3) channels regulate neuronal excitability and are thought to play a key role in mediating pathological tremor-producing oscillations in conditions like essential tremor (ET). Suvecaltamide (JZP385), a potent, selective CaV3 modulator, improved function in adults with moderate-to-severe ET in a phase 2 study (T-CALM/NCT03101241). We

present potency-concentration relationships and combined pharmacological effects for suvecaltamide and its 2 active metabolites (JZZ05000034 = M01, JZZ05000035 = M02; total active moiety [TAM]).

Methods: Automated patch-clamp recordings in HEK293 cells stably overexpressing human CaV3 subtypes were used to generate steady-state inactivation curves with/without analyte treatments; concentration-response curves used protocols enriching for resting or inactivated channel states. Off-target effects were tested in enzyme and receptor binding panels.

Results: All analytes inhibited all CaV3 channels in a concentration- and state-dependent manner (Table) and slowed recovery from inactivation. Selectivity (<50% [10 μM]) was demonstrated for all targets/analytes, except suvecaltamide at CB2 receptor (IC50 = 5.3 μM) and M01 at human PPAR-gamma (54% at 10 μM) and guinea-pig adenosine transporter (IC50 = 2.9 μM), which are likely not relevant at projected therapeutic doses.

Table. Suvecaltamide and Its Active Metabolites Inhibited Ca_V3 in a Concentration- and State-Dependent Manner

Mean Potency (IC_{50}, nM) and State Dependency	Suvecaltamide	M01 (JZZ05000034)[a]	M02 (JZZ05000035)[a]
	(n=25[b])	(n=7[b])	(n=6[b])
Partially Inactivated $Ca_V3.1$ ($V_{0.5}$)	58	40	1050
Resting $Ca_V3.1$	3628	2958	>30,000
Fold difference[c]	98	110	>50
Partially Inactivated $Ca_V3.2$ ($V_{0.5}$)	365	264	8540
Resting $Ca_V3.2$	8015	9607	>30,000
Fold difference[c]	37	46	>4
Partially Inactivated $Ca_V3.3$ ($V_{0.5}$)	37	20	878
Resting $Ca_V3.3$	1271	1090	25,501
Fold difference[c]	40	68	35

[a]Metabolite of suvecaltamide.
[b]Refers to number of individual assays performed (n=4 wells/assay).
[c]Mean of individual ratios of resting:partially-inactivated Ca_V3 IC_{50} values.
IC_{50}, concentration resulting in 50% inhibition of peak current.

Suvecaltamide and Its Active Metabolites Inhibited CaV3 in a Concentration- and State-Dependent Manner.

Conclusion: Suvecaltamide and its active metabolites demonstrate selective, state-dependent modulation of all CaV3 subtypes with markedly higher affinity for partially inactivated channels. Modelling TAM shows that, at clinically relevant concentrations, suvecaltamide and its metabolites may selectively inhibit channels enriched under hyperexcitable conditions (eg, pathological neuronal firing) while sparing channels involved in normal signalling, which may contribute to a more optimal clinical profile. Two ongoing phase 2 studies are evaluating suvecaltamide in adults with moderate-to-severe ET (NCT05122650) or residual Parkinson's disease tremor (NCT05642442).

Disclosure: Supported by Jazz Pharmaceuticals. All authors are full-time employees of Jazz Pharmaceuticals who, during this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc.

EPO-343 | Reprogramming options after IPG replacement in STN DBS for Parkinson's disease: Is the upgrade worth the cost?

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Background and Aims: People with Parkinson's disease (PD) having motor fluctuations can be treated with deep brain stimulation targeting the subthalamic nucleus (STN DBS)1. The lifetime of non-rechargeable implantable pulse generators (IPG) requires battery replacements every 3-5 years2. Recently, IPGs with more programming features have become readily available.

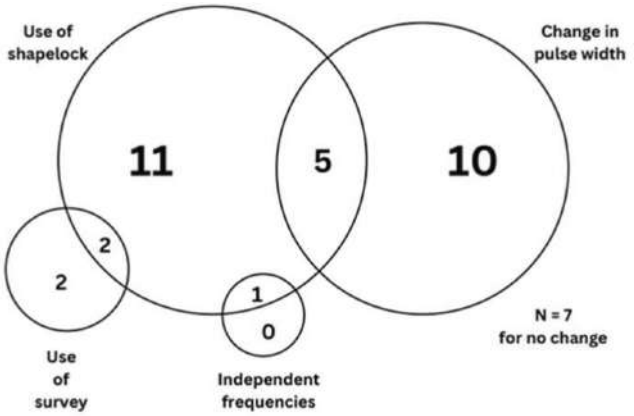
Methods: This double-blind cross-over randomized study recruited consecutive PD patients undergoing IPG replacement surgery in whom the Activa PC was replaced with a Percept PC (Medtronic, Minneapolis, MN, USA). Reprogramming was done to reduce stimulation-induced side effect and/or to lower battery consumption (i.e. avoiding bipolar or interleaving settings). Change of active contact could only be done based on the Brainsense Survey (contact with highest beta peak). Bipolar and interleaving settings were replaced by monopolar, double, triple or quadruple monopolar settings (Shapelock). Pulse width could be shortened beyond 60 mcsec. Change in frequency was only allowed when switching to independent frequencies per hemisphere.

Results: 19 patients (38 STNs) were included (four females). In 19 STNs (50%), the stimulation settings were changed from bipolar or interleaving to a (multiple) monopolar configuration using the Shapelock feature. Pulse width was shortened in 15 STNs (39.5%). A change in contact was done in 4 STNs (10.5%) after an average of 6.5 years on another contact. Eleven patients (57.9%) preferred the novel stimulation paradigm, while 6 patients (31.6%) preferred their established program. Two patients were undecided.

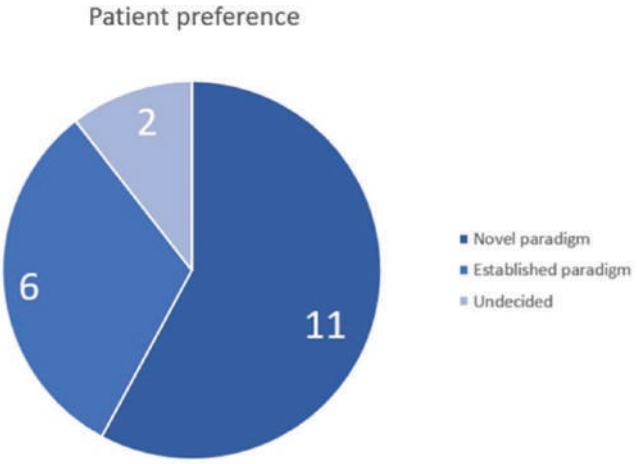
Conclusion: DBS reprogramming using novel additional features after IPG replacement can lead to improved outcomes and/or reduced battery consumption in a sizable proportion of patients.

Disclosure: AL received honoraria and research support from Medtronic. SK received honoraria and research support from

During the baseline visit, patients underwent reprogramming in medication-off condition using novel stimulation features. They were randomized between the established and the novel stimulation paradigm for a month. Thereafter, they were crossed over.



Features used when reprogramming after battery replacement surgery.



Pie chart of patient preference between the novel stimulation paradigm ($n = 11$) and the established stimulation paradigm ($n = 6$). Two patients did not have a preference between the two programs.

Medtronic. AF received honoraria and research support from Medtronic.

EPO-344 | Incidence and risk factors of glaucoma in Parkinson's disease: A population-based study

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Background and Aims: The potential association between Parkinson's disease (PD) and glaucoma remains unclear. We aimed to investigate glaucoma incidence in PD patients, explore the differences by age and sex, and identify potential risk factors for glaucoma in Korean PD patients.

Methods: We conducted a comprehensive study using data from the Korean National Health Insurance System database, encompassing 97% of the Korean population from 2002 to 2019. We calculated the incidence of newly developed glaucoma among PD patients and estimated the adjusted hazard ratio (aHR) with 95% confidence intervals (CI) using Cox proportional-hazards models to elucidate glaucoma risk factors.

Results: Among 176,673 patients with PD, 9,718 patients developed glaucoma during the follow-up period (3,670 men and 6,048 women), yielding an overall incidence of 8.02 per 1,000 person-years. Stratified by age group and sex, we observed an increasing incidence with age until 80, with minimal sex differences. In particular, older age (aHR = 1.78, 95%CI: 1.55-2.05 in the 60s), diabetes mellitus (DM) (aHR = 1.19, 95%CI: 1.14-1.25), and hyperlipidemia (aHR = 1.06, 95%CI: 1.01-1.10) emerged as significant risk factors for glaucoma in PD patients.

Conclusion: Our study suggests that PD patients face an elevated risk of glaucoma compared to the general population, with no substantial sex differences. Older age, the presence of DM, or hyperlipidemia were identified as risk factors for glaucoma in PD patients. These findings emphasize the significance of considering regular ophthalmologic evaluation as part of their management in PD patients, particularly among those with a history of DM or hyperlipidemia, regardless of age or the presence of visual symptoms.

Disclosure: Nothing to disclose.

EPO-345 | Neuroleptic malignant syndrome in Huntington's disease

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Background and Aims: Huntington's disease (HD) is often treated with tetrabenazine (TBZ) and dopamine receptor blocking agents (DRBAs). Few data are available regarding the likelihood of neuroleptic malignant syndrome (NMS) development in HD patients. In this article we investigate the main risk factors that lead to the development of NMS in HD patients, and discuss the measures to avoid this potentially life-threatening condition.

Methods: We gathered data from the 5th data set of the Enroll-HD study (PDS5), a literature review, and described a case report. We selected HD patients treated with TBZ and/or DRBAs, who presented at least one of the core symptoms of NMS, therefore including atypical forms.

Results: We identified 12 cases of NMS in HD patients in total, three of which showed atypical forms of NMS. Only one out of 5108 patients, treated with DBRA and/or TBZ, was identified in the

Enroll-HD dataset. All patients developed NMS in conjunction with drug-therapy changes, with average onset within a month, except one patient during ongoing treatment with TBZ. Five out of the twelve patients developed NMS while undergoing TBZ. Overall, the patients showed a long clinical history of HD.

Conclusion: NMS is likely underestimated in HD patients partly due to missed diagnosis of cases with atypical presentation. Therefore, careful monitoring of symptoms may allow early detection of this potentially fatal condition. Abrupt changes in therapy, are the main risk factors for NMS development, hence the importance of periodic revision of treatment and cautious drug management, especially in advanced stages of HD.

Disclosure: Nothing to disclose.

EPO-346 | Deep brain stimulation as an effective therapy in atypical two stage evolution adult-onset KMT2B-related dystonia

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Background and Aims: In KMT2B-related dystonia (DYT-KMT2B), onset occurs typically, in the first decade of life with focal involvement progressing to generalized dystonia, prominently affecting the cranial, cervical and bulbar regions. Later onset has been reported, with upper body parts and oromandibular involvement. We report an adult-onset case of severe DYT-KMT2B with improvement after bi-pallidal deep brain stimulation (GPi-DBS).

Methods: We report the phenomenology and genetic data of an adult with DYT-KMT2B.

Results: Cervical dystonia initiated at 33y, evolving through two phases: an initial calm period and a subsequent exacerbation phase. While botulinum toxin injections provided relief from 33 to 47 years, the dystonia significantly worsened from 47 to 49 years, manifesting a cranio-caudal progression with blepharospasm, oromandibular dystonia, upper limb and trunk dystonia, and a myoclonus component (Video). Chewing difficulties necessitated a gastrostomy. The Burke-Fahn-Marsden Movement and Disability Subscales (BFMMS and BFMDS) scores were 30 and 21, respectively, with ineffective conventional therapies and botulinum toxin injections. Genetic analysis unveiled a heterozygous variant in KMT2B: NM_014727.2:c.631T>G/p.(Cys211Gly). GPi-DBS led to a postoperative dystonic crisis, requiring a one-week stay in intensive care. Rapid clinical improvement ensued within a month, with BFMMS and BFMDS scores reduced to 5 and 1, respectively (monopolar stimulation,3.2 mA, 210 μs pulse width, 130 Hertz). Although oral feeding resumed, blepharospasm persisted, prompting medication discontinuation.

Conclusion: Only a few studies demonstrate the benefit of GPi-DBS in adult-onset DYT-KMT2B. Our case highlights that GPi DBS appears to be as effective in adult-onset as in childhood-onset DYT-KTM2B and emphasized the importance of postoperative monitoring.

Disclosure: The authors declare that there are no conflicts of interest relevant to this work.

EPO-347 | Striatal dopamine correlates to spatial gait parameters in dual task conditions

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Background and Aims: Parkinson's disease (PD) is clinically defined by motor symptoms and the underlying mechanism is determined by loss of dopaminergic neurons in the substantia nigra, leading to dopamine depletion in the basal ganglia circuit. Despite this, the MDS-UPDRS-III, the standard motor assessment, does not correlate with the dopaminergic deficit. The aim of this study was to investigate the relationship between dopamine uptake and motor changes using inertial sensors.

Methods: Forty de novo PD patients were enrolled. They underwent a comprehensive motor assessment including MDS-UPDRS-III and digital assessment of gait parameters in normal, fast and dual-task conditions using mobile health technologies (MHT) in a supervised setting. All patients underwent 123I-FP-CIT-SPECT imaging to quantify dopaminergic uptake. The relationship between motor parameters and dopamine binding was assessed using partial correlations corrected for age, sex and height.

Results: No correlation was observed between MDS-UPDRS-III and dopamine uptake in the striatal circuit. Step length in single and dual task conditions correlates directly with MDS-UPDRS-III (p: 0.001 R: 0.376), while reduced step length in dual task conditions is associated with reduced DAT availability in both putamen and pallidum (p: 0.022 and 0.013 with R: 0.417 and R: 0.428).

Conclusion: Dopamine depletion is known to be the pathological mechanism underlying motor changes in PD. Our study suggests that the use of more sensitive parameters, specifically spatial parameters in dual task conditions, can identify this relationship.

Disclosure: Nothing to disclose.

EPO-348 | Efficacy of safinamide in Parkinson's disease: Focus on gender differences

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Background and Aims: There is an increasing evidence of gender differences in the epidemiology and clinical manifestation of both motor and non-motor symptoms of Parkinson's disease (PD). Nevertheless, few data are available on gender differences in the

response to antiparkinsonian drugs. Safinamide has a unique dopaminergic and non-dopaminergic mechanism of action that might improve patients' care in both sexes.

Methods: The gender differences in safinamide efficacy were investigated using the data from two clinical trials, studies SYNAPSES (Europe) and XINDI (China).

Results: 616 (38%) out of 1610 patients enrolled in the SYNAPSES study were women and 994 (62%) men, while in the XINDI study 128 (42%) out of 305 patients enrolled were women and 177 (58%) men. Safinamide significantly improved motor symptoms ($p<0001$), motor fluctuations ($p=0.0007$) and quality of life ($p=0.0014$) in both genders, with a good safety profile and without requiring any change in the concomitant dopaminergic therapy. Moreover, safinamide improved three out of four PD cardinal symptoms and reduced tremor in females and rigidity in males, the two peculiar gender features of PD.

Conclusion: Safinamide, administered as add-on therapy in fluctuating PD patients, improved motor symptoms and motor complications without increasing troublesome dyskinesia in both male and female subjects. Further prospective studies specifically addressing potential gender differences in response to PD therapies are needed to develop tailored management strategies.

Disclosure: Carlo Cattaneo is an employee of Zambon SpA; Ivan Marjanovic is a consultant of Zambon SpA.

EPO-349 | Navigating the maze: Unmasking the influence of cerebral small vessel disease on non-motor symptoms burden in PD

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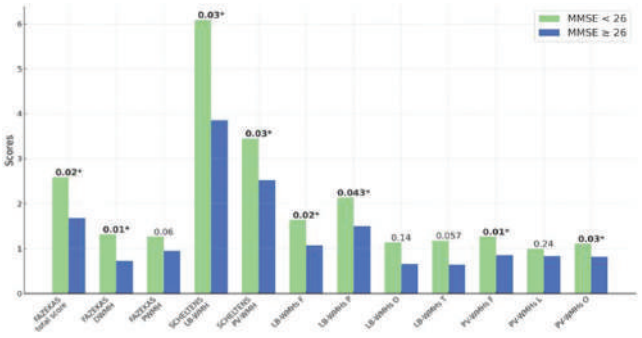
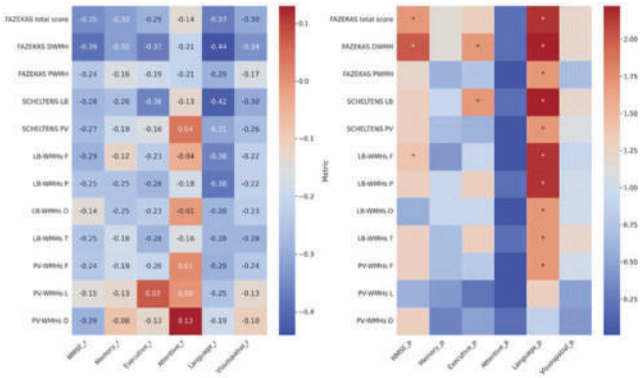
Background and Aims: Managing Parkinson's disease (PD) poses a significant challenge, primarily due to the prevalence of non-motor symptoms (NMS). While the impact of Lewy-Body and Amyloid pathology on PD-related cognitive impairment is known, the role of vascular co-pathology remains uncertain. This study explores potential links between white matter hyperintensities (WMH) and specific NMS-clusters.

Methods: A cohort of 66 PD patients underwent comprehensive assessments, including clinical evaluations of both motor and NMS, neuropsychological tests covering five major cognitive domains and brain 3.0T magnetic resonance imaging. The severity and distribution of WMH were visually rated using Fazekas and Scheltens scales. Statistical analyses, including Mann-Whitney tests and Spearman correlations, were employed to assess associations between WMH burden, cognitive functions, and NMS.

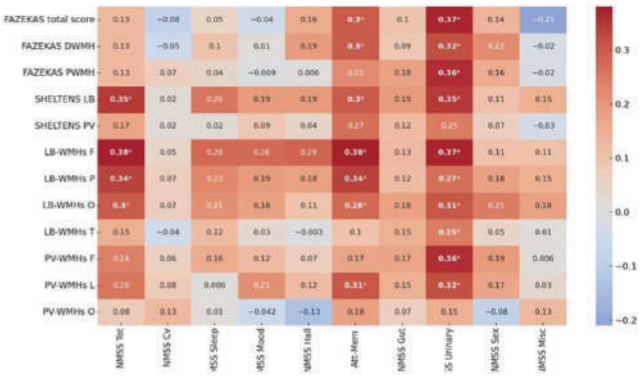
Results: Prominent connections with NMS, particularly urinary dysfunction, were observed in the frontal and parietal lobes. Significant correlations were found between WMH burden and cognitive functions. MMSE scores negatively correlated with Fazekas WMH total



Examining two groups (MMSE < 26, $n=22$; MMSE > 26, $n=44$), this chart reveals significant associations between lower MMSE scores and increased Fazekas and Scheltens total burden and sub-scores especially in the deep lobar areas.



The left heatmap shows Spearman correlation coefficients exploring the interplay between cognitive domains (including MMSE) and white matter lesion severity and distribution; the right one instead highlights *p*-values post-Benjamini correction.



This heatmap illustrates Spearman correlation coefficients (r) examining the relationship between the vascular burden of WMH (measured by Fazekas and Scheltens scales) and various domains of NMS assessed by NMS scale.

and frontal deep white matter loads. Executive dysfunction was linked to greater Fazekas and Scheltens lobar WMH loads, while language impairment was associated with frontal and parietal WMH burdens.

Conclusion: Our findings suggest significant associations between radiological WMH sites and distinct NMS that might be unintentionally overlooked in clinical contexts. We propose a cortical-subcortical "disconnection syndrome," indicating disruptions in communication between different cortical and subcortical regions. This syndrome may play a crucial role in the development or progression of distinct non-motor and cognitive patterns in PD. Recognizing regional-specific white matter damage enriches cognitive and NMS assessments, offering refined options for personalized medicine.
Disclosure: Nothing to disclose.

EPO-350 | Beta power circadian modulation in patients with Parkinson's disease and conventional or adaptive deep brain stimulation

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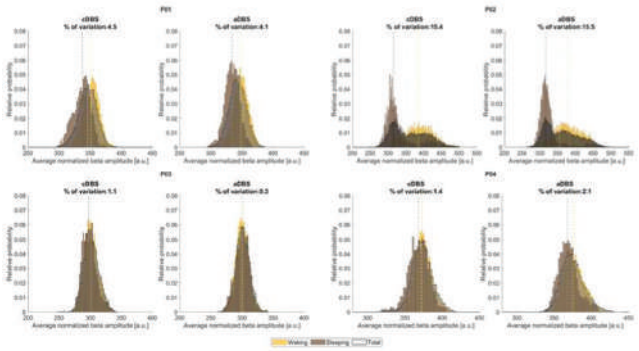
Background and Aims: Increased beta power oscillations in the subthalamic nucleus (STN) are a key feature of Parkinson's disease (PD). However, their physiological contribution to motor and non-motor tasks, such as the sleep-awake cycle, is still poorly understood, and may influence the effect of deep brain stimulation (DBS), both in conventional (cDBS) and adaptive (aDBS) modes. The aim of the study is to investigate the impact of cDBS and aDBS on sleep-wake subthalamic beta power fluctuations in PD
Methods: We acquired subthalamic local field potentials (LFP) in four patients with idiopathic PD and implanted with the AlphaDBS device (Newronika SpA). This device can operate in either cDBS, with constant stimulation parameters, or aDBS, adjusting linearly the current amplitude with respect to subthalamic beta power. Patients were recorded consecutively for 10 days in both stimulation modes and with unchanged drugs doses. We calculated the amplitude of the STN-LFP in a patient-specific frequency range centered around the most prominent beta peak with 1 min resolution and analyzed the distribution of the beta amplitude separately for the sleeping and waking time
Results: One patient showed a median reduction in subthalamic beta power during sleep compared to waking hours of 15%, under both



Sleep-awake beta power distribution.

stimulation modes. All other patients had sleep-awake beta power modulation <5% in both stimulation modes. The stimulation modes did not affect the sleep-awake modulation of subthalamic beta power.
Conclusion: Our preliminary data show a variable modulation of subthalamic beta power during sleep-wake cycle in parkinsonian patients with comparable impact of cDBS and aDBS
Disclosure: Nothing to disclose.

EPO-351 | Effects of loading, tapping performance, and ballistic movements on tremor features in patients with essential tremor

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Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy

Background and Aims: In recent years, a comprehensive set of neurophysiological tests, including the loading test, tapping performance analysis, and the evaluation of response to ballistic movements, has been proposed to formulate laboratory-supported criteria for diagnosing functional tremor. Our aim is to comprehensively evaluate the effects of these manoeuvres on tremor features in patients with essential tremor (ET).
Methods: ET patients were evaluated using a standardized clinical scale, the Fahn-Tolosa-Marin Tremor Rating Scale (FTM-TRS). A comprehensive tremor evaluation at baseline and during loading, finger tapping (at 1, 3, and 5 Hz), and ballistic movements was conducted using an optoelectronic system. Data were analyzed through non-parametric Friedman Analysis of Variance (ANOVA).
Results: Thirteen ET patients were included (6 females, 64.9±17.6 years), with a mean disease duration of 15.6±10.9 years and a FTM-TRS score of 20.6±10.1. At baseline, postural tremor had a mean frequency of 5.98±1.42 Hz and a mean amplitude of 0.053±0.036 GRMS^2. ANOVA unveiled a difference in amplitude ($p = 0.03$), with lower values during 1 Hz finger-tapping movements, compared to the other conditions. Moreover, we found an inverse correlation between baseline tremor amplitude and the reduction in tremor amplitude during 1 Hz tapping ($p = 0.021$). No variation

in tremor frequency was revealed across different manoeuvres ($p = 0.62$).

Conclusion: Gaining insights into the impact of loading, tapping performance, and ballistic movements on tremor features in patients with ET holds relevance for clinical applications, especially within the diagnostic process. Expanding the analysis to larger patient samples could contribute to a deeper understanding of how clinical factors influence the observed effects.

Disclosure: Nothing to disclose.

EPO-352 | Altered motor cortex excitability in Parkinson's disease patients

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Background and Aims: In Parkinson's disease (PD), pathological activity of basal ganglia-thalamocortical circuits affect neural networks subtending motor and non-motor symptoms. This disruption could be unveiled by exploring primary motor cortex (M1) with transcranial magnetic stimulation (TMS). We extensively assessed a combined neurophysiological-neuropsychological evaluation in a cognitively spared population of PD patients (PDp).

Methods: 15 PDp and 11 healthy controls (HC) were enrolled. Fatigue was evaluated with Parkinson Fatigue Scale (PFS-16), attention was measured with computerized Sustained Attention Task (SAT) and Stroop Task (ST). Global cognition in PDp was evaluated with Montreal Cognitive Assessment (MoCA). Following TMS of dominant M1, we assessed Resting Motor Threshold (RMT), Motor Evoked Potential (MEP) amplitude and Silent Period (SP) duration. Intracortical activity was explored with Short-Interval Intracortical Inhibition (SICI), Intracortical Facilitation (ICF) and Long-Interval Intracortical Inhibition (LICI).

Results: Mean MoCA score was 24.2 (SD $\pm$3.3). PFS score was higher in PDp ($p = 0.03$). Reaction times were longer in PDp in SAT ($p = 0.002$), ST-incongruent condition and ST-interference ($p = 0.005$ and $p = 0.036$, respectively). In PDp, RMT was higher ($p = 0.43$), MEP amplitude was lower ($p = 0.26$), SP duration was shorter ($p = 0.001$) and LICI at 100 ms interstimulus interval (ISI) was reduced ($p = 0.013$). SICI at 2 and 3 ms ISI was disrupted (MEPs were facilitated) in both groups. No difference was observed in ICF.

Conclusion: Neurophysiological findings suggest that M1 hypoexcitability and altered GABAB activity possibly affect motor control and attention in PD. Aging-related GABAA circuits disruption we found in both groups may contribute to fatigue perception in PD.

Disclosure: Nothing to disclose.

EPO-353 | The influence of deep brain stimulation on saccades in Parkinson's disease: A transversal and longitudinal study

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Background and Aims: Saccades are disrupted in Parkinson's disease (PD), both involuntary (i.e., saccadic intrusions [SI]), reflexive (i.e., prosaccades [PS]) and more voluntary (i.e., antisaccades [AS]) saccades, eventually deteriorating vision. Deep Brain Stimulation (DBS) seems to improve saccadic parameters in PD patients. There is need to evaluate if such effect is sustained over time and if saccades' planes are individually influenced by DBS.

Methods: We recruited 23 PD patients (14 males, mean age 65$\pm$8.2 years) with bilateral subthalamic nucleus-DBS that underwent eye-tracking assessment at baseline and one year follow-up, both with DBS on- and off-state. Number of SI, velocity, latency and gain of PS and AS, and AS errors/corrected errors were analysed.

Results: At baseline, when compared to off-state, DBS significantly decreased SI number, increased the gain/velocity of correct horizontal/vertical AS and the gain of corrected horizontal/vertical errors, while decreasing the latency of incorrect vertical AS. At one year follow-up, DBS increased the gain of horizontal PS, the gain/velocity of correct horizontal/vertical AS and the gain of corrected horizontal/vertical errors, while decreasing the latency of correct/incorrect vertical AS. Saccadic parameters remained unchanged in off-state after one year and there was no interaction between DBS status and time of assessment.

Conclusion: DBS significantly improves fixation instability, speeds up and widens predominantly voluntary eye movements in PD patients, in addition to accelerate their start strictly along the vertical plane. Remarkably, these effects are sustained over time. This data highlights the overlooked benefit of DBS on vision of PD patients.

Disclosure: Nothing to disclose.

Movement disorders 4

EPO-354 | HeBA-online Parkinson disease risk factors survey diffusion: Digital versus traditional approaches

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Background and Aims: The Healthy Brain Ageing (HeBA) is a European multicenter project using innovative approaches for early detection and intervention in Parkinson's disease. In the first phase, the project aims to gather comprehensive data through online surveys. This study specifically focuses on evaluating and comparing the effectiveness of various dissemination strategies, particularly digital platforms like META's platforms and Google Ads against traditional media in collecting data from Catalonia's population.

Methods: We gathered data from META campaigns (Facebook, Instagram), Google Ads, and traditional media (radio, press, online press, and television). Analyzed metrics included clicks for HeBA online survey in META and Google, along with audience size for traditional media. Quantitative analysis assessed campaign clicks, and audience engagement trends.

Results: In the context of HeBA diffusion strategies, digital dissemination methods, such as META campaigns, achieved a total of 102,248 clicks (Figure 1A). For Google Ads campaigns, there were a total of 2,089 clicks to the HeBA survey (Figure 1B). Notably, our traditional media campaigns reached an impressive overall audience of approximately 97,432,694. Newspapers emerged as the medium with the highest reach (Figure 1C). Additionally, in the HeBa survey response distribution, we obtained 6,943 complete responses and 6,749 partial responses out of a total of 13,692 responses collected between June 13, 2022, and January 15, 2024 (Figure 1D).

Conclusion: The HeBA Project's media strategy effectively merges the broad audience reach of traditional media with the targeted engagement of digital platforms, providing a valuable blueprint for future health communication campaigns.

Disclosure: Nothing to disclose.

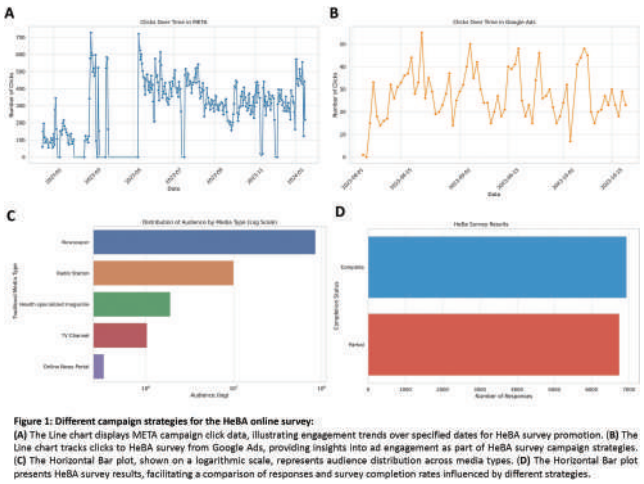

FIGURE 1 Different campaign strategies for the HeBA online survey.

EPO-355 | Clinical features and outcomes of neuroacanthocytosis: A single center experience

Z. Huseynli; B. Samanci; E. Sahin; S. Yusifli; B. Bilgic; H. Hanagası
Neurology, Istanbul Unıversity, Topkapı, Istanbul, Turkey

Background and Aims: Neuroacanthocytosis (NA) is a rare disorder with multisystem involvement, and characterized by progressive basal ganglia degeneration. We aimed to report clinical characteristics and outcomes of NA patients in a Turkish cohort.

Methods: Eleven patients with NA diagnosis of our database were included. Clinical characteristics, laboratory and MRI examinations were recorded.

Results: The mean age of the patients (5 male, 6 female) was 39.5±3.65 years, with symptom onset at 29±4.86 years. Mean follow-up duration was 3.9±2.1 years. Psychiatric symptoms ($n=4$), tics ($n=3$), dystonia ($n=2$), chorea ($n=1$), seizure ($n=1$) were noted as first symptoms. Self-mutilation were observed in 5 patients. In the follow up, vocal ($n=5$) and motor tics ($n=3$), choreiform movements ($n=11$), dystonia ($n=6$), dysarthria ($n=11$), dysphagia ($n=11$), weight loss ($n=11$), psychiatric issues ($n=7$) were observed. Seizures occurred in 10, with 4 focal and 6 generalized. Acanthocytes ratio were seen in 10-50% of blood smears. MRI revealed caudate in all, and parietal atrophy in 2 patients. Three patients had sensory neuropathy, 1 had motor neuropathy, and 2 showed myogenic changes in EMG. VPS13A mutation was detected in 4 patients for whom molecular analysis was available. Six started on olanzapine, five on haloperidol, and two underwent deep brain stimulation for severe dystonia. Significant worsening of involuntary movements and dysphagia was observed in all patients during follow-up, and three patients died after 11±2.82 years follow-up.

Conclusion: It is crucial to assess patients showing multisystem involvement such as early psychiatric issues, self-mutilation, movement disorders, acanthocytosis, and caudate atrophy for an accurate NA diagnosis.

Disclosure: The authors affirm that there are no conflicts of interest pertinent to this study.

EPO-356 | Experience with safinamide in Parkinson's disease patients after STN-DBS

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Background and Aims: Subthalamic nucleus -Deep Brains Stimulation (STN-DBS) has been stablished as a well-defined therapy for treating Parkinson's disease (PD) motor symptoms; however, some non-motor symptoms may not respond as expected, which significantly impact on quality of life of the patients (QoL). Antiparkinsonian drugs with dopaminergic and non-dopaminergic properties like "safinamide" have been suggested to have a positive effect on non-motor symptoms. The aim of this study was to investigate the efficacy of safinamide to improve apathy, fatigue and QoL in PD patients after STN-DBS.

Methods: We studied prospectively 13 PD patients that presented bothersome nonmotor symptoms after intensive setting of electrical parameters, stimulation contacts and optimal drug therapy. Patients were evaluated 32 week after 100mg of safinamide was started. Clinical assessment included Apathy Scale Starktein (AS), Parkinson Fatigue scale-16 (PFS-16) and Parkinson´s Disease Quality of life questionnaire -8 (PDQ-8).

Results: Thirteen PD patients were analyzed. The median age was 59 years old, with a median disease duration of 10 years at surgery. All patients were H&Y 2 in the ON state, and median of 400 levodopa equivalent daily dose. An improvement of 58.3% on the AS, 38% on the PFS-16 and 41.6% on the PDQ-8 was observed.

Conclusion: In this pilot study, safinamide proved to be an effective add-on treatment in PD patients treated with bilateral STN-DBS, leading to an improvement of non-motor complications, such as apathy, fatigue and QoL. Further studies with a higher number of patients are necessary to establish the value of this drug in the clinical practice.

Disclosure: Nothing to disclose.

EPO-357 | Clinicians' information provision during diagnostic consultations regarding Parkinson's disease

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Background and Aims: People with Parkinson's disease (PD) have reported feeling insufficiently informed by clinicians during diagnostic consultations, which might hinder patients' ability to manage their day-to-day lives. We aimed to (1) assess the amount and content of provided information during diagnostic consultations; and to test if the provided information is associated with (2) patients' evaluation thereof and (3) clinician and patient characteristics.

Methods: This observational longitudinal study video recorded diagnostic consultations of PD patients at seven neurology outpatient clinics in The Netherlands. We systematically coded the recordings for time spent on pre-defined information topics. Clinician and patient characteristics, a priori information needs, and retrospective perception and evaluation of received information were assessed using questionnaires. Analyses included descriptive statistics and regressions.

Results: Patients' information need was high overall ($M = 4.5 \pm 0.8$, potential range 1–5). Clinicians' information provision varied across patients ($n = 50$) and clinicians ($n = 37$). All patients were provided with information regarding their diagnosis, treatment options, and the follow-up plan. About half were not informed about PD being incurable (44%) and the long-term effects of dopaminergic medication (58%). Patients reported to have perceived quite some information ($M = 2.8 \pm 0.9$, PR 1-5), and were quite satisfied ($M = 3.4 \pm 0.9$, PR 1-5). 30% reported a wish for more information, particularly regarding the prognosis. Regression analyses will be completed at the time of the conference.

Conclusion: Most clinicians mainly focus on treatment during PD diagnostic consultations, and may not sufficiently meet patients' prognostic information needs. We recommend clinicians to actively inquire about patients' information preferences during diagnostic consultations, and tailor their information provision accordingly.

Disclosure: Nothing to disclose.

EPO-358 | Diagnostic accuracy of Parkinson's disease by neurologists in an outpatient setting: The Parklink Bologna cohort

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[1]*DIBINEM Dipartimento di Scienze Biomediche e Neuromotorie;* [2]*IRCCS Istituto delle Scienze Neurologiche di Bologna*

Background and Aims: The diagnosis of Parkinson's disease (PD) is still mainly clinical and with variable accuracy in different settings. The Parklink Bologna project is an ongoing record linkage system started in 2015 in the Local Health Trust of Bologna (LHTB), devised for epidemiological and research purposes, including prevalent and incident cases of PD or atypical parkinsonism. The objective of this study is to evaluate the accuracy of the diagnosis of PD recorded by neurologists participating in the Parklink project. Interobserver agreement between two movement disorder experienced neurologists was assessed.

Methods: Diagnostic accuracy cross-sectional study on a random sample of 220 patients representative of the ParkLink cohort. Sensitivity, specificity, positive/negative predictive value (PPV/NPV) were calculated by assuming as reference standard the blinded diagnosis of two movement disorder experienced neurologists, applying Postuma international diagnostic criteria for PD, and as index-test the diagnosis recorded by outpatients neurologists within

the ParkLink project. Interobserver agreement was assessed using Cohen's Kappa.

Results: In 193 patients (mean age 72.8 years) clinical documentation for a diagnosis was available. A sensitivity of 94.1% (95% CI: 88.7-97.4) and specificity of 63.2% (49.3-75.6), PPV of 85.9% (79.3-91.1) and NPV of 75% (59.7-86.8) were found for the first assessor. Interobserver agreement was "substantial" (Kappa 0.77, 95% CI: 0.67-0.87) between the two experts.

	1° assessor	CI 95%	2° assessor	CI 95%
Sensitivity	94.1%	88.7-97.4	92.7%	87.3-96.3
Specificity	63.2%	49.3-75.6	78.6%	63.2-89.7
PPV	85.9%	79.3-91.1	94%	88.8-97.2
NPV	81.8%	67.3-91.8	75%	59.7-86.8

Accuracy parameters

Conclusion: Diagnosis of PD according to the 2015 Postuma criteria showed good PPV and NPV in an outpatient real-world setting. It is possible to build reliable cohorts of people with PD for epidemiological research, based on both community neurologists and neurologists from movement disorder centres.

Disclosure: Nothing to disclose.

EPO-359 | TremAn3: A new tool for the analysis of tremor and other oscillatory movements in video recordings

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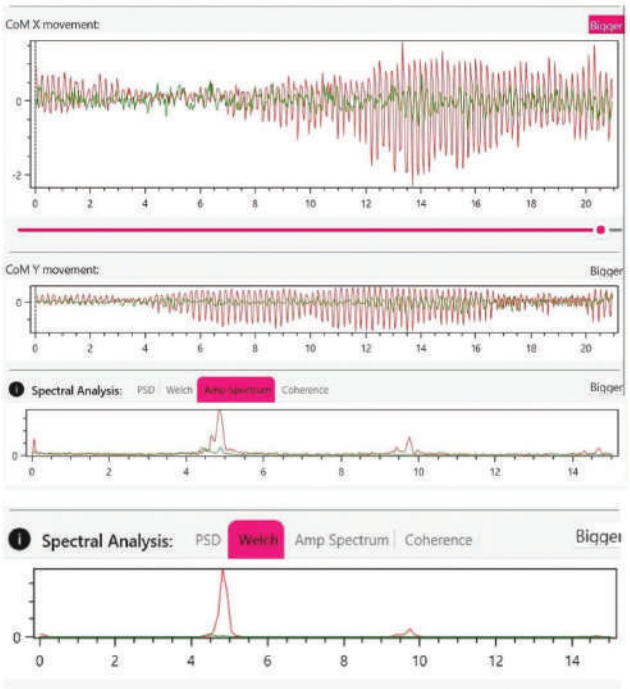
Background and Aims: Neurophysiological techniques used to quantify tremor are not readily available in clinical practice, whereas video recording is a part of routine evaluation. We describe TremAn3, a novel application that enables kinematic analysis of tremor or other rhythmic movements from standard video recordings of patients.

Methods: We analyzed video recordings of 17 patients with essential tremor (ET) and 19 patients with functional tremor (FT) diagnosed at the General University Hospital in Prague, Czechia and of 9 subjects with leg stereotypy syndrome (LSS) recruited at the Baylor College of Medicine in Houston, Texas. In the video recordings, oscillating part(s) of the body are delineated in TremAn3 as the region(s) of interest. The algorithm then calculates the center of motion (CoM) derived from the normalized frame differences and defines the motion trajectory, followed by a fast Fourier transform (FFT) generating an amplitude spectrum of oscillations.

Results: In patients with ET, analysis demonstrated stable frequency spectra with intraindividual variation below 1 Hz. In FT patients, increased intraindividual variability of tremor frequency exceeding 1 Hz was found, with marked distractibility and entrainment by contralateral rhythmic movements. Of the 9 individuals with LSS, regular rhythmic oscillations of the lower limbs were present in 7 cases, ranging between 4.5 and 6.5 Hz, with a variance below 0.5 Hz in individual cases (Yilmaz et al., manuscript in preparation).



Sample output from TremAn3: video analysis of a patient with ET.

Conclusion: TremAn3 appears as a tool suitable for supporting the differential diagnosis of tremor in daily practice and to analyze video recordings obtained in large participant cohorts.

Disclosure: Nothing to disclose.

EPO-360 | Prospective study of gait and multimodal MRI biomarkers Multiple System Atrophy (MSA)

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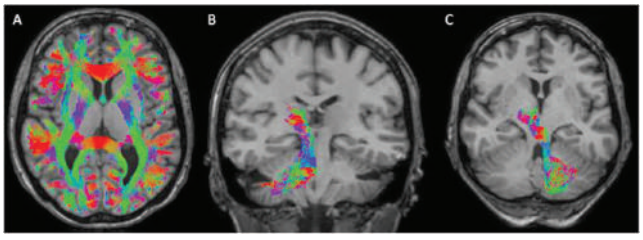
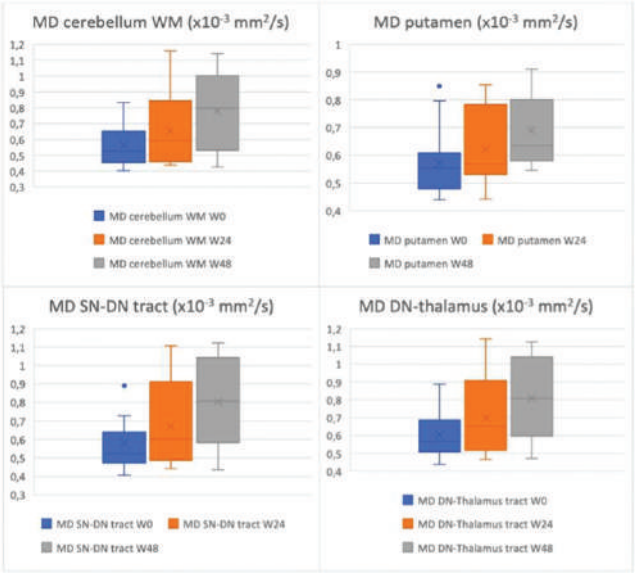
Background and Aims: MSA is a rare neurodegenerative condition characterized by a rapid gait deterioration with severe prognosis. Currently, no treatment is available to slow down disease progression. We aimed to develop new multimodal biomarkers allowing objective monitoring of early MSA progression to improve outcome definition for future neuroprotective trials.

Methods: This analysis focuses on 19 MSA patients, enrolled in the Gait'N'Park multicentric cohort (NCT04653688). Longitudinal data, including clinical scales (UMSARS), unsupervised gait analysis (at home using smart insoles), and multimodal MRI data (volumetric, R2*, QSM for iron load, and DTI for microstructural alterations), were collected at baseline (W0) and 24 weeks (W24).

Results: At W24, there was a significant increase of mean diffusivity in cerebellar white matter (pFDR = 0.029) and in fiber bundles between: Substantia Nigra and Dentate Nuclei (pFDR = 0.0013); and Dentate Nuclei and Thalamus (pFDR = 0.0013). No significant worsening was observed at W24 for other parameters, such as UMSARS, gait speed (95th centile) or stride length (mean), putamen, cerebellum or pons volume, or putamen R2* and QSM values.



Tractography: (A) Whole brain; (B) Substantia Nigra-Dentate Nucleus; (C) Dentate Nucleus-Thalamus.



Mean diffusivity evolution along time (MD = Mean Diffusivity; WM = White Matter; SN = Substantia Nigra; DN = Dentate Nucleus).

MD ($x10^{-3}mm^2/s$)	W0 (median; Q1-Q3)	W24 (median; Q1-Q3)	Difference	p	p_{FDR}	$p_{Bonferroni}$
Cerebellum WM	0.525 (0.460-0.639)	0.592 (0.480-0.767)	+0.067 (+12.8%)	**0.0067***	**0.029***	0.0871
Putamen	0.553 (0.486-0.600)	0.570 (0.533-0.716)	+0.017 (+3.1%)	**0.0293***	0.0596	0.3809
SN-DN tract	0.523 (0.481-0615)	0.602 (0.494-0.850)	+0.08 (+15.2%)	**0.0001***	**0.0013***	**0.0013***
DN-Thalamus tract	0.568 (0.514-0.670)	0.653 (0.529-0.853)	+0.085 (+15%)	**0.0002***	**0.0013***	**0.0026***

Mean diffusivity analysis at W24 vs W0 (MD = Mean Diffusivity; WM = White Matter; SN = Substantia Nigra; DN = Dentate Nucleus).

Conclusion: Our data confirm the low sensitivity to early change of UMSARS, currently use as the gold standard to monitor disease progression. Whereas diffusion imaging of white matter appears to be sensitive to change as early as 6 months of follow-up, with high statistical significance, supporting early involvement of oligodendrocytes. This kind of biomarker should be considered to enhance outcome definition for future neuroprotection trials.

Disclosure: This study was sponsored and funded by H. Lundbeck A/S, FeetMe, France Parkinson, Vaincre Parkinson. Félix Marchand has nothing to disclose.

EPO-361 | Improvement of troublesome dyskinesia in people with Parkinson's disease treated with foslevodopa/foscarbidopa

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Background and Aims: Troublesome dyskinesia, a complication from Parkinson's disease (PD) progression and pulsatile dopaminergic stimulation, impairs daily living. Foslevodopa/foscarbidopa (LDp/CDp), a formulation of levodopa/carbidopa prodrugs delivered as a continuous (24-hour/day) subcutaneous infusion, increased "On" time without troublesome dyskinesia in 2 phase 3 clinical trials. This post hoc analysis evaluated LDp/CDp efficacy by baseline duration of troublesome dyskinesia.

Methods: Patients with levodopa-responsive idiopathic PD aged ≥30 years who were inadequately controlled by current therapy and had ≥2.5 "Off" hours/day received LDp/CDp in a 52-week, phase 3, open-label trial (NCT03781167). The change from baseline (CFB) to final visit was assessed for "On" time with troublesome dyskinesia (PD diary; normalized to 16-hour waking day), time spent with dyskinesias (Movement Disorder Society-Unified PD Rating Scale [MDS UPDRS] Part 4.1), functional impact of dyskinesias (MDS-UPDRS Part 4.2), and 39-item PD Questionnaire (PDQ-39) in patient subgroups with >0.5 and >1.0 hours of troublesome dyskinesia at baseline.

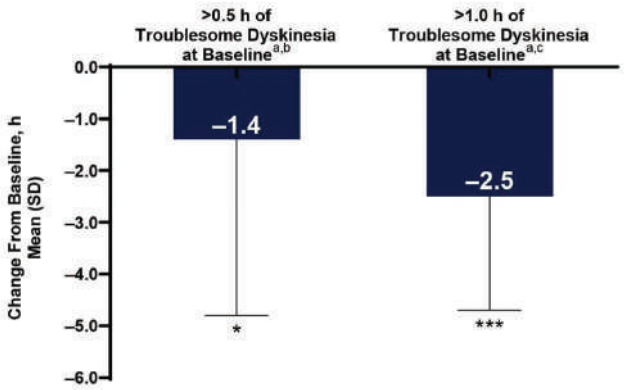
Results: Baseline characteristics were similar across subgroups with >0.5 ($n=83$) and >1.0 hours ($n=66$) of troublesome dyskinesia at baseline; mean (SD) duration of troublesome dyskinesia was 2.7 (2.0) and 3.1 (2.0) hours, respectively (Table). In both subgroups, LDp/CDp led to numerical or significant improvements from baseline in troublesome dyskinesia (mean [SD] CFB −1.4 [3.4] and −2.5 [2.2] hours, respectively; $p<0.05$; Figure1), time spent with dyskinesias ($p\leq0.001$), functional impact of dyskinesias ($p\leq0.001$), and PDQ-39 ($p<0.05$ for >0.5 hour subgroup; Figure 2).

Table. Baseline Demographics and Disease Characteristics by Duration of Troublesome Dyskinesia at Baseline

Characteristic	>0.5 h of Troublesome Dyskinesia[a] n=83	>1.0 h of Troublesome Dyskinesia n=66
Age, years, mean (SD)	63.5 (9.3)	63.9 (9.2)
Sex, male, n (%)	45 (54.2)	33 (50.0)
Race, White, n (%)	71 (85.5)	59 (89.4)
MMSE total score	28.8 (1.8)	28.8 (2.0)
PD duration since onset, years, mean (SD)	12.7 (5.1)	12.7 (5.3)
"Off" time, h, mean (SD)[b]	5.2 (2.3)	5.2 (2.4)
"On" time without troublesome dyskinesia, h, mean (SD)[b]	8.1 (2.8)	7.7 (2.9)
"On" time with troublesome dyskinesia, h, mean (SD)[b]	2.7 (2.0)	3.1 (2.0)
MDS-UPDRS Part II, mean (SD)	16.5 (7.6)	16.6 (7.8)
MDS-UPDRS Part IV, mean (SD)	11.2 (3.1)	11.3 (3.3)
PDQ-39, mean (SD)	37.4 (16.0)	38.0 (16.0)

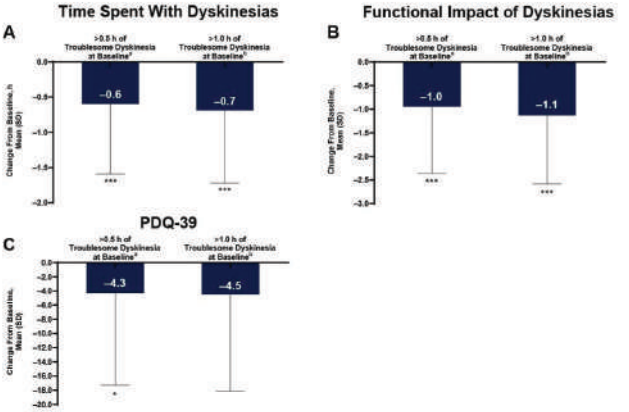
h, hour; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; MMSE, Mini Mental State Evaluation; PD, Parkinson's disease; PDQ-39, 39-item Parkinson's Disease Questionnaire.
[a]Patients with >1.0 h of troublesome dyskinesia at baseline were also included.
[b]Normalized to a 16-hour waking day.

Figure 1. Change From Baseline in "On" Time With Troublesome Dyskinesia With LDp/CDp Treatment



h, hour; LDp/CDp, foslevodopa/foscarbidopa.
[a]"On" time with troublesome dyskinesia was normalized to a 16-hour waking day.
[b]Data were available from 83 patients at baseline and from 35 patients at the final visit.
[c]Data were available from 66 patients at baseline and from 26 patients at the final visit.
*$P<.05$; ***$P<=.001$ vs baseline.

Figure 2. Improvement of Efficacy Outcomes With LDp/CDp Treatment By Duration of Troublesome Dyskinesia at Baseline



h, hour; LDp/CDp, foslevodopa/foscarbidopa; PDQ 39, 39-item Parkinson's Disease Questionnaire.
[a]Data were available from 83 patients at baseline and from 42 patients at the final visit.
[b]Data were available from 66 patients at baseline and from 32 patients at the final visit.
*$P<.05$; ***$P<=.001$ vs baseline.

Conclusion: Continuous delivery of LDp/CDp was associated with significant improvements in dyskinesia and quality of life in patients with relevant/significant troublesome dyskinesia at baseline.

Disclosure: MB has received research funding from Aptinyx Inc. T-WL has served as a site principal investigator for the AbbVie M15-736 study and for the Abbott PROGRESS trial. ELP has received research and grant support from Sunovion Pharmaceuticals and has conducted prior and/or ongoing clinical trials with AbbVie, Acadia Pharmaceuticals, Cala Health, Cerevance, Cerevel, Covance, Evidera, Lilly, Lundbeck, Osmotica Pharmaceutical, Revance Therapeutics, Roche, Sunovion Pharmaceuticals, and Sun Pharma. SEZ has received research support for clinical trials from AbbVie, Abbott, and Boston Scientific. LB, RG, LH, and MS are full-time employees of AbbVie, and may hold AbbVie stock or stock options. FB has received financial compensation for lectures and advisory services as well as in-kind donations of PKG reports for clinical studies from GKC, and honorarium for an advisory board from AbbVie. He owns stock options in Dizlin Pharmaceuticals AB. AbbVie funded

this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the abstract. All authors had access to relevant data and participated in the drafting, review, and approval of this abstract. No honoraria or payments were made for authorship. AbbVie and authors thank all the trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Jay Parekh, PharmD, ISMPP CMPP™, of JB Ashtin, and funded by AbbVie.

EPO-362 | Opicapone as first-line strategy for the treatment of wearing-off in Korean patients with Parkinson's disease

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Background and Aims: Opicapone (OPC) proved effective for end-of-dose motor fluctuations in patients with Parkinson's disease (PD) treated with levodopa (L-dopa)/dopa decarboxylase inhibitor (DDCi). This study aimed to explore the efficacy of OPC 50 mg versus an extra 100 mg L-dopa dose to treat early wearing-off in Korean patients with PD.
Methods: This was a prospective, multicentre, randomised, active-controlled study in which 169 levodopa-treated patients with PD and wearing-off were randomly assigned (1:1) to OPC 50 mg once-daily ($n=88$) or an additional 100 mg L-dopa dose ($n=81$). A 1-week screening period was followed by a 4-week maintenance phase. Main endpoint was change from baseline in absolute OFF-time. Secondary endpoints included tolerability, Movement Disorder Society-Unified-PD-Rating-Scale (MDS-UPDRS), 8-item PD Questionnaire (PDQ-8), Clinical Global Impression of Improvement (CGI-I), and Patient Global Impression of Change (PGI-C).
Results: At week 4, mean (standard error [SE]) change from baseline in absolute OFF-time was -62.1 min (9.8) for the OPC 50 mg group and -16.7 min (10.0) for the L-dopa 100 mg group, resulting in a significant difference of -45.4 min ($p=0.0015$). No significant differences were observed in MDS-UPDRS and PDQ-8 scores between the two groups. The OPC group tended to show greater improvements on CGI-I/PGI-C than the L-dopa group. OPC was well tolerated, but adverse events (AEs) were more frequent in the OPC than the L-dopa group (37.9% vs 18.5%), with dyskinesia (6.9%) being the most common drug-related AE.
Conclusion: OPC can be considered a potential first-line therapy to treat early wearing-off versus the standard L-dopa dose increase approach.
Disclosure: Supported by BIAL.

EPO-363 | Early-onset Parkinson's disease in women: A comparison of hormonal exposure with late-onset PD and unaffected controls

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Background and Aims: PD is almost twice as common in men than in women. There is a paucity of studies evaluating the role of hormonal exposure in EOPD women. The objective was to compare the demographic characteristics and exposure to endogenous, exogenous estrogens and progestins between patients with EOPD, LOPD, and EOPD-matched unaffected controls.
Methods: We identified all female patients with EOPD in an incident cohort study from 1991 to 2010. EOPD patients were defined as having motor symptoms onset before age 50, after age 50 as LOPD. Each EOPD patient was matched to an unaffected control. Their medical records were reviewed to determine demographic characteristics, medical, reproductive, and menopausal history.
Results: 318 women with EOPD and 170 women with LOPD were identified. Of these, 87 EOPD patients, 91 controls, and 84 LOPD patients had sufficient hormonal exposure data in their records to be included. There were no significant differences in demographic characteristics between the three groups. EOPD patients were significantly more likely to have used hormonal contraception compared to controls and LOPD patients ($p<0.001$). The number of pelvic surgeries and the use of perimenopausal hormonal therapy preceding the onset of motor symptoms (both $p<0.001$) was significantly higher in LOPD compared to EOPD.
Conclusion: Our study reports that there are no significant differences in hormonal exposure between controls and EOPD patients, except for exposure to hormonal contraception. The differences in the history of hormonal contraception, oophorectomy and perimenopausal treatment between EOPD and LOPD are probably linked to the age gap between the two cohorts.
Disclosure: Nothing to disclose.

EPO-364 | Dopaminergic medication and STN-DBS increase motor, but not reflection and cognitive impulsivity in PD

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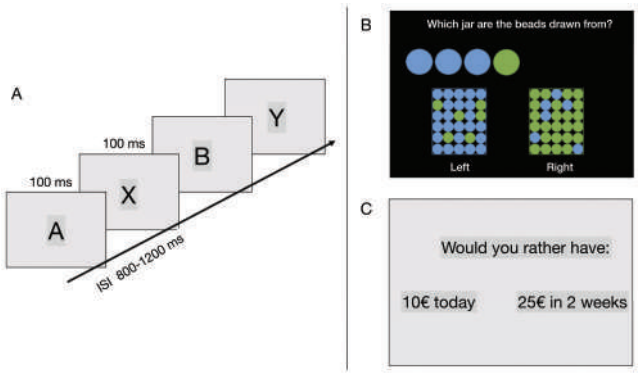
[1]*Department of Neurology, University Medical Centre Ljubljana, Ljubljana, Slovenia;* [2]*Department of Neurosurgery, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Centre, Nijmegen, The Netherlands;* [3]*Department of Neurosurgery, University Medical Centre Ljubljana, Ljubljana, Slovenia;* [4]*Department Clinical and Motor Neurosciences, Institute of Neurology, University College London, London, UK*

Background and Aims: Parkinson's disease is associated with increased impulsivity, which can be divided into several domains: motor (consisting of proactive and reactive subdomains), reflection and cognitive impulsivity. Evidence suggests that both dopaminergic medication and subthalamic nucleus deep brain stimulation can affect impulsivity. Therefore, we set out to investigate the effect of dopaminergic medication and subthalamic nucleus deep brain stimulation on motor, reflection and cognitive impulsivity in PD patients.
Methods: Twenty consecutive Parkinson's disease patients operated with subthalamic nucleus deep brain stimulation were tested ON and OFF dopaminergic medication and ON and OFF subthalamic nucleus deep brain stimulation. They performed three different impulsivity tasks: AX Continuing Performance Task to test for motor impulsivity, Beads Task for reflection impulsivity and Delay Discounting Task for cognitive impulsivity.
Results: The combination of subthalamic nucleus deep brain stimulation and dopaminergic medication led to an increase in motor impulsivity ($p=0.036$), both proactive ($p=0.045$) and reactive ($p=0.006$). There was no effect of either dopaminergic medication or subthalamic nucleus deep brain stimulation on reflection and cognitive impulsivity.



A - AX continuous performance task, B - Beads task, C - Delay discounting task. ISI = Interstimulus interval.

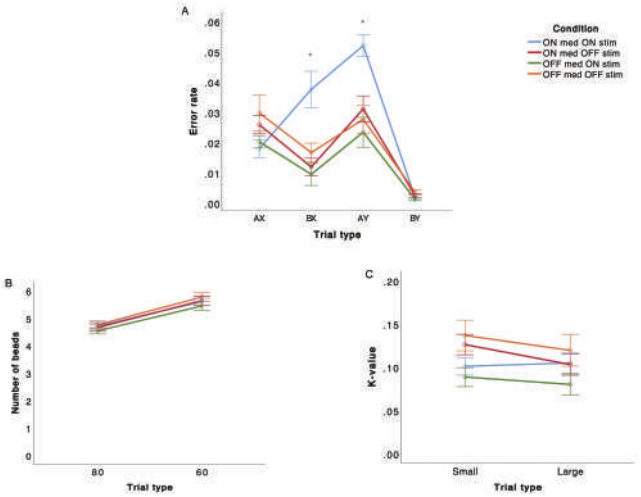


FIGURE 2 The performance on different tasks (A - AX-CPT, B-Beads task, C - Delay Discounting Task) in STN-DBS PD patients in four different conditions are presented.

Conclusion: The combination of dopaminergic medication and subthalamic nucleus deep brain stimulation leads to increased motor, but not cognitive or reflection impulsivity in patients with Parkinson's disease. Both, proactive and reactive motor impulsivity were impaired by the combination of dopaminergic medication and subthalamic nucleus deep brain stimulation.
Disclosure: Nothing to disclose.

EPO-365 | Gender differences in patients with Parkinson's disease treated with STN or GPi DBS: Results from a single center

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Background and Aims: We investigated gender-differences in response to DBS of the STN or GPi in a group of patients with advanced PD
Methods: 123 patients with PD (30% F, 70% M) and DBS targeting the STN (93 patients, 32.2 % females) or GPi (30 patients, 23.3% females) were enrolled. At baseline, MDS-UPDRS part III was collected in both OFF and ON state; at 1 year follow up, it was assessed in the ON state with the stimulator turned on. Dopaminergic therapy was converted in Levodopa Equivalent Daily Dose (LEDD)
Results: At baseline, there were no gender differences as regards disease duration, LEDD and MDS-UPDRS part III score. At 1-year follow-up, we found reduced MDS-UPDRS III scores for both GPi- and STN-DBS and a significant LEDD reduction compared to baseline only after STN-DBS ($p=0.0001$), with no gender-specific differences. The percentage of patients with dyskinesias decreased from 86% to 20% in females and from 91% to 50% in males after GPi-DBS. After STN-DBS the decrease was from 93.3% to 66% in females, and from 73% to 34% in males. The percentage of patients with clinical fluctuations decreased from 86% to 14% in females and from 39% to 13% in males after GPi-DBS, while after STN-DBS the decrease was from 56.6% to 27% in females, and from 44% to 28% in males. Overall, the effect of sex was not statistically significant
Conclusion: Bilateral STN- and GPi-DBS are equally effective in males and females as a treatment for motor complications of PD
Disclosure: Nothing to disclose.

EPO-366 | Mapping cortical nodes for targeted neuromodulation in focal dystonia: A TMS-EEG study

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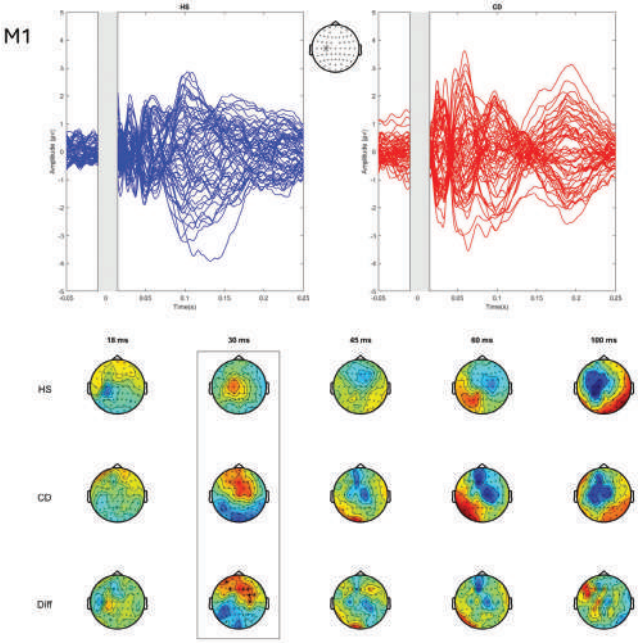
Background and Aims: Focal dystonia (FD) manifests as involuntary movements and abnormal postures in specific body regions, often with non-motor symptoms, due to brain network dysfunctions. Our objective is the therapeutic modulation of these networks using non-invasive brain stimulation. We present preliminary Transcranial Magnetic Stimulation-Electroencephalography (TMS-EEG) findings that identify dysfunctional cortical nodes in motor and non-motor networks of cervical dystonia (CD) patients. Pinpointing these nodes is vital for developing targeted neuromodulatory strategies.

Methods: Eighteen CD patients and 15 healthy subjects (HS) were evaluated using TMS-EEG to record TMS-evoked potentials (TEPs) from the primary motor cortex (M1), supplementary motor area (SMA), and dorsolateral prefrontal cortex (DLPFC), key nodes involved in the pathophysiology of motor and non-motor symptoms in CD. The Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) was employed for clinical assessment.

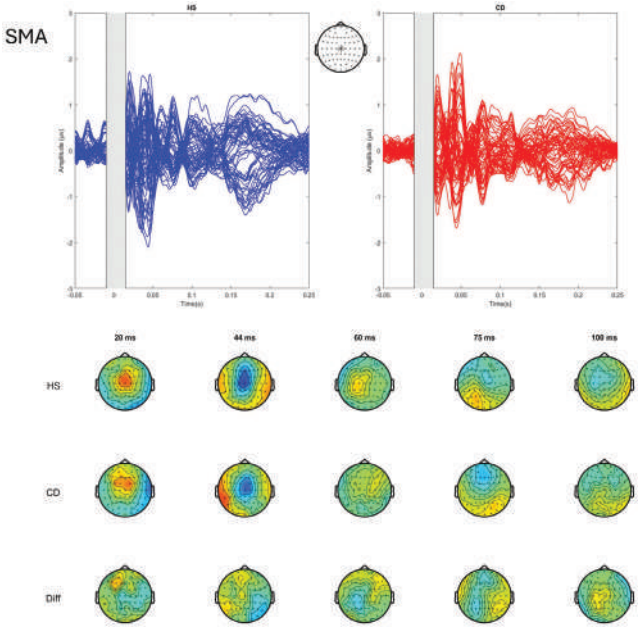
Results: Preliminary findings revealed a significantly larger early local M1 TEP amplitude in CD patients versus HS. Conversely, DLPFC showed a non-significant trend toward reduced early local TEP amplitude in CD patients. SMA TEPs did not differ significantly between groups. No significant correlations were found between TEP amplitudes and TWSTRS scores.

Conclusion: Identifying dysfunctions in specific cortical nodes within CD patients' motor and frontoparietal networks lays the groundwork for developing neuromodulation strategies aimed at symptom relief. This study is ongoing, and it includes data collection from other pathophysiologically relevant areas in various forms of FD, and correlations with an extensive array of clinical parameters.

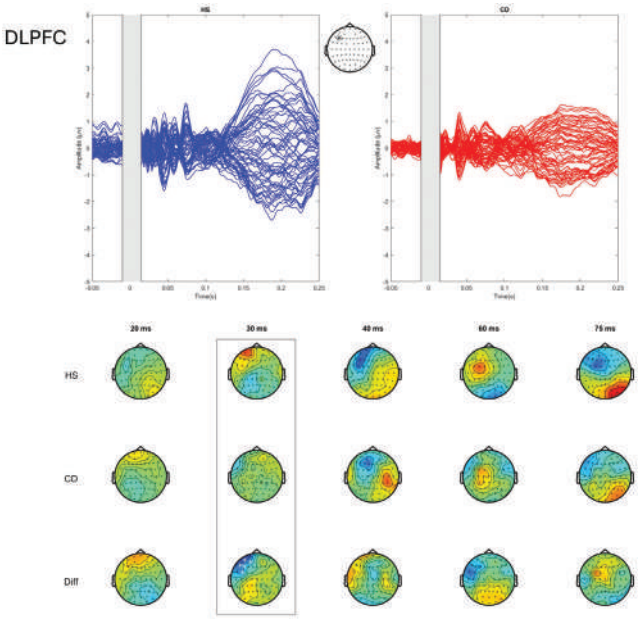
Disclosure: Nothing to disclose.



Butterfly plots (top) and topoplots (bottom) of TEPs from M1 stimulation in cervical dystonia (CD) compared to healthy subjects (HS). Top: Stimulation site marked by an asterisk. Bottom: Asterisks highlight significant electrodes in CD vs HS.



Butterfly plots (top) and topoplots (bottom) of TEPs from SMA stimulation in cervical dystonia (CD) compared to healthy subjects (HS). Top: Stimulation site marked by an asterisk.



Butterfly plots (top) and topoplots (bottom) of TEPs from DLPFC stimulation in cervical dystonia (CD) compared to healthy subjects (HS). Top: Stimulation site marked by an asterisk. Bottom: Asterisks mark electrodes with a trend towards significant comparison.

EPO-367 | Abstract withdrawn

EPO-368 | Olfactory and gustatory function is associated with global cognition in early-stage Parkinson's disease

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Background and Aims: Hyposmia and hypogeusia is a prevalent non-motor symptom of Parkinson's disease (PD). Although there have been reports linking hyposmia to the development of dementia in PD, the association between cognitive and olfactory and gustatory function remains largely unexplored. This study evaluate the olfactory, gustatory function in early-stage of PD patients without dementia.
Methods: This study included drug-naive early PD patients with normal cognition (PD-NC) or mild cognitive impairment (PD-MCI). Olfactory function was evaluated using the YSK olfactory function test, which consisted of threshold, discrimination, and identification. The gustatory function was assessed using the YSK function test, which measures thresholds for the sweet, bitter, salty, sour, and umami tastes.
Results: Among the 84 individuals with PD, the average value of the olfactory function test fell within the hyposmia range, while taste function remained within the normal range. The study encompassed 39 patients with PD-NC and 45 with PD-MCI. Notably, no significant disparities were identified in olfactory and gustatory function tests between the two groups, with this trend persisting across the subdomains of each respective test. The result indicated a direct correlation between diminished global cognition (Montreal Cognitive Assessment scores) and decreased performance in both odor discrimination and gustatory function in all patients with early PD.
Conclusion: This study demonstrates that olfactory and gustatory function was associated with global cognition in the early stages of PD without dementia. Further study is warranted to ascertain whether early olfactory or gustatory dysfunction in PD could serve as an indicator for future dementia development.
Disclosure: None.

MS and related disorders 3

EPO-369 | Intrathecal synthesis biomarkers in late-onset multiple sclerosis: Any difference from adult-onset cases?

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Background and Aims: The clinical and radiological features of Late-Onset Multiple Sclerosis (LOMS), characterized by onset after the age of 50, have been recently described, while limited data are available about fluid biomarkers. This multicenter retrospective study aims to compare intrathecal synthesis index markers between LOMS and Adult-Onset MS (AOMS).
Methods: A total of 152 patients (LOMS $n=39$, AOMS $n=113$) undergoing lumbar puncture for MS-diagnosis were included. We confirmed homogeneity between the groups, except for age, using Pearson's chi-square analysis. We collected Cerebrospinal Fluid (CSF) biomarkers, including kappa-free light chains to calculate K-index, immunoglobulin-G for Link-index, and Oligoclonal Bands (OB). Median (IQR) differences were analyzed using Mann-Whitney analysis (normality excluded with Shapiro-Wilk test).
Results: Among clinical variables (gender, EDSS, brain and spinal lesion load, type of onset, autoimmune comorbidities), only mean age at onset differed between the groups (LOMS: 55.9 ± 5.4; AOMS: 31.3 ± 8.0). The OB-positivity was similar in LOMS and AOMS (82% vs. 93%), whereas we observed significantly lower values of intrathecal synthesis indexes in LOMS, with median K-index at 18.95 (32.35) and median Link-index at 0.5 (0.28), compared to AOMS, with 32.60 (67.44; $p=0.008$) and 0.6 (0.3; $p=0.001$). No other significant differences were found in CSF proteins.
Conclusion: LOMS exhibits lower values of the intrathecal synthesis markers, both K-index and Link-index, whereas they do not differ in OB status. These results may reflect a less pronounced inflammatory component in LOMS. Quantitative markers of intrathecal synthesis may help in understanding pathological differences for LOMS, with future potential therapeutic implications. Larger cohort confirmation is needed.
Disclosure: Nothing to disclose.

EPO-370 | Ten years of Kappa Index: Revision of intrathecal synthesis biomarkers in multiple sclerosis on a cohort of 1,000 cases

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Background and Aims: Cerebrospinal fluid (CSF) kappa free light chains (KFLC) are becoming a diagnostic biomarker for multiple sclerosis (MS). We aimed to compare the diagnostic performances of intrathecal synthesis biomarkers to that of oligoclonal bands (OB) in diagnosing MS, radiological and clinical isolated syndromes (RIS-CIS) on a large cohort of patients collected over 10 years.
Methods: We collected 1057 patients (59% females) in 10 years, who underwent CSF analysis for intrathecal synthesis in the diagnostic work-up, and they were classified according to their diagnosis

as: 395 MS, 260 with other neurological inflammatory (including 76 RIS-CIS), and 402 non-inflammatory diseases (excluding lymphoproliferative and infective diagnosis).

Results: MS patients significantly differ from all other groups (including if considering the RIS-CIS cohort) for: CSF KFLC, KFLC intrathecal fraction, Kappa index, and OB. Evaluating diagnostic performance, the Kappa index cut-off was 5.6 for the diagnosis of MS, and 5.7 in predicting OB (that showed the best diagnostic accuracy).

Conclusion: The KFLC index confirmed the accuracy in MS diagnosis in this large Italian cohort, adding information also in the RIS-CIS population.

Disclosure: None.

EPO-371 | Reassessing Balo's concentric sclerosis: Diverse clinical presentations and therapeutic implications

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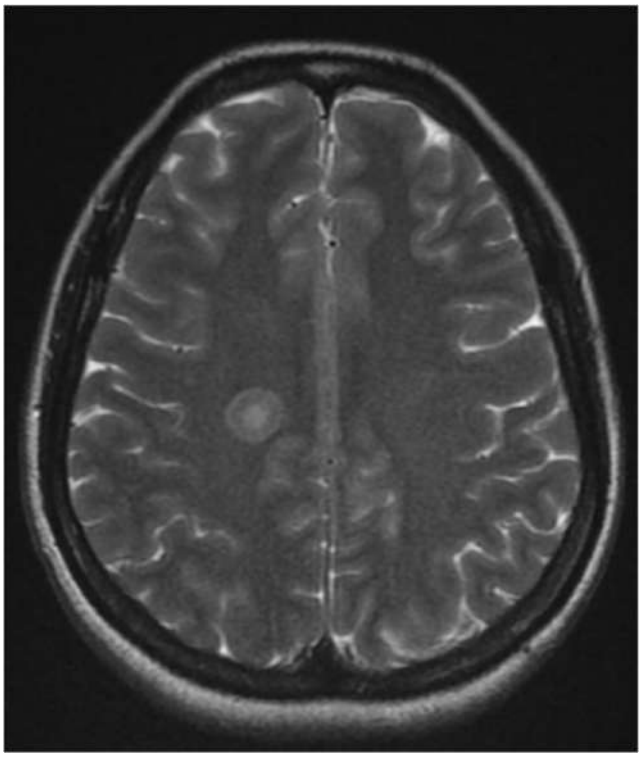
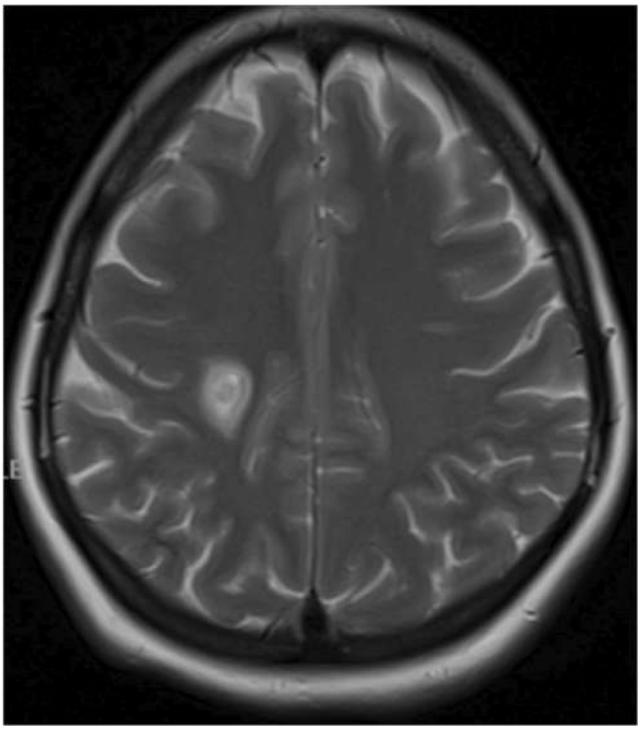
Background and Aims: Balo's concentric sclerosis (BCS) represents a rare variant of multiple sclerosis (MS), characterized by concentric lamellae of alternating demyelinated and partially myelinated tissues. Historically considered to have a severe and often fatal course, recent imaging studies have identified cases with a more benign evolution.

Methods: This descriptive retrospective study involved seven BCS patients from the neurology department at the National Institute Mongi Ben Hamida of Neurology. Demographic, clinical and paraclinical data were analyzed.

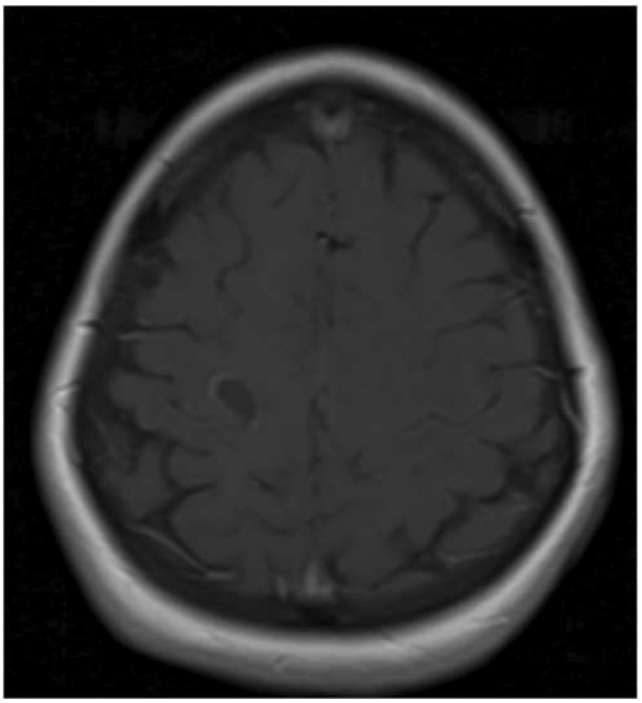
Results: At diagnosis, the average age was 31.71 years [18; 47], with a sex ratio of 2:5. Inaugural relapses included motor ($n=4$), visual ($n=1$), multifocal ($n=1$) presentations, and focal seizures ($n=1$). The initial Expanded Disability Status Scale (EDSS) averaged 2 [1; 4], reaching a maximum of 5.5 during relapse. Imaging revealed a single concentric Balo lesion in most of the cases and multiple Balo lesions in one case, the majority exhibiting contrast enhancement ($n=6$). All cases presented associated lesions in typical MS areas. Treatment outcomes showed that most patients responded well to corticosteroid therapy ($n=6$). One patient with corticosteroid-resistant optic neuritis underwent plasmapheresis with a poor outcome. First-line treatment was initiated for two patients, with an indication for escalation after four years in one case.



Right periventricular hyperintense signal on T2-weighted sequence showing concentric layering.



Hyperintense signal on T2-weighted sequence in the right annular semi-oval center showing typical 'onion-like' appearance.



Peripheral incomplete ring enhancement on T1 post contrast (gadolinium).

Conclusion: This study challenges the historical perspective on BCS, emphasizing the need for ongoing research to refine its clinical course and treatment. For cases meeting MS diagnostic criteria, first-line therapy is recommended, while immunosuppressive treatment may be considered for more severe progression.
Disclosure: Nothing to disclose.

EPO-372 | Analysing B-cell depletion kinetics and clinical outcomes of ocrelizumab and rituximab in multiple sclerosis

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Background and Aims: Rituximab and ocrelizumab deplete B-lymphocytes from the pre-B stage to the mature B stage and are used for multiple sclerosis (MS) treatment. This study aims to compare their effects on overall lymphocyte levels and subpopulations over 12 months in MS patients and explore possible clinical correlates.
Methods: We included 107 patients with MS, treated with rituximab ($n=84$) or ocrelizumab ($n=23$). We used flow cytometry in the peripheral blood to count total lymphocytes and B-lymphocytes subpopulations, before treatment and after 6 and 12 months.
Results: After 6 and 12 months, patients treated with Rituximab and Ocrelizumab were similar in total B-cell count and in B-cell subpopulations except for Naïve B-cells at 6 months ($p<0.001$) and at 12 months ($p=0.001$) and Memory B-cells at 12 months ($p=0.002$). Regarding EDSS progression, relapse occurrence and treatment discontinuation rate, no significant differences between the two treatment groups were found. In the whole sample, total B-cell count after 12 months of treatment was significantly lower in patients with treatment discontinuation due to infectious complications ($p=0.024$) and with EDSS progression ($p=0.014$). Naïve and Immature B-cells counts after 12 months were also significantly lower in patients with EDSS progression ($p=0.014$ and $p=0.006$ respectively).
Conclusion: Both anti-CD20 treatments equally decreased total B-cell counts in the peripheral blood. No between-treatment difference in clinical outcomes was found. B-cell subpopulation counts may be used as predictors of disability progression and infectious adverse events.
Disclosure: Nothing to disclose.

EPO-373 | Multiple Sclerosis Implementation Network: A patient-engaged practiced based research network to improve patient care

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Background and Aims: The Multiple Sclerosis Implementation Network (MSIN) is a patient-centric collaboration between MS providers, patient advocacy organizations, academia, and industry, aimed at improving MS care and patient outcomes through the development of a practice-based research network.
Methods: The goals for MSIN Phase I are to: 1) establish an MSIN governance structure; 2) develop a practice-based research network composed of a diverse group of clinicians and practice settings providing care for people living with MS, and 3) establish a patient registry providing multilevel data enabling the assessment of both implementation and patient care outcomes across diverse clinical settings. The MSIN leadership designed and administered a survey assessing preliminary interest and capacity for joining the network. In Phase II MSIN will establish an implementation research program focused on the design and evaluation of implementation strategies to accelerate the adoption, implementation and sustainment of evidence-based interventions to improve MS care.
Results: Led by the Multiple Sclerosis Association of America (MSAA), the MSIN governance structure includes people living with MS, the University of Texas Health Science Center at Houston, Dell Medical School at The University of Texas at Austin, and Novartis Pharmaceuticals Corporation. The initial recruitment effort includes 12 providers, with an anticipated 24 providers expected to join the

network in 2024. Through coordinated data collection MSIN will enable rapid cycle implementation research a collaborative learning community.

Conclusion: MSIN will accelerate the translation of best MS practices into routine clinical care, improving the outcomes for people living with MS equitably.

Disclosure: AM: Nothing to disclose MF: Nothing to disclose LF: Has received fees for consultancy and/or advisory board participation from Bristol Myers Squibb, EMD Serono, Genetech, Horizon Therapeutics, Novartis, Sanofi, and TG Therapeutics; has received speaker fees from EMD Serono, MSAA, and Sanofi; has received honorarium for participation in educational programs from Medscape, Inc and MSAA; has received program sponsorship from EMD Serono; and grant support from EMD Serono, Genentech, NIH/NINDS, and PCORI through her institution. JF: Is an employee of Novartis Pharmaceuticals Corporation.

EPO-374 | Longitudinal changes in hippocampal subfield volumes of relapsing remitting multiple sclerosis patients

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Background and Aims: Due to the coexistence of neurogenesis and neurodegeneration, the hippocampus represents an interesting structure to analyze the interplay between these two processes in MS patients. We aimed to identify longitudinal trajectories of hippocampal subfield volume loss and its contribution to clinical disability and cognitive impairment.

Methods: We analyzed 3DT1-weighted images from 108 early relapsing remitting MS patients at baseline and yearly for a maximum of 8 years, together with clinical and cognitive evaluation. We segmented hippocampal subfields by using Freesurfer version 7.2.0.

Results: All the hippocampal subfields showed progressive volume loss over disease course, but with different trajectories. On the right hippocampus dentate gyrus and cornus ammonis 1 (CA1) – related to neurogenesis – showed a bimodal pattern: early volume stability, then rapid volume decrease, and finally again stability. We identified an index of relative progression "gamma", considering the shared variance among hippocampal subfields. Significant associations were observed between gamma and performance at visuo-spatial memory and attention.

Conclusion: The different pattern of progression of hippocampal subfield volume loss suggests an initial resilience of hippocampal regions related to neurogenesis, which then experience volume exhaustion after few years of disease. Gamma might become a relevant index for monitoring specific cognitive abilities.

Disclosure: Nothing to disclose.

EPO-375 | Predictors of longitudinal cognitive decline assessed using processing speed test in patients with multiple sclerosis

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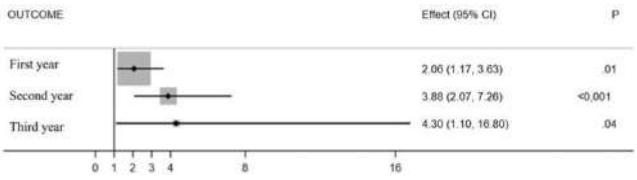
Background and Aims: Cognitive impairment is highly prevalent in multiple sclerosis (MS) with a profound impact on quality of life and socio-economic levels. Our objective was to longitudinally evaluate predictors of deterioration in the Processing Speed Test (PST) using the CogEval® application.

Methods: A prospective single-center study of MS patients with PST evaluations every 3-6 months from October 2019 to May 2023. Significant deterioration in PST was defined as declines of ≥10% from the baseline value each year. Multivariate logistic regressions were performed for each year of follow-up.

Results: Eight hundred eighty-one patients with ≥1 year of follow-up were included: 604 (68.6%) women, with a mean age of 45.3 (SD±11.41) years in the first test. The majority (79.8%) had relapsing-remitting MS. Follow-up was at least at two and three years was achieved in 455 and 65 patients, respectively. Confirmed worsening on the Expanded Disability Status Scale (EDSS), whether due to relapse or independent of it, was significantly associated with PST deterioration in all models, increasing each year: OR 1.85, 95% CI 1.03-3.32, $p=0.04$ in the first year; OR 2.01, 95% CI 1.1-3.69, $p=0.02$ in the second year; and OR 4.25, 95% CI 1.02-17.6, $p=0.046$ in the third year. Other factors were not consistently associated with cognitive deterioration in all models.



Forest plot graph to estimate the risk of annual decline in PST.

Conclusion: Cognitive impairment measured by PST in MS patients is common and is associated with worsening EDSS, regardless of clinical phenotype, disability acquisition pathways, and treatments received.

Disclosure: None.

EPO-376 | The MS-LOTUS initiative, a digital cohort collecting real-world evidence on multiple sclerosis relying on MSCopilot®

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Background and Aims: Several pharmaceutical companies are actively developing novel treatments for multiple sclerosis (MS). However, there is still a need for a more comprehensive characterization of MS-related disability to achieve a holistic understanding of the disease. Additionally, there are no coordinated patient registries across Europe and North America. The MS-LOTUS cohort will gather valuable insights that will enhance patient care by harnessing the power of digital biomarkers.
Methods: MS-LOTUS is an international, decentralised research initiative facilitating the direct enrolment of patients by their respective hospitals or private neurologists in France, Germany, Italy, Spain, Canada, amongst others. Circa 8000 participants will be recruited around the world. 300 digital biomarkers will be derived from assessments such as mobility, cognition, vision, and hand dexterity through MSCopilot®, a smartphone-based medical device evaluating MS-related disability. Quality of life and treatment-related variables will be assessed using in-app validated scales.
Results: The MS-LOTUS study, with its innovative design, will collect data directly from the patients at home in unsupervised conditions, to complement national registries data. MS-LOTUS will provide new information on the progression of MS and the dynamics of treatments. Healthcare providers will be able to access the data generated by the patients through a web dashboard. Agnostic MS-LOTUS data will be published regularly, to better inform the whole MS community (learned societies, neurologists and rehabilitation specialists, pharmaceutical companies and patient associations).
Conclusion: The interest for MS-LOTUS is strong in the community and presents a promising approach to advance our collective understanding of MS and improve patients' care pathways.
Disclosure: P. Vermersch received honorarium for contributions to meeting from Biogen, Sanofi-Genzyme, Novartis, Teva, Merck, Roche, Imcyse, AB Science, Janssen, Ad Scientiam and BMS-Celgene and research supports from Novartis, Sanofi-Genzyme and Merck. G. Comi received consulting and speaking fees from Novartis, Sanofi Genzyme, Merck, Bristol-Myers Squibb, Janssen, Rewind L. Leocani received research support from Novartis, Almirall, Biogen, Merck and consultancy or speaker fees from Novartis, Almirall, Biogen, Merck, Janssen-Cilag, Bristol-Myers Squibb, Roche. T. Ziemssen reports consulting or serving on speaker bureaus for Almiral, Biogen, BMS, Roche, Novartis, Sandoz, Viatris, TEVA, Merck, and Sanofi as well as research support from Biogen, Novartis, Roche, TEVA and Sanofi. L. Carment, A.Vivès, S. Bieuvelet, and S. Zinaï are employees of Ad Scientiam.

EPO-377 | Late-onset myelin oligodendrocyte glycoprotein antibody-associated disease: An unusual case

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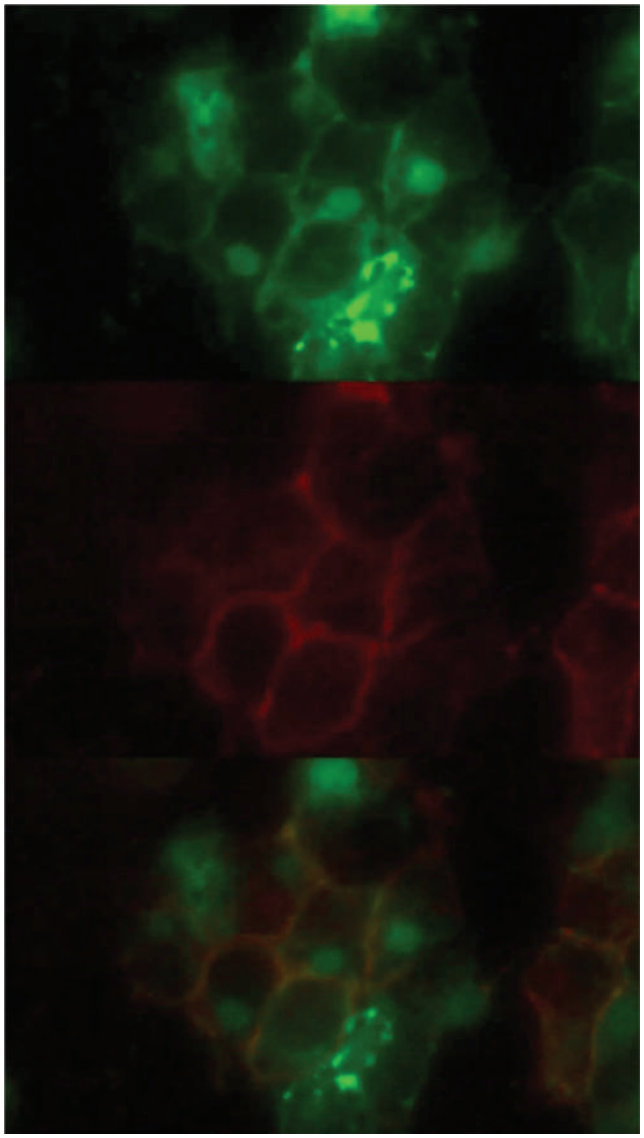
Background and Aims: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an inflammatory disease of the nervous system characterized by a wide range of symptoms that vary according to age. It's usually more common in pediatric-aged patients and young adults, although it can also debut in older patients.
Methods: We present the case of a 72-year-old female patient diagnosed with MOGAD, with uncommon symptoms for late-onset patients.
Results: We have a 72-year-old woman who starts with acute paraparesis and is admitted for complementary tests. Brain resonance showed multiple hyperintense lesions in T2/FLAIR in periventricular white matter, subcortical, both internal capsules and bilateral temporobasal level. At the medullary level there was extensive myelitis, from T2 to L1, with areas of contrast uptake. In the cerebrospinal fluid there was proteinorrachia (48.2 mg/dL), leukocytosis (20 leu/μL) and positivity of anti-MOG antibodies analyzed with indirect immunofluorescence. In blood tests there was also positivity for anti-MOG antibodies at 1/40 titer. After treatment with corticosteroids and plasmapheresis she improved, but after 2 weeks she was readmitted due to a new outbreak.



Indirect immunofluorescence in cerebrospinal fluid. Green = anti-MOG antibodies in native form. Red = patient's antibodies. Yellow = Colocalization of the prior confirming positive to anti-MOG antibodies.

Conclusion: According to the literature, late-onset MOGAD is a rare condition, with a usually more subacute, monophasic clinical picture, with more cerebral symptoms, without many cases of extensive myelitis at the onset and with less inflammatory burden. The patient that we present differs greatly from what has been described so far on late-onset MOGAD. Therefore, we consider that this diagnosis should be kept in mind in elderly patients, although it is not the most common clinical presentation.

Disclosure: Nothing to disclose.

EPO-378 | Longitudinally extensive myelitis in MS: A single centre experience

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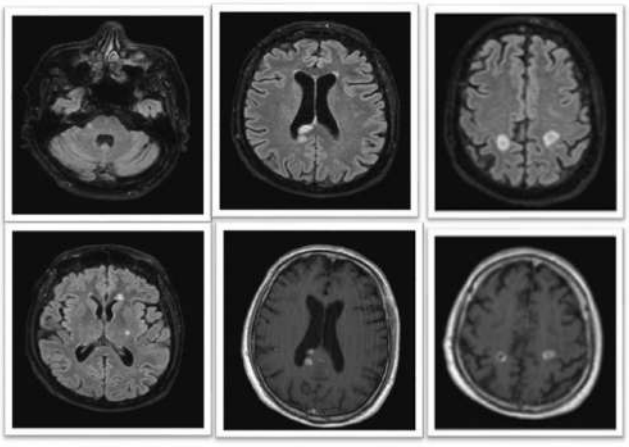
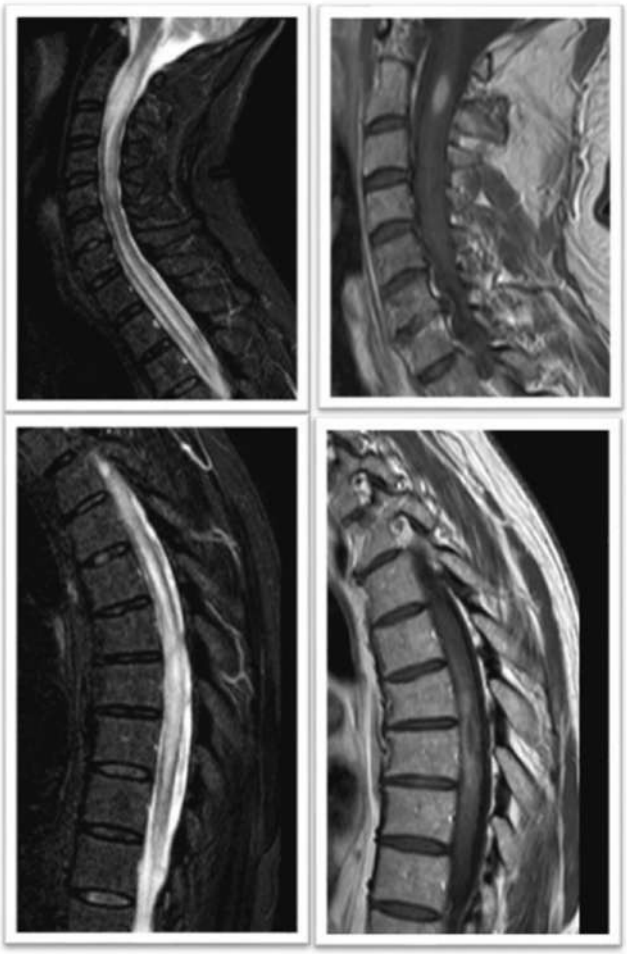
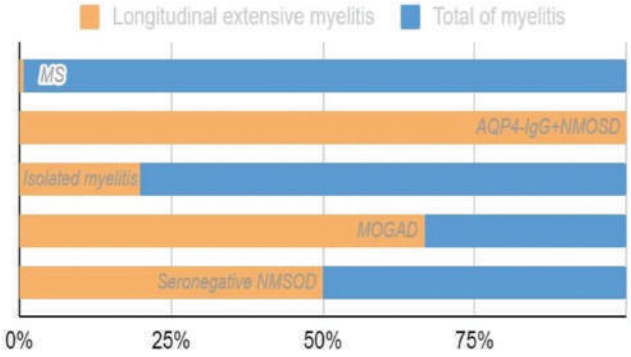
Background and Aims: The reported frequency of longitudinally extensive myelitis lesions - LEMs in MS varies, ranging from 0% to 32%. Most prior studies, however, predate the discovery of AQP4-IgG and MOG-IgG, potentially resulting in overestimation of LEMs. We sought to determine the frequency of LEMs at first myelitis attack in a single-centre cohort of patients with CNS demyelinating disorders.
Methods: We retrospectively identified patients with CNS demyelinating disorders seen at the University-Hospital of Sassari from January 1, 2017 to December 31, 2022. We included the following inclusion criteria: 1) First myelitis attack; and 2) available spinal cord MRI during the myelitis attack. The frequency of LEMs was determined and classified according to the diagnosis at last follow-up.
Results: Among 336 patients with CNS demyelinating disorders consecutively seen over 6 years, 158 were included in the study. The frequency of LEMs in MS was 0.7% (1/138). The only MS patient with LEMs was a 55-year-old man who developed subacute weakness of right limbs, accompanied by numbness and gait instability. Spinal cord MRI showed a longitudinally extensive T2-hyperintense enhancing lesion extending from C2-D11. Brain MRI showed typical MS lesions. CSF analysis revealed moderate pleocytosis and absence of oligoclonal bands; AQP4-IgG and MOG-IgG were absent in both serum and CSF by live cell-based assay.



Axial T2 FLAIR brain MRI showing brainstem, periventricular and cortico-juxtacortical white matter lesions (A-E), some of which presents gadolinium enhancement (D,F) consistent with multiple sclerosis.



Sagittal T2-weighted spinal cord MRI showing one short cervical lesion (A) and one longitudinally extensive lesion in the thoracic cord extending over >3 contiguous vertebral body segments (C), showing intense gadolinium enhancement in a nodular and ring.



Distribution of LEM in patients with CNS demyelinating diseases with at least one episode of myelitis attack.

Conclusion: LEMs is rare among adult MS patients at first myelitis attack. Although our MS patient with LEMs met the 2017 diagnostic criteria for MS, he showed several atypical features that raise the possibility of an alternative aetiology of the myelitis.

Disclosure: No disclosures.

EPO-379 | Modified Charlson Comorbidity Index as new tool to predict prognosis in multiple sclerosis

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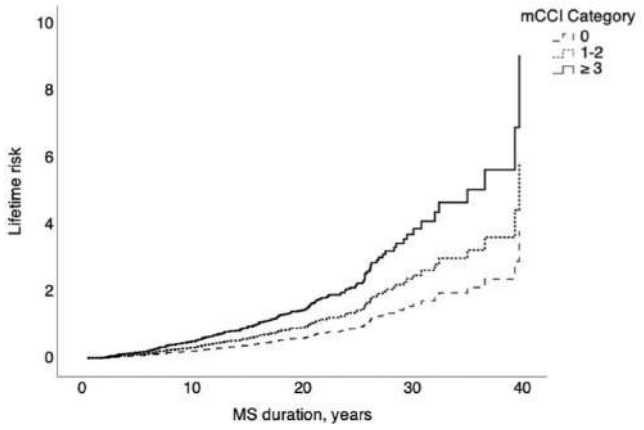
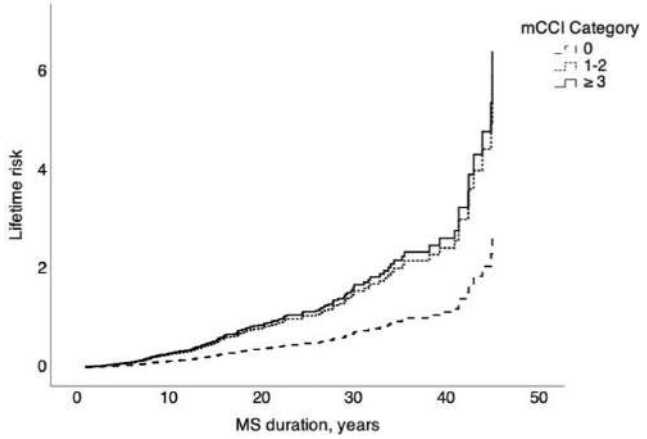
Background and Aims: Comorbidities have recently attracted increasing interest because of their impact in MS outcomes. The aims of this study are to predict the risk of reaching two disability milestones evaluated trough the Expanded Disability Status Scale (EDSS) and the risk of conversion from relapsing-remitting MS to Secondary Progressive MS (SPMS) by using a modified version of the Charlson Comorbidity Index (mCCI).

Methods: comorbidity data of people included in our local MS database were extracted. The mCCI was obtained by incorporating the grade of pyramidal functional system scores into the original CCI version. The capability of mCCI at first visit to predict the reaching of EDSS 4, EDSS 6 and SPMS conversion was estimated by carrying out multivariable Cox regression models.

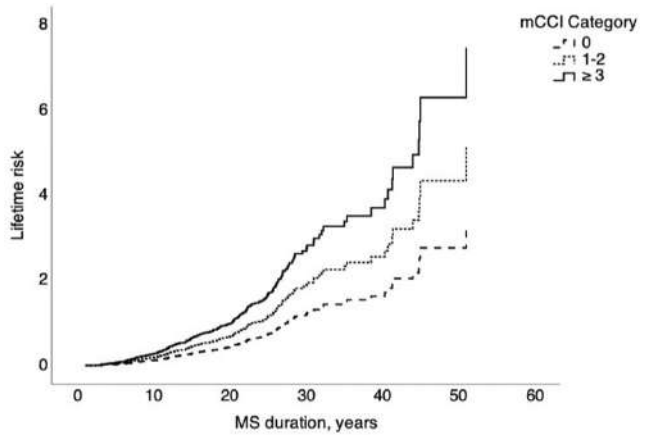
Results: a total of $n=622$ pwMS were included (72.7% women; median age 30.8 years [24-40]). The mCCI at first visit comprised between 1 and 2 was associated with higher risk of reaching EDSS 4 (HR = 1.53 [1.1-2.1], $p=0.011$), EDSS 6 (HR = 2.17 [1.48-2.96], $p<0.0001$) and SPMS conversion (HR = 1.57 [1.16-2.1], $p=0.003$). The mCCI at first visit >3 was associated with higher risk of reaching EDSS 6 (HR = 2.34 [1.44-3.8], $p=0.001$) and SPMS conversion (HR = 2.38 [1.29-4.01], $p=0.004$).



Lifetime risk of reaching the milestone EDSS 4 by mCCI categories according to MS duration on the x axis and the risk on the y axis.



Lifetime risk of reaching the milestone EDSS 6 by mCCI categories according to MS duration on the x axis and the risk on the y axis.



Lifetime risk of reaching the SPMS conversion according to mCCI categories according to MS duration on the x axis and the risk on the y axis.

Conclusion: comorbidity significantly affects MS prognosis as well as patient's age and motor impairment. In this study, the mCCI calculated at first visit appeared a simple and faster tool to predict MS prognosis by estimating the risk of disability worsening and SPMS conversion.
Disclosure: Nothing to disclose.

EPO-380 | The first study of real-world efficacy and safety of Natalizumab (Tysabri) in Iran

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Background and Aims: This study was aimed to evaluate the real-world effectiveness of Natalizumab in a referral center in Tehran, Iran. This study is the first real world analysis of efficacy and safety of Natalizumab in our country.
Methods: In this retrospective study, patients with RRMS were investigated in a high-volume center in Tehran from 2019 to 2021. MS patients under treatment with Natalizumab who have received at least 3 infusions of the drug and had completed follow-up data, have been evaluated for safety and efficacy of Natalizumab.
Results: 100 patients were included in the final analysis. The mean follow-up time was 20 months (6-33 months). The median EDSS score [1] of patients reached to 2 from 2.5 after the treatment course ($p<0.0001$). The annualized relapse rate (ARR) decreased from 0.81 (95% CI: 0.73-0.87) to 0.023 (95% CI 0.009 – 0.061). The median JCV index [2] remained unchanged before treatment 0.85 (IQR: 0.21-2.41) compare to after the treatment 0.85 (IQR: 0.21-2.31). The number of patients with active brain and cervical MRI lesions decreased significantly ($p=0.001$). NEDA-3 (No evidence of disease activity) was improved from 9% to 87% after the treatment with Natalizumab. No serious adverse events except than one progressive multifocal encephalopathy (PML) case have been found.
Conclusion: Natalizumab is a safe and effective choice in RRMS patients for reducing relapse rate, disability score, active MRI lesion, and improving the NEDA.
Disclosure: Nothing to disclose.

EPO-381 | Treatment failure rates in patients with neuromyelitis optica spectrum disorder included in an Argentinean registry

V. Tkachuk[1]; E. Carnero Contentti[2]; P. López[2]; L. Patrucco[3]; J. Miguez[4]; S. Liwacki[5]; C. Vrech[6]; N. Deri[7]; J. Correale[8]; M. Ysrraelit[8]; F. Leguizamon[9]; G. Luetic[10]; M. Menichini[11]; D. Tavolini[12]; C. Mainella[13]; G. Zanga[14]; M. Burgos[15]; J. Hryb[16]; A. Barboza[17]; R. Alonso[18]; B. Silva[18]; N. Fernández Liguori[19]; A. Carrá[20]; O. Garcea[18]; J. Rojas[21]
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Background and Aims: Immunosuppressive therapies such as azathioprine (AZA), mycophenolate mofetil (MMF) and rituximab (RTX) are commonly used to prevent relapses in NMOSD. However,

the response rate to these traditional therapies are unknown in Argentina. We aimed to describe and compare treatment failure rates in NMOSD (seropositive and seronegative for aquaporin-4 antibody) patients included in the Argentinean MS and NMOSD registry (RelevarEM, NCT 03375177)

Methods: Retrospective cohort study conducted in NMOSD patients. Only who received AZA or MMF for at least 6 months or RTX for at least 1 month were included. Patients who had initially received AZA, MMF, or RTX and then switched to another 1 of these 3 therapies were included if they met the specified criteria. Data on patient demographics, clinical and neuroradiological findings, and treatments administered were collected. Treatment failure was defined as any new attack/relapse that occurred despite immunosuppressive treatment

Results: We included 139 NMOSD patients: AZA ($n=105$), MMF ($n=5$) or RTX ($n=29$) with a mean follow-up time of 41.3 ±11.4 months and a median EDSS at treatment initiation of 3. We observed a reduction in the annualized relapse rate from pretreatment to post treatment of 56%, 48%, and 79% respectively, with a Hazard Risk relative to RTX (95% CI) of 1.67 (1.34-3.54, $p=0.01$) for AZA and 2.01 (1.86-4.43, $p=0.008$) for MMF. AZA, MMF and RTX failure was observed in 45 (42.8%), 2 (40%) and 3 (10.3%) patients, respectively.

Conclusion: Treatment failure rates were higher for AZA and MMF than RTX in Argentinean NMOSD patients in a real-word setting

Disclosure: Nothing to disclose.

EPO-382 | Treatment strategies for neuromyelitis optica spectrum disorder relapses: A study from a nationwide registry in Argentina

V. Tkachuk[1]; E. Carnero Contentti[2]; P. López[2]; J. Miguez[3]; L. Patrucco[4]; S. Liwacki[5]; C. Vrech[6]; N. Deri[7]; J. Correale[8]; M. Ysrraelit[8]; F. Leguizamón[9]; G. Luetic[10]; M. Menichini[11]; D. Tavolini[12]; C. Mainella[13]; G. Zanga[14]; M. Burgos[15]; J. Hryb[16]; A. Barboza[17]; R. Alonso[18]; N. Fernandez Liguori[18]; D. Nadur[19]; J. Rojas[20]

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Background and Aims: We aimed to assess treatment strategies selected in patients with neuromyelitis optica spectrum disorder (NMOSD) experiencing relapses: frequency, types, and response after 6 months based on the Expanded Disability Status Scale (EDSS) score.

Methods: We conducted a retrospective study from the Argentinean MS and NMOSD registry (RelevarEM, NCT 03375177). We collected data: patient demographics, clinical and radiological findings, and treatments. Treatment response at 6 months was categorized as "good" if the EDSS score decreased by ≥1 point after a nadir EDSS score ≤3, or by ≥2 points after a nadir EDSS score >3, "poor" if the EDSS score decrease was slighter, and as "absent" if the EDSS score remained unchanged or worsened. We used ordinal logistic regression to identify statistical associations with the outcome

Results: We included 131 patients (120 NMOSD [seropositive $N=75$ and seronegative $N=45$] and 11 myelin oligodendrocyte glycoprotein-antibody-positive [MOGAD]), who experienced 262 NMOSD-related relapses and received 270 treatments. Most common treatment: intravenous methylprednisolone (81.4%), followed by plasmapheresis (15.5%). At 6 months, complete recovery was achieved in 74/102 (74.5%) of the NMOSD patients. In NMOSD we did not observe differences in treatment response based on serostatus. Predictors of "good" response were: younger age at disease onset (OR: 3.54, CI95% 2.45-5.01, $p<0.0001$) and a short delay from onset of relapse to treatment initiation (OR: 1.56, CI95% 1.22-2.13, $p=0.004$)

Supplementary table 3. Predictors of complete remission in NMOSD (positive and negative) patients from relapses

	P	OR	95%CI
Age at disease onset	**0.002**	**2.27**	**2.11-4.12**
Female	0.461	0.57	0.12-2.52
Symptom at onset	0.862	0.77	0.43-1.23
Time from onset of relapse to start of treatment	0.885	0.95	0.82-1.56
Duration of long-term immunosuppressive treatment	0.421	0.88	0.65-1.65
First line treatment for relapse	0.223	1.03	0.67-1.78

Predictors of complete remission in NMOSD (positive and negative) patients from relapses.

Conclusion: In Argentina, plasmapheresis is not commonly used to treat NMOSD relapses. Approximately two-thirds of patients experienced complete recovery, and younger age and a short delay to start treatment were independent predictors of a "good" response.

Disclosure: Nothing to disclose.

EPO-383 | Tocilizumab treatment in naïve adult MOGAD patients: A single center experience

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Background and Aims: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare autoimmune oligodendrocytopathy. Differential diagnosis from multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) is challenging, and diagnostic criteria have been recently proposed. Moreover, treatment guidelines are still lacking, and traditional MS treatments are ineffective. Several case reports have documented the efficacy and safety of tocilizumab (TCZ), a humanized antibody targeting the IL-6 receptor, as a rescue therapy from other immunotherapies. Experience for naïve patients is otherwise lacking in adult patients.
Methods: In this single-center case series, we report three female (mean age at diagnosis 28±10 years) adult MOGAD naïve patients treated with TCZ. MOG antibodies tested positive on serum using fixed or live cell-based assay. Two patients presented with myelitis and one with bilateral optic neuritis (ON) (median EDSS at diagnosis 4, range 4-9). All patients fulfilled the 2023 diagnostic criteria.
Results: All patients were initially treated with steroids. Myelitis needed plasma exchanges and immunoglobulin for short-term worsening or relapses (one patient with extending myelitis and the other developing bilateral ON). After a mean time of 2.5 (SD1.5) months from diagnosis, TCZ 8 mg/kg every 4 weeks was started. Clinical and radiological stability was obtained for all patients (median EDSS 3.5, range 2-9). No adverse events were recorded.
Conclusion: MOGAD is rare but highly disabling and must be treated effectively early. TCZ is reported as a useful second-line immunotherapy in MOGAD patients. However, our observations highlight its efficacy and safety as a first-line disease-modifying treatment.
Disclosure: Nothing to disclose.

MS and related disorders 4

EPO-384 | Neuromyelitis Optica Spectrum Disorder (NMOSD) and effects of AQP4 status: A multicenter Turkish cohort

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Background and Aims: The detection of serum immunoglobulin G (IgG) autoantibodies to aquaporin-4 (AQP-4) is an important diagnostic tool for Neuromyelitis Optica Spectrum Disorder (NMOSD). While the precise mechanisms remain elusive, the pathogenic role of AQP-4 antibodies is well-established. However, the influence of variables such as gestation and menopause on NMOSD remains largely unknown. Exploring these factors within AQP-4 serostatus may reveal a linkage between AQP-4 IgG and hormonal dynamics, namely in the case of pregnancy where hormonal changes are fairly pronounced.
Methods: This retrospective analysis leverages medical records from nine centers in Turkiye, comprising 120 NMOSD patients (94 Females: F, 26 Males: M) diagnosed per the 2015 IPDN diagnostic criteria. A spreadsheet, filled out by the primary neurologists and was analysed using IBM SPSS Statistics Version 28.
Results: In the AQP-4 seropositive group, a significant association was revealed between presenting symptoms and treatment response ($p = 0.043$) (Figure 1, Table 1). In 41 women, 87 pregnancies before the disease onset were evaluated. Pregnancy exhibited a remarkable relationship with the onset age, in which multiple gestations postponed disease manifestation ($p < 0.001$) (Figure 2).

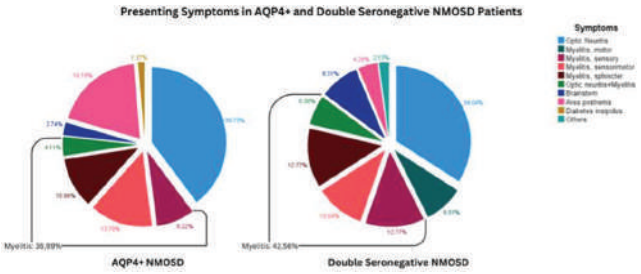

FIGURE 1 Presenting symptom of the first attack of the patients according to serostatus.

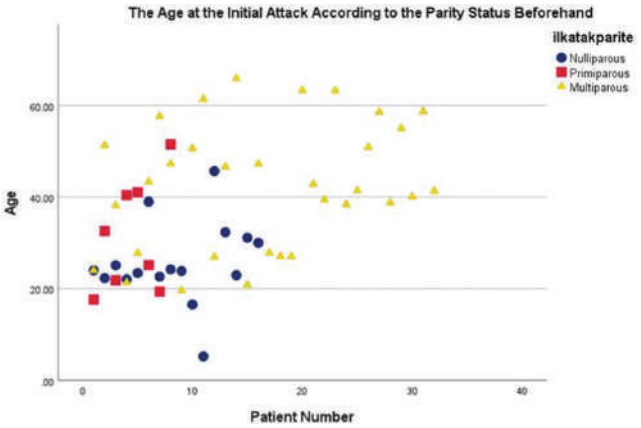

FIGURE 2 The age at the first attack of the patients categorised according to the parity status before the onset of the disease.

	Groups in AQP4+				Groups in DN			
Presenting Symptom / Response to Long Term Treatment	ON	Myelitis	ON+Myelitis	Total	ON	Myelitis	ON+Myelitis	Total
No response	3	1	0	4 (8.7%)	1	3	1	5 (17.9%)
Mild improvement	6	13	1	20 (43.5%)	3	5	1	9 (32.1%)
Moderate improvement	5	3	0	8 (17.4%)	2	4	0	6 (21.4%)
Full recovery	12	1	1	14 (30.4%)	6	2	0	8 (28.6%)
Total	26 (39.1%)	18 (56.5%)	2 (4.3%)	46	12 (50.0%)	14 (42.9%)	2 (7.1%)	28

TABLE 1 Long term treatment responses of the AQP4+NMOSD patients according to their presenting symptoms.

Conclusion: This study provides valuable insights into the interplay of clinical, reproductive, and immunological factors in NMOSD, focusing on serostatus and diverse patient profiles. The AQP4+ serostatus emerges as a potential prognosis predictor, prompting physicians to initiate targeted diagnostic assessments earlier which could guide therapeutic strategies and mitigate disability. Compared to double seronegative (25 F, 13 M), AQP4-NMOSD (66 F, 13 M) predominantly affects females and manifests later in life. Pregnancy initially delays disease onset, potentially influencing prognosis and disability in ways yet to be fully discovered.

Disclosure: Nothing to disclosure.

EPO-385 | Replacing PASAT with SDMT in the MSFC score improves the prediction of thalamic volume in multiple sclerosis

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Background and Aims: Multiple Sclerosis Functional Composite (MSFC) is a disability measure in Multiple Sclerosis that includes the "Timed 25-Foot Walk" (T25FW) to evaluate leg function, the "9-Hole Peg Test" (9HPT) to evaluate arm function and the "Paced Auditory Serial Addition test 3 seconds" (PASAT) to assess cognitive function. An alternative MSFC version replace the PASAT (MSFCp) with the Symbol Digit Modalities Test (SDMT) (MSFCs), that is less influenced by patient's psychological status. Among other MRI structural measures, thalamic volume is strictly associated to physical/cognitive disability in MS. The objective is to evaluate which is the best predictor of thalamic volume between MSFCs and MSFCp.

Methods: One hundred and fifteen relapsing remitting MS (RRMS) patients and 46 sex, age and education-matched healthy controls (HC) underwent clinical evaluation (EDSS, MSFCp and MSFCs), and a 3T–MRI protocol including high resolution 3D–T1 imaging. Brain and Thalamic volumes were calculated using SIENAX and FIRST tool of the FMRIB Software Library. To compare the different relationship between the thalamic volumes and disability measures we applied linear regression models, introducing the thalamic volumes as dependent variable and EDSS, MSFCp and MSFCs as independent variables.

Results: Compared to HC, MS patients showed a significant thalamic atrophy ($p<0.001$). Thalamic volume was independently predicted only by MSFCs ($\beta=0.67$, t 4.16, $p<0.001$), while not by EDSS and MSFCp.

Conclusion: MSFCs score performs better than MSFCp in prediction of thalamic volume in MS. Therefore MSFCs might be a better outcome measure in clinical trials in MS.

Disclosure: Nothing to disclose.

EPO-386 | Association of CSF levels of osteopontin with cortical atrophy and disability in early multiple sclerosis

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Background and Aims: We aimed to evaluate cerebrospinal fluid (CSF) inflammatory markers of accumulation of cortical damage as well as disease activity in patients with early relapsing remitting MS (RRMS).

Methods: CSF levels of Osteopontin (OPN) and 66 inflammatory markers were assessed using an immune-assay multiplex technique in 107 patients with RRMS (82F/25M, mean age 35.7±11.8 years). All patients underwent regular clinical assessment and yearly 3T MRI scans for 2 years, while 39 patients had a 4-year follow-up. White matter lesion number and volume, cortical lesion (CLs) and volume and global cortical thickness (CTh) were evaluated together with the 'no evidence of disease activity' (NEDA-3) status.

Results: The random forest algorithm selected OPN and CXCL13 as most related to CTh changes after 2 and 4 years. In a regression model, OPN ($p < 0.001$), CXCL13 ($p = 0.001$), and sTNFR1 ($p = 0.024$) were increased in those patients with accumulating atrophy (adjusted R-squared 0.615). The markers were added in a model that included all clinical, demographic and MRI variables: OPN ($p = 0.002$) and IL19 ($p = 0.022$) levels were confirmed to be significantly increased in patients developing more CTh change over the follow-up (adjusted R-squared 0.619). CXCL13 and OPN also revealed the best association with NEDA-3 after two years, with OPN significantly linked to disability accumulation (OR 2.468 [1.46-5.034], $p = 0.004$).

Conclusion: The data emphasize a crucial role of OPN in predicting changes in cortical pathology and disease activity in early MS.

Disclosure: Nothing to disclose.

EPO-387 | Neuro-physiological evidences of cerebellar impairment unrelated to structural damage in early multiple sclerosis

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Background and Aims: Despite early radiological involvement, clinically-evident cerebellar impairment (CI) is uncommon in early multiple sclerosis (MS). We used transcranial magnetic stimulation (TMS) to assess cerebellar function and explore its relationship with structural damage in this population.

Methods: Early, right-handed MS patients without clinically-evident CI underwent 3T-MRI and TMS assessment. FLAIR and Double-Inversion Recovery (DIR) sequences were analyzed to detect both white-matter and grey-matter cerebellar lesions (CLs). Cortico-spinal tract (CST) and middle cerebellar peduncle (MCP) masks from Johns Hopkins University atlas were registered to Diffusion-Tensor Imaging (DTI)-maps to obtain mean fractional-anisotropy (FA). CST excitability was studied through TMS recruitment curve (RC). Cerebellar-brain inhibition (CBI) was computed as the ratio between test stimulus and motor evoked potential amplitudes recorded after a paired-pulse protocol stimulating the cerebellum and the primary motor cortex with an interstimulus interval of 5ms.

Results: Seventeen MS patients (F: 12; mean (SD) age: 35.2 (11.3)) with disease-duration 6.7 (2.6) months and ten healthy-controls (HCs) (F: 5; age: 32.7 (11.2)) were included. ANCOVA analysis showed CBI reduction (MS: 0.18 (0.11) mV; HCs: 0.28 (0.12) mV; $p = 0.05$) and RCs slope reduction (MS: 0.56 (0.26) μV/%; HCs: 1.01 (0.36) μV/%; $p = 0.01$) in MS. No differences in CBI were shown comparing MS patients with and without CLs ($p = 0.92$). MCP-FA and CST-FA showed no effect on CBI ($p = 0.86$) and RC slope ($p = 0.28$) reduction respectively.

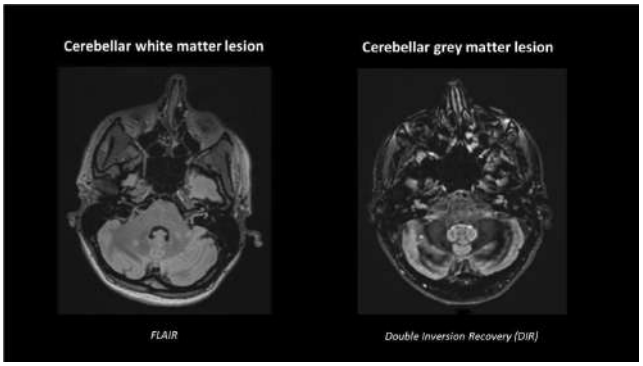

FIGURE 1 FLAIR and Double-Inversion Recovery (DIR) sequences allow for the detection of both white-matter and grey-matter cerebellar lesions.

Conclusion: CBI and RC slope reduction may indicate CI and decreased cortico-spinal excitability in early-MS. TMS-detected functional deficits appeared unrelated to lesion-related and microstructural damage. TMS may unveil distinct intracortical damage mechanism inaccessible to traditional MRI.

Disclosure: This research was funded by the Italian Ministry of Research through the 5x1000 project 'Cortical Excitability and MS.

EPO-388 | Post-pandemic pneumonia cases excess in multiple sclerosis patients treated with intravenous anti-CD 20 drugs

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Background and Aims: Pneumonia is rare in multiple sclerosis (MS) disease-modifying therapies (DMT) trials. In particular pneumonia in ocrelizumab (OCR) was 0.12% in OPERA I and II, 0.41% in ORATORIO trials. In rituximab (RTX) OLYMPUS trial was 1.4%.

Methods: From January 2023 we collected radiologically confirmed pneumonia cases among MS patients. Our cohort included 1543 subjects, distributed among the different DMTs as shown in the graph.

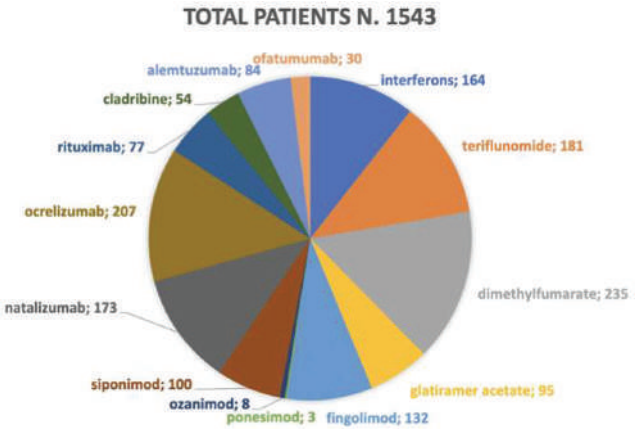

TABLE 1

	Cases	Range	Notes
Total N of Ocrelizumab patients	207	-	
Total N of Rituximab patients	77	-	
Total N of pneumonia cases	17	-	
N in Rituximab (%) among pneumonia cases	6 (35)	-	
N in Ocrelizumab (%) among pneumonia cases	11 (65)	-	
% of pneumonia cases among total patients in rituximab	7,8%	-	
% of pneumonia cases among total patients in ocrelizumab	5.3%	-	
Females (%) among pneumonia cases	15 (88)	-	
Age medium (standard deviation, SD) pneumonia cases	56 (7)	43-69	
Progressive course (%) among pneumonia cases	9 (53)	-	
Relapsing remitting course (%)among pneumonia cases	8 (47)	-	
EDSS medium and median (SD) among pneumonia cases	4.0 (2.0)	1.0-8.0	No differences RTX vs OCR
Medium time between starting anti-CD20 treatment and pneumonia in months (SD)	51 (35)	0-116	
Medium time from last infusion of anti CD 20 and pneumonia in months (SD)	3 (2.65)	0-8	
SARS COV2 pneumonia among all pneumonia cases	3 (18)	-	2 in RTX, 1 OCR
Hospitalisation (%) among pneumonia cases	7 (41)	-	
Hospitalisation (%) among pneumonia cases in rituximab	4 (67)	-	
Hospitalisation (%) among pneumonia cases in ocrelizumab	3 (27)	-	
Orotracheal intubation need (%) among pneumonia cases	1 (5.9)	-	In OCR
Grade 1 Neutropenia (%)among all pneumonia cases	1 (6)	-	In RTX, COVID+
Hypogammaglobulinemia (%)among all pneumonia cases	5 (29)	-	2 (33) in RTX, 3 (27) in OCR
Death by pneumonia (%) among all pneumonia cases	0 (0)	-	

Table 1. Demographic and clinical characteristics of patient with pneumonia in anti-CD 20 treatment.

Results: We found 17 pneumonia cases, 11/207 treated with OCR and 6/77 with RTX (5.3% and 7.8% of total patients respectively). No cases occurred in other DMTs. Three cases were COVID related; 7 patients were hospitalized (one with hypogammaglobulinemia in ICU). All patients recovered. Demographic and clinical data are reported in table 1.

Conclusion: We observed a higher incidence of pneumonia among patients in intravenous anti-CD20 therapies compared with clinical trials data. We suppose that risk of pneumonia increases according to treatment duration. A shorter treatment may account for absence of pneumonia cases in ofatumumab treated patients. Considering the age of pneumonia cases, immunosenescence could have an addictive role in increasing infective risk, while hypogammaglobulinemia does not seem as much. Cases mainly occurred in winter, in accordance with epidemic flu peaks; in long lasting immunosuppressed older patients, the post- pandemia abandoning of the use of masks and social distancing could account for the recent increase of incidence of pneumonia. Further and larger case-control study are needed, focused on others environmental factors like smoking and air pollution. Selection bias could account for imbalance between DMTs.

Disclosure: -D. Quartana received speaking fee in events sponsored by Merck and Novartis. Merck, Roche and Novartis sustained his travel and accommodation expenses during scientific events. -M. Lo Re received speaking fee in events sponsored by Merck and writing fee from Novartis. Biogen sustained her travel and accommodation expenses during scientific events. -M. Malentacchi received a grant from Alexion and Novartis. -R. Bottero received writing fee from Novartis and speaking fee in events sponsored by Sanofi and Novartis. Bristol Myers and Janssen sustained her travel and accommodation expenses during scientific events. -F. Sperli received speaking fee in events sponsored by Novartis. Bristol Mayers sustained her travel and accommodation expenses during scientific events. -A. Oggero declared nothing to disclose -S. Malucchi received speaking fee in events sponsored by Biogen, Merck, Novartis and Roche. -A. Di Sapio received honoraria for speaking and consulting by Biogen, Novartis, Roche, Sanofi, Merck, Alexion and Sandoz and has been reimbursed by Merck, Biogen, Sanofi, Novartis and Roche for attending several conferences.

EPO-389 | Secondary autoimmune diseases in multiple sclerosis after autologous hematopoietic stem cell transplantation

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Background and Aims: Autologous hematopoietic stem cell transplantation (aHSCT) has been described as an effective treatment strategy for aggressive multiple sclerosis (MS). Between the possible side effects, secondary autoimmune diseases (SAD) are reported, depending mostly on conditioning regimen (CR) intensity. We aimed to describe the occurrence of both clinical and subclinical SADs in a cohort of MS patients (pwMS) treated with intense immunosuppression followed by aHSCT.
Methods: All pwMS treated at our center with aHSCT with minimum one-year follow-up were included and we analysed clinical-radiological data, blood samples for SADs and lymphocitary-immunophenotype at baseline and every year.
Results: We evaluated 21 pwMS treated from 2015 to 2022. Medium FU was 3.5 years (range 1-7). All patients underwent the same CR (carmustine-cytarabine-etoposide-melphalan plus anti-thymocyte-globulin), besides one that received high-dosage cyclophosphamide (Cy). No clinical SADs were noted. Eight out of 21 (38.1%) patients already presented clinical/laboratorical (lab)-autoimmunity (AI) before aHSCT; of these, in 4 (50.0%) cases lab-AI disappeared or reduced, in 2 (25.0%) lab-thyroid-AI temporarily compared and 2 (25.0%) presented mild anti-cyclic-citrullinated-peptide (CCP) positivity. Of the remaining 13 negative at basal screening, 4 (30.8%) presented transient lab-AI, 4 (30.8%) mild but persistent lab-AI (mostly anti-nuclear antibody, CCP or gastric-parietal-cells; one of these patient received high-dosage Cy as CR) and 5 (38.4%) none. Lab-AI occurred even after long time from procedure (4 years).
Conclusion: Isolated subclinical positivity with no clinical significance can occur in pwMS after aHSCT with myeloablative CR even after a long FU. Interestingly, previous laboratoristic autoantibodies might disappear.
Disclosure: Nothing to disclose.

EPO-390 | Ketogenic diet as a promising intervention for fatigue management in multiple sclerosis: Results of the CHE-FATICA study

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Background and Aims: Fatigue is a frequent, disabling and difficult to treat symptom of multiple sclerosis. Low grade inflammation and energetic dysfunction are proposed mechanisms in the pathogenesis of this symptom. Due to its anti-inflammatory and metabolic properties, there is a rational for ketogenic diet application in this setting.
Methods: We conducted a single arm open label interventional study on a strictly selected group of 16 non obese patients with multiple sclerosis who were prescribed a KD for three months.
Results: With respect to baseline, at 3 months we observed a significant reduction of fatigue severity scale (5.18±1.02 v.s. 4.16±0.98; $p=0.042$), Epworth Sleepiness Scale (5.64±2.46 v.s 8.46±3.05; $p<0.001$), Pittsburgh Sleep Quality Index (5.64±3.53 v.s. 7.62±2.59; $p=0.009$), Depression Anxiety Stress Scales-21 depression (3.18±2.93 v.s. 6.15±3.81; $p=0.036$) and anxiety (5.15±4.10 v.s. 1.55±1.92; $p=0.019$) sub-scales, and an improvement in energy sub-scale of Multiple Sclerosis Quality of Life-54 (52.49±12.83 v.s. 37.43±14.26; $p=0.042$).
Conclusion: These findings suggest that ketogenic diet may be useful in the treatment of fatigue and other symptoms frequently encountered in multiple sclerosis.
Disclosure: Nothing to disclose.

EPO-391 | A case of multiple sclerosis combined with polyradiculoneuropathy associated with antiCASPR-1 antibodies

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Background and Aims: Multiple Sclerosis (MS) is an inflammatory demyelinating and neurodegenerative disease of the Central Nervous System (CNS) with almost complete sparing of the Peripheral Nervous System (PNS). Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) is the most common acquired inflammatory polyneuropathy worldwide. It can be associated with Antibodies to molecules of the paranodal complex, such

as Contactin-associated protein-1 (CASPR-1). Cases of CIDP in MS have been reported.

Methods: We report the case of a 50-year-old woman with a ten-years history of CIDP related to Anti-CASPR-1 Antibodies who developed MS.

Results: During the diagnostic work-up for CIDP, to exclude alternative diagnosis, she underwent Magnetic Resonance Imaging (MRI) of the brain in 2010 that was unremarkable. In May 2014 she had diplopia related to right abducens nerve palsy. In November 2014 she had optic neuritis. Therefore she was admitted to our Neurology Department. The neurological examination showed mild right upper limb weakness, facial nerve palsy and absent lower limbs reflexes. Expanded Disability Status Scale was 2.0. She repeated brain and spinal cord MRI that revealed multiple T2 hyperintense lesions involving juxtacortical and periventricular white matter and dorsal segment of the spinal cord. All paraclinical and laboratory tests were normal; the cerebrospinal fluid analysis showed Oligoclonal Bands. A diagnosis of MS was made according to 2017 McDonald criteria.

Conclusion: The co-existence of MS and CIDP has been reported. It can be due to a shared immune pathogenesis with common antigen between CNS and PNS. It may cause an additional disability burden in patients.

Disclosure: Nothing to disclose.

EPO-392 | A multicentric Italian project: Family functioning and multiple sclerosis

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Background and Aims: The impact of Multiple Sclerosis (MS) on family dynamics includes effects on both marital relationships and parental bonding1. In this study we aim to evaluate family functioning and related factors in patients with MS and their families.

Methods: To fill-out the questionnaires for MS patients and their families, a dedicated platform was employed2. Families without members reporting chronic diseases were selected as healthy controls (HC), and data on socio-demographics and clinical information were gathered. The administered questionnaires included: The short form of the Family Assessment Measure Third Edition (FAM3), The Hospital Anxiety and Depression Scale (HADS), The Multidimensional Scale of Perceived Social Support (MSPSS), 20-item Toronto Alexithymia Scale (TAS-20), Dyadic Adjustment Scale (DAS) and Inventory of Parent and Peer Attachment (IPPA).

Results: Out 164 MS patients enrolled, we selected those individuals for whom a family member had completed the questionnaires. Two patients were excluded due to language limitations, resulting in a final cohort of 50 individuals. Sociodemographic characteristics are displayed in table 1. Compared with HC, MS patients (>20 years) relatives tend to perceive greater support from "others" ($p = 0.044$), while MS patients partners exhibit a higher dyadic agreement (on finances, leisure time, home organization) ($p = 0.005$)(Table 2). Moreover, young individuals (13 – 20 years), who have at least one family member with MS, have higher overall IPPA scores (table 3).

	Patients (N=50)	Partners (N=34)	Children (N=25)	Other family members (N=25)
Relationship with the MS patient				
Partner	---	34(100%)	---	---
Child	---	---	25(100%)	---
Father	---	---	---	5 (20.0%)
Mother	---	---	---	9 (36.0%)
Sister/Brother	---	---	---	10 (40.0%)
Other	---	---	---	1 (4.0%)
Cohabitation, N(%)	---	---	25 (100.0%)	25 (100.0%)
Mean age (ds)	42.6 (11.4)	45.2 (10.6)	16.2(3.6)	47.2 (17.7%)
Italian nationality N(%)	49 (98.0%)	34 (100.0%)	25 (100.0%)	25 (100.0%)
Women, N(%)	34 (68.0%)	15 (44.1%)	10 (40%)	16 (64%)
Job, N(%)				
Student	5 (10.0%)	0 (0.0%)	24(96.0%)	5 (20.0%)
Worker	30 (60.0%)	24 (70.6%)	1(4.0%)	13 (52.0%)
Unemployed	3 (6.0%)	3 (8.8%)	0 (0.0%)	2 (8.0%)
Retired	4 (8.0%)	3 (8.8%)	0 (0.0%)	1 (4.0%)
Housewife	8 (16.0%)	4 (11.8%)	0 (0.0%)	4 (16.0%)
Qualification, N(%)				
None	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Elementary Licence	0(0.0%)	0(0.0%)	1(4.0%)	0(0.0%)
Middle school diploma	1 (2.0%)	0(0.0%)	3(12.0%)	2 (8.0%)
Diploma	6 (12.0%)	5 (14.7%)	17(68.0%)	6 (24.0%)
Bachelor's Degree	25 (50.0%)	18 (52.9%)	2(8.0%)	9 (36.0%)
Master's Degree	6 (12.0%)	1 (2.9%)	2(8.0%)	7 (28.0%)
Old Degree	5 (10.0%)	3 (8.8%)	0(0.0%)	0(0.0%)
Postgraduate specialisation/Master's degree	3 (6.0%)	2 (5.9%)	0(0.0%)	0(0.0%)
Missing	4 (8.0%)	5 (14.7%)	0(0.0%)	1 (4.0 %)
Education, N(%)				
< 5	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
5	1(2.0%)	0(0.0%)	1(4.0%)	0(0.0%)
8	3(6.0%)	3 (8.8%)	10(40.0%)	7 (28.0%)
12-13	16 (32.0%)	11 (32.3%)	8(32.0%)	5 (20.0%)
> 13	30 (60.0%)	20 (58.8%)	6(24.0%)	13 (52.0%)
Marital status, N(%)				
Single	8 (16.0%)	2 (5.9%)	20 (80.0%)	4 (16.0%)
Cohabiting	4 (8.0%)	5 (14.7%)	0(0.0%)	0(0.0%)
Married	31 (62.0%)	27 (79.4%)	0(0.0%)	14 (56.0%)
Separated	2 (4.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Divorced	0 (0.0%)	0(0.0%)	0(0.0%)	1 (4.0%)
Widowed	0(0.0%)	0(0.0%)	0(0.0%)	3 (12.0%)
Missing	5 (10.0%)	0(0.0%)	5(20.0%)	3 (12.0%)
Children, N(%)				
No	21 (42.0%)	13 (38.2%)	---	---
Biological parent	28 (56.0%)	19 (55.9%)	---	---
Adoptive parent	0 (0.0%)	1 (2.9%)	---	---
Missing	1 (2.0%)	1 (2.9%)	---	---
Number of children among parents, N(%)				
1	11 (39.3%)	6 (30.0 %)	---	---
2	12 (42.9%)	11 (55.0%)	---	---
3	5 (17.9%)	3 (15.0%)	---	---
PDDS, median (IQR)	1 (0 - 3)	---	---	---

Characteristics of the included participants.

	Family members>20	Controls	p-value
AnxietyHADS	6(3.5;12)	8(7;10)	0.132
DepHADS	5(2;8)	5(3;7)	0.889
FAM3tot	10(7;15)	11.5(8;20)	0.054
MSPSStot	73(62;79)	67(58;73)	0.068
Significant other	26.5(23;28)	24(20;26.5)	**0.044**
Family	26.5(21.5;28)	24(20.5;26)	0.186
Friends	20.5(19;25)	20(16;23.5)	0.128
TAStot	57(49;65.5)	59(50;65.5)	0.950
Describing	14(11;17)	15(12;17)	0.647
identifying	15(11;21)	17.5(11;22)	0.391
externally oriented thinking	28(25;30.5)	26(24;29)	0.077
DASTot (N=28)	110(104;115)	96.5(86.5;112)	**0.039**
dyadic agreement	56.5(53;60.5)	44.5(38;56.5)	**0.005**
dyadic satisfaction	28(26;29)	28(25.5;30)	0.963
dyadic coesion	14(12.5;18)	15(13.5;17.5)	0.560
Display of emotional responses	10(8;11)	8.5(6.5;11)	0.137

Family members >20 matched with controls based on sex and age.

	Family members<=20	Controls	p-value
TotMother	94(85;103)	83(77;86)	**0.001**
Confidence	32(28;35)	19(14;24)	**<0.001**
Trust	41(37;44)	38(33;41)	**0.022**
Communication	33(27;36)	32(27;36)	0.681
Disaffection	21(16;23)	14(9;16)	**<0.001**
TotFather	92.5(85;102)	76.5(72;82)	**0.001**
Confidence	34(32;37)	19(15;25)	**<0.001**
Trust	43(37;46)	37(32;38)	**0.021**
Communication	28.5(26;35)	27(24;32)	0.648
Disaffection	22.5(19;24)	12.5(10;16)	**<0.001**
TotalePeer	98(89;108)	90(81;96)	**0.016**
Confidence	31(28;35)	18(13;21)	**<0.001**
Trust	43(38;46)	42(39;46)	0.761
Communication	29(27;34)	33(27;37)	0.338
Disaffection	26(25;31)	16(12;20)	**<0.001**

Family members ≤20 matched with controls based on sex and age.

Conclusion: MS influences dynamics of interpersonal relationships within families, Specifically, it molds relationships with partners, showing an higher level of dyadic consensus and leading to a positive impact on MS younger family members.

Disclosure: Nothing to disclose.

EPO-393 | White matter integrity and the brief repeatable battery: A combined neuropsychological and MRI study

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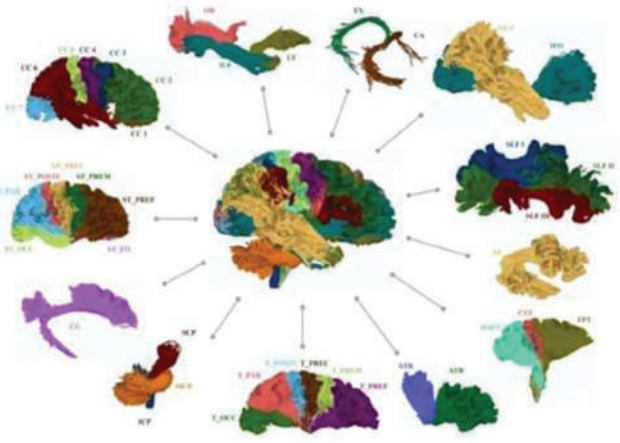
Background and Aims: Cognitive impairment is frequent in people with multiple sclerosis (pwMS) and the brief repeatable battery (BRB) is a sensitive measure for its early detection. Our aim was to test BRB in recently-diagnosed (<2 years from diagnosis) relapsing-MS in association with white matter (WM) integrity as measured by diffusion tensor imaging tractography to find possible correlations between cognitive performances and microstructural WM damage

Methods: BRB and 3T-MRI were acquired in 26 pwMS (16 F, 10 M). WM fibers density and cross-section (FDC) were measured by fixel-based analysis within 72 WM tracts of interest using TractSeg. Correlations between WM-tracts FDC and BRB-scores were assessed by Pearson correlations (setting $p<0.05$) and regression analyses for potential confounders were carried out. Sex differences in Paced Auditory Serial Addition Test (PASAT) scoring were tested by t-test.

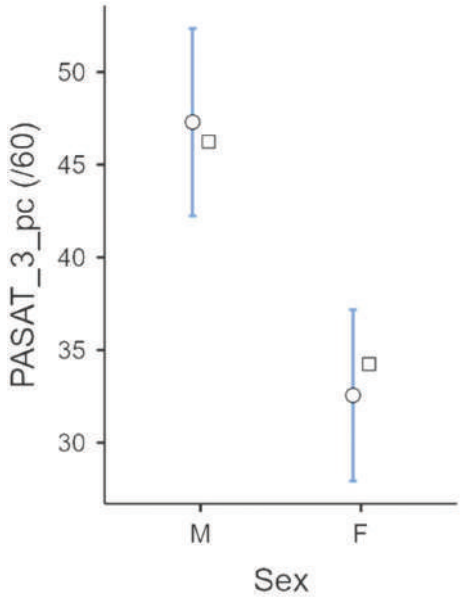
Results: BRB scores were not significantly correlated with clinical and radiological activity, EDSS, depression or fatigue. We found a significant correlation between PASAT 3, 2 and word list generation (WLG) scores and FDC within certain WM tracts, as shown in figure 2. Linear regression found that sex significantly affects PASAT scoring, with males showing higher performances (Fig.3).



Overview of the 72 WM tracts. WM fiber density and cross-section (FDC) measures were extracted from 72 WM tracts, by using fixel-based analysis (MRtrix and TractSeg) (picture from Wasserthal J et al. 2018).

FDC	PASAT 2	PASAT 3	WLG
ATR_left	r = 0.503 p = 0.009	r = 0.608 p < 0.001	r = 0.533 p = 0.005
ATR_right	r = 0.555 p = 0.003	r = 0.689 p < 0.001	r = 0.556 p = 0.003
CA	N.S.	r = 0.509 p = 0.008	N.S.
CC_1	N.S.	r = 0.478 p = 0.014	N.S.
CC_2	r = 0.584 p = 0.002	r = 0.685 p < 0.001	r = 0.479 p = 0.013
CC_3	r = 0.412 p = 0.037	r = 0.431 p =0.028	r = 0.404 p = 0.04
CC	r = 0.452 p = 0.02	r = 0.496 p < 0.01	N.S.
CG_left	r = 0.479 p = 0.013	r = 0.594 p = 0.001	N.S.
CG_right	r = 0.418 p = 0.034	r = 0.565 p = 0.003	r = 0.426 p = 0.03
FPT_right	N.S.	N.S.	r = 0.408 p = 0.039
FX_left	r = 0.401 p = 0.042	r = 0.547 p = 0.004	r = 0.411 p = 0.037
FX_right	N.S.	r = 0.483 p = 0.012	r = 0.398 p = 0.044
IFO_ left	r = 0.430 p = 0.028	r = 0.548 p = 0.004	r = 0.449 p = 0.021
IFO_right	N.S.	r = 0.452 p = 0.02	N.S.
ILF_left	r = 0.424 p = 0.031	r = 0.524 p = 0.006	N.S.
ILF_right	N.S.	r = 0.461 p = 0.018	r = 0.701 p = 0.042
MLF_left	N.S.	r = 0.426 p = 0.03	N.S.
SLF_III_left	N.S.	r = 0.398 p = 0.044	r = 0.41 p = 0.037
SLF_III_right	N.S.	r = 0.438 p = 0.044	N.S.
ST_FO_left	r = 0.531 p = 0.005	r = 0.680 p < 0.001	N.S.
ST_FO_right	r = 0.469 p = 0.016	r = 0.644 p < 0.001	r = 0.456 p = 0.019
ST_OCC_left	N.S.	r = 0.438 p = 0.025	N.S.
ST_PREF_left	r = 0.440 p = 0.024	r = 0.593 p = 0.001	r = 0.395 p = 0.046
ST_PREF_right	r = 0.485 p = 0.012	r = 0.647 p < 0.001	r = 0.448 p = 0.022
ST_PREM_left	r = 0.423 p = 0.031	r = 0.446 p = 0.022	r = 0.549 p = 0.004

Significant correlation between scoring of PASAT 2, PASAT 3 and WLG with FDC within different WM tract. Pearson correlations were used ($p < 0.05$). *Persistance of statistical significance when inserting sex as a covariant during regression analyses.



T-test shows higher PASAT 3 scores in the male group. The same was confirmed for PASAT 2.

Conclusion: In people with recently-diagnosed-MS, PASAT and WLG scoring are affected by regional WM axonal damage within specific WM tracts as measured by FDC reduction. From our preliminary results sex seems to affect PASAT performance in MS patients. Larger sample is needed to confirm preliminary result.
Disclosure: Nothing to disclose.

EPO-394 | Treatment switch or retreatment with cladribine tablets during CLARIFY-MS & CLARIFY-MS extension studies: Patient profile

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Background and Aims: The objective of CLARIFY-MS Extension (NCT04776213), a follow up study to CLARIFY-MS, was to assess long-term effects on cognition and health-related quality of life in patients with relapsing multiple sclerosis treated with cladribine

tablets (CladT). We also evaluated the individual characteristics of patients who switched to other disease modifying therapies (DMTs) or were retreated with CladT during CLARIFY-MS and CLARIFY-MS Extension.

Methods: We evaluated potential reasons for switching to other DMTs or CladT retreatment during the total 4-year observation period of the CLARIFY-MS Extension study ($N = 280$), during which no CladT treatment was planned, as per protocol. Decisions to switch to other DMTs or re-treat with CladT were based on the investigators´ discretion.

Results: Overall, 37/280 patients (13.2%) switched to another DMT, among whom 33 (89%) showed evidence of disease activity (EDA, i.e., 6-month confirmed disability progression, qualifying relapse, or magnetic resonance imaging [MRI] activity) before switch; MRI activity was the most frequently observed EDA event (28/37; 75.7%). None of the patients switched to another DMT during Year 1 of CladT treatment; 4, 17 and 16 patients switched during Years 2, 3, and 4, respectively. One patient in Year 3 and 7 patients in Year 4 (2.9% in total) were retreated with CladT; all had an EDA event before CladT retreatment. Individual patient profiles and reasons for switching or CladT retreatment will be presented.

Conclusion: A low proportion of patients switched to other DMTs or required CladT retreatment during the CLARIFY-MS and CLARIFY-MS Extension studies, suggesting durable CladT efficacy.

Disclosure: This study was sponsored by Merck (CrossRef Funder ID: 10.13039/100009945). Detailed author disclosures will be included in the presentation.

EPO-395 | Ocrelizumab versus siponimod: A real life comparison study

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Background and Aims: Ocrelizumab (OCR) and Siponimod (SIP) are licensed to treat patients with Progressive Multiple Sclerosis with disease activity (paMS). This study aims to compare the effectiveness and side effects of OCR and SIP in paMS patients.

Methods: This is a multicenter, retrospective, real-world study conducted in Italy on paMS patients treated with SIP or OCR. Clinical data, including demographics and laboratory information, were collected at baseline, 6, 12 and 18 months during routine clinical visits. A propensity score matching approach (PSMA) was used to compare the effectiveness and safety of the two treatments.

Results: We enrolled 116 paMS patients treated with OCR and 76 with SIP. These groups showed significant differences in age and annualized relapse rate (ARR) one and two years before treatment. After PSMA, both groups consist of 76 paMS patients, with a mean age of 50.8 (SD 6.95) for the OCR and 51.8 (SD 8.10) for the SIP group (Table 1). No differences in relapses and EDSS scores at 6, 12, and 18 months follow-up, and Gd+ lesions at MRI at 6 and 18 months follow-up. The SIP compared to the OCR group showed lower white blood cells and lymphocytes count at 6, 12, and 18 months ($p < 0.001$); no significant differences were found in the two groups for the number of infections at 6, 12, and 18 months follow-up.

TABLE 1 Demographic and clinic characteristics of paMS patients.

		paMS patients treated with OCR n=76	paMS patients treated with SIP n=76
Age (y)	Mean (SD)	50.8 (6.95)	51.8 (8.10)
	Median (min-Max)	52.4 (34.0-62.1)	54.8(27.3-61.4)
Sex	F % (n)	30.9%	32.2%
ARR one year before the start of OCR/SIP	Mean (SD)	0.513(0.554)	0.421(0.572)
ARR one year before the start of OCR/SIP	Mean (SD)	0.401 (0.408)	0.349(0.469)
Percentage of DMTs of paMS patients before starting OCR/SIP	%		
Naive		11.5%	4.7%
Interferon		7.4%	10.8%
Glatiramer Acetate		5.4%	6.1%
Dimetilfumarate		1.4%	4.7%
Teriflunomide		3.4%	6.1%
Fingolimod		11.5%	14.2%
Siponimod		1.4%	0%
Natalizumab		0.7%	1.4%
Ocrelizumab		0%	0.7%
Lemtrade		2%	0.7%
Cladiribine		0%	0.7%
Rituximab		1.4%	0%
Azatioprine		3.4%	0.7%

ARR, annualized relapse rate; paMS, Progressive Multiple Sclerosis with disease activity; OCR, Ocrelizumab; SD, standard deviation; SIP,Siponimod;

Conclusion: Despite a short 18-month follow-up, similar treatment outcomes in elderly paMS patients in SIP or OCR therapy suggest that both treatments are similarly effective and safe in elderly patients.

Disclosure: Nothing to disclose.

EPO-396 | Comparing lymphocyte count among different S1P modulators in multiple sclerosis: A multicenter real-world study

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Background and aims: Sphingosine-1-phosphate (S1P) modulators are a class of molecules targeting S1P receptors (S1PR) with different S1PR-subtype selectivity. They cause a reduction in circulating lymphocytes by inhibiting lymphocytes egress from lymph nodes. Our study aims to compare the absolute lymphocytes counts (ALCs) of MS patients treated with Fingolimod (FTY), Siponimod (SIP), Ozanimod (OZA), and Ponesimod (PON).

Methods: We enrolled 219 pwMS from eleven Italian Centers. Out of 219 pwMS, 69 (31.5%) were treated with SIP, 62 (28.3%) with OZA, 46 (21%) with FTY and 42 (19.2%) with PON. We excluded patients who had already received previous treatment with S1P modulators.

Results: OZA showed a significantly higher ALCs compared either to SIP in all time points ($p < 0.001$ at T1 and T3; $p = 0.003$ at T6), or FTY at T1 ($p < 0.001$) and T3 ($p = 0.02$). PON showed significantly higher ALCs compared to SIP at T1 and T3 ($p = 0.003$; $p = 0.03$ respectively). Furthermore, we analyzed the percentage of severe lymphopenia (including grade 3 and grade 4) among the different S1P modulators. PON and OZA showed a significantly lower percentage of patients with severe lymphopenia (23.8 % $p = 0.006$, 25.8% $p = 0.005$ respectively) compared to FTY (52.2%) and SIP (60.9%).

Conclusion: Despite a short follow-up, our study demonstrated a different degree of induced-lymphopenia among S1P modulators, as OZA and PON showed higher ALCs and a lower percentage of severe lymphopenia in pwMS.

Disclosure: Nothing to disclose.

EPO-397 | Identifying multiple sclerosis patients within a control population using online cognitive and motor assessments

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Background and Aims: Multiple Sclerosis (MS) is characterised by a complex interplay of motor, cognitive and neuropsychiatric features which vary between individuals and across time. Whilst MS diagnosis has improved over time, there remains a need for more rapid and reliable diagnostic tools. We use classification algorithms to investigate the feasibility of online cognitive and motor assessments in identifying MS patients from controls.

Methods: We trained a random forest classifier on cognitive metrics from a randomly sampled population of 1777 patients with MS (pwMS), 1189 patients with depression and anxiety (pwDA) and 1777 healthy controls (HC) from Cognitron. The model uses performance metrics (response time and accuracy) from 7 online cognitive tasks specific to MS, as features to predict the participant's group label. We also trained a support vector machine (SVM) classifier on motor performance metrics from pwMS and HC. This model uses the MS Impact Scale (MSIS-29v2) from the UKMS Register to determine the participant's group label.

Results: The random forest classifier discriminates between HC and pwMS (ROC AUC = 0.81), and between pwDA and pwMS (ROC AUC = 0.85) using online cognitive testing metrics. Our SVM classifier robustly distinguished pwMS from HC (ROC AUC = 0.96) using the MSIS-29v2. A sub-analysis of pwMS (five years from onset) also showed high classification accuracy (ROC AUC = 0.94).

Conclusion: Online cognitive testing and motor MSIS-29v2 can accurately distinguish pwMS from controls. Our findings provide a novel data-driven approach to MS identification, offering an opportunity for earlier intervention and tailored treatment approaches in the clinical setting.

Disclosure: RN: Advisory boards for Roche/Novartis.

EPO-398 | Longer-term safety and efficacy of ofatumumab in people with relapsing multiple sclerosis for up to 6 years

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Background and Aims: Ofatumumab demonstrated superior efficacy and favourable safety versus teriflunomide in the Phase 3 ASCLEPIOS I/II trials in people with relapsing multiple sclerosis (pwRMS). Previously reported data showed sustained efficacy and a favourable safety profile of ofatumumab in pwRMS up to 5 years. Here, we aim to present the safety and efficacy of ofatumumab treatment for up to 6 years.

Methods: Efficacy analyses will include all participants randomised in ASCLEPIOS I/II and their data from first dose in ASCLEPIOS I/II, whereas safety analyses will include all participants who received at least one dose of ofatumumab in either ASCLEPIOS I/II, APOLITOS, APLIOS or ALITHIOS (cut-off date: 25-Sep-2023). Efficacy will be analysed by randomised treatment in the core study, with those randomised to ofatumumab referred to as continuous group and to teriflunomide as switch group.

Results: Previously reported 5-year data (cut-off: 25-Sep-2022) showed a sustained low annualised relapse rate (ARR) and almost complete suppression of MRI lesion activity in the continuous group. In the switch group, ARR was markedly reduced from Year 2–3 (0.16–0.06) and remained low through Years 3–5 (0.05), and MRI lesion activity was almost completely suppressed through Years 3–5. At Year 5, 90% of patients reached NEDA-3 in both groups. The safety profile of ofatumumab remained consistent with no new safety signals over 5 years. Updated 6-year efficacy and safety results will be presented at the congress.

Conclusion: These analyses will help inform physicians on the longer-term safety and efficacy profile of ofatumumab in pwRMS.

Disclosure: The study was supported by Novartis Pharma AG, Switzerland. The detailed author disclosures will be presented in the subsequent presentation.

Muscle and neuromuscular junction disorder 2

EPO-399 | Association of the initiation timing of oral steroids with clinical prognosis in adult generalized myasthenia gravis

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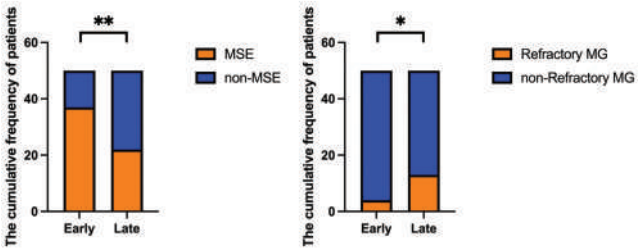
Background and Aims: To explore the association of the initiation timing of oral corticosteroids with the prognosis of adult generalized myasthenia gravis (GMG) patients.

Methods: We retrospectively screened adult GMG patients and divided them into early treatment group (initiation of oral steroids within one year from disease onset) and late treatment group. The clinical information at baseline and one-year follow-up were collected. The propensity score matching (PSM) analysis was used to select the candidates of two cohorts. The prognosis after one year therapy between the two groups was compared after matching.

Results: 50 patients were enrolled in both groups after PSM. Both quantitative MG (QMG) and MG-activities of daily living (MG-ADL) points were significantly lower in the early-treatment group than in the late-treatment group. In particular, the QMG and MG-ADL points of appendicular muscles were significantly lower in the early-treatment group than in the late-treatment group. The proportion of minimal symptom expression (MSE) is significantly higher in early treatment group compared to late treatment group (74% vs 44%, $p = 0.0223$), while the proportion of refractory MG is lower (8% vs 26%, $p = 0.0166$).

	early treatment (N=50)	late treatment (N=50)	P Value
MSE	37 (74.0%)	22 (44.0%)	0.0223
Refractory MG	4 (8.0%)	13 (26.0%)	0.0166
Immunosuppressants	22 (44.0%)	28 (56.0%)	0.2301
QMG, mean±SD	5.4 ± 4.1	8.0 ± 4.6	0.0040
Extraocular and facial muscle	1.0 ± 1.4	1.2 ± 1.7	0.4480
Bulbar muscle	0.1 ± 0.6	0.1 ± 0.4	0.8396
Appendicular muscle	4.3 ± 3.1	6.7 ± 3.7	0.0007
MG-ADL, mean±SD	1.2 ± 2.3	2.2 ± 2.1	0.0330
Extraocular and facial muscle	0.7 ± 1.3	1.0 ± 1.2	0.2022
Bulbar muscle	0.3 ± 0.8	0.4 ± 0.8	0.4453
Appendicular muscle	0.2 ± 0.6	0.7 ± 1.1	0.0051



Clinical prognosis of the patients between early treatment and late treatment groups after propensity score matching. Values are presented as the mean±SD or *n* (%). MSE, minimal symptom expression; MG, Myasthenia Gravis; QMG, Quantitative Myasthenia Gravis.

Conclusion: Adult GMG patients who received corticosteroid therapy within one year of the onset date show a higher rate of MSE and a lower rate of refractory status than the late-treatment GMG patients, indicating that treatment of corticosteroids starting within 12 months gave rise to a more favorable prognosis in GMG patients.

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EPO-400 | Safety profile of intravenous efgartigimod from clinical trials in immunoglobulin G–mediated autoimmune diseases

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Background and Aims: Efgartigimod (EFG), a human immunoglobulin G (IgG)1 Fc fragment, blocks the neonatal Fc receptor, selectively decreasing IgG levels. The safety profile of intravenous (IV) EFG was assessed across different IgG-mediated diseases.

Methods: EFG IV was assessed in different dosing regimens (10–25 mg/kg IV, including cyclical and continuous weekly dosing) in generalised myasthenia gravis (gMG; Phase 2 trial and Phase 3 placebo-controlled ADAPT and open-label extension ADAPT+ trials), in primary immune thrombocytopenia (ITP; Phase 3 placebo-controlled ADVANCE IV and ongoing open-label extension ADVANCE IV+ [data cut-off: 24 November 2023] trials) and in pemphigus vulgaris and foliaceus (Phase 2 trial). Pooled data represent participants receiving EFG 10 mg/kg IV in the Phase 2, ADAPT and ADAPT+ trials for gMG and in the ADVANCE IV and ADVANCE IV+ trials for ITP.

Results: EFG IV was well-tolerated and demonstrated a consistent safety profile across all indications and doses studied, with comparable rates of treatment-emergent adverse events (TEAEs) to placebo and across indications (Table 1; TEAEs ranged from 77.4–95.6% across studies and pooled analyses). Most TEAEs across studies were mild to moderate in severity. Discontinuation rates due to TEAEs were consistently low across studies and pooled analyses (ranged from 0–9.1%). There was no increase in TEAE or infection event rates with repeated treatment (Table 1). EFG treatment did not reduce albumin levels or increase cholesterol levels.

Table 1 Incidence and event rates of adverse events for intravenous efgartigimod in phase 2 generalised myasthenia gravis, ADAPT, ADAPT+, ADVANCE IV, ADVANCE IV+ and phase 2 pemphigus trials

Indication	Generalised myasthenia gravis				Primary immune thrombocytopenia			Pemphigus foliaceus and pemphigus vulgaris
Phase	Phase 3		Phase 3	Pooled data	Phase 3	Phase 3	Pooled data	Phase 2
Trial	ADAPT (NCT03669588)		ADAPT+ OLE (NCT03770403)	Phase 2 (NCT02965573), ADAPT and ADAPT+ OLE	ADVANCE IV (NCT04188379)	ADVANCE IV+ OLE (NCT04225156)	ADVANCE IV and ADVANCE IV+ OLE	NCT03334656
Incidence, n (%) [event rate]	EFG 10 mg/kg IV (N=84; PYFU=34.3)	PBO IV (N=83; PYFU=34.1)	EFG 10 mg/kg IV (N=145; PYFU=229.0)	EFG 10 mg/kg IV pooled (N=104; PYFU=263.8)	EFG 10 mg/kg IV (N=88; PYFU=38.0)	PBO IV (N=45; PYFU=23.2)	EFG 10 mg/kg IV (N=101; PYFU=68.1)	EFG 10 mg/kg IV pooled (N=124; PYFU=105.2)	EFG 10 mg/kg IV (N=33)	EFG 25 mg/kg IV (N=15)	Overall EFG IV (N=34)
Any TEAE	65 (77.4) [7.2]	70 (84.3) [7.8]	134 (85.5) [3.5]	143 (87.2) [4.3]	80 (93.0) [13.6]	43 (95.6) [17.8]	93 (92.1) [6.2]	118 (95.2) [10.2]	26 (84.2)	13 (86.7)	29 (85.3)
Any SAE	4 (4.8) [0.1]	7 (8.4) [0.3]	36 (24.8) [0.2]	38 (23.1) [0.2]	7 (8.1) [0.3]	3 (15.6) [0.4]	12 (11.9) [0.2]	19 (15.3) [0.3]	3 (10.5)	0	3 (5.9)
Any severe TEAE (or grade ≥3)	9 (10.7) [0.3]	8 (9.6) [0.4]	40 (27.6) [0.3]	43 (26.2) [0.3]	11 (12.8) [0.6]	9 (20.0) [0.7]	16 (15.8) [0.5]	26 (21.0) [0.5]	3 (15.8)	2 (13.3)	5 (14.7)
Any treatment-related TEAE	26 (31.0) [1.8]	22 (26.5) [1.6]	44 (30.3) [0.8]	66 (40.2) [1.0]	15 (17.4) [0.8]	10 (22.2) [0.9]	11 (10.9) [0.3]	30 (16.1) [0.5]	5 (26.3)	5 (33.3)	10 (29.4)
Discontinued due to TEAEs	3 (3.6) [0.2]	3 (3.6) [0.3]	12 (8.3) [0.1]	15 (9.1) [0.08]	4 (4.7) [0.1]	3 (2.2) [0.05]	1 (1.0) [0.01]	5 (4.0) [0.05]	1 (5.3)	0	1 (2.9)
Any TEAEs of infections and infestations*	39 (46.4) [1.6]	31 (37.3) [1.2]	80 (55.2) [0.7]	101 (61.6) [0.9]	25 (29.1) [1.0]	10 (22.2) [0.6]	34 (33.7) [0.8]	52 (41.1) [0.8]	11 (57.9)	10 (66.7)	21 (61.8)

EFG, efgartigimod; IV, intravenous; OLE, open-label extension; PBO, placebo; PYFU, patient-year(s) of follow-up; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
*Infections and infestations are grouped under System Organ Class (Medical Dictionary for Regulatory Activities v. 24.1).
Event rates were calculated as the number of events divided by the PYFU. PYFU and event rates were not calculated for pemphigus as it was a Phase 2, open-label trial and therefore are not reported above.

Conclusion: EFG IV was well-tolerated across indications and doses studied. Most TEAEs were mild to moderate in severity and event rates did not increase with repeated treatment.

Disclosure: AM: Alexion, argenx, Axunio, Grifols, Hormosan, Janssen, Merck, Octapharma, UCB, Vitaccess. KG: Alexion, argenx, UCB, Xeris Pharmaceuticals. CMB: Alexion, Apellis, argenx, Sanofi. MG: Almirall, argenx, Biotest, GSK, Janssen, Leo Pharma, Lilly, Novartis, UCB. HM: Alexion, argenx, Chugai, Japan Blood Products Organization, Roche, UCB. ZBC: NKFI Hungary, Orvostovábbképzo Szemle, Sanofi Genzyme Hungary. AN: Amgen, Angle, argenx, Dova, Novartis, Ono, Rigel, Shionogi. PU, RK, JTG, SA, and MJ: Employees of argenx. JFH: AcademicCME, Ad Scientiam, Alexion, AstraZeneca Rare Disease, argenx, Biologix Pharma, Cartesian Therapeutics,

Centers for Disease Control and Prevention, CheckRare CME, F. Hoffmann-LaRoche Ltd, Amgen, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Toleranzia AB, UCB, Zai Lab. KGC: Alexion, Alnylam, Amicus, argenx, Biogen, CSL Behring, Ipsen, Janssen, Roche, UCB.

EPO-401 | Adverse pregnancy outcomes in myasthenia gravis: A retrospective cohort study in a US health insurance claims database

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Background and Aims: Pregnancy is common among individuals with autoantibody conditions and adverse perinatal outcomes have been documented. However, previous studies in myasthenia gravis (MG) have produced mixed results.

Methods: We conducted a retrospective cohort study in the United States (US) Marketscan Commercial Claims and Encounters database between 2000-2022. Pregnancies in females aged 18-49 were identified and among live births, maternal and infant records were linked. MG was defined by ≥1 inpatient or ≥2 outpatient diagnoses within a 365-day period, with ≥1 diagnosis required before pregnancy end. The prevalence of six perinatal outcomes was calculated in the MG and total populations: live birth, spontaneous abortion, Cesarean section, preeclampsia, preterm birth, and small for gestational age (SGA). Outcome prevalence in the total population was standardized to the MG population age distribution.

Results: A total of 694 individuals with MG had 900 pregnancies and 3,928,256 individuals in the total population had 5,185,726 pregnancies. The prevalence of live birth (75.0% vs. 73.9%) and spontaneous abortion (20.4% vs. 20.8%) was similar in the MG and age-adjusted total population, respectively. Preeclampsia and Cesarean section were more frequent among MG than the total population (10.7% vs. 7.1%; 42.9% and 35.0%, respectively). The largest differences were noted for preterm birth and SGA, which were more prevalent among MG than the total population (18.0% vs. 9.7%; 4.3% vs. 1.7%, respectively).

Conclusion: MG was associated with a greater burden of certain adverse perinatal outcomes, occurring in both mother and infant. Further research is needed to understand drivers of pregnancy outcomes in MG.

Disclosure: This study was conducted by Johnson & Johnson. All authors are employed by, and hold stock in, Johnson & Johnson.

EPO-402 | Rituximab alone is as effective as associated with steroids on naive patients with generalized myasthenia gravis

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Background and Aims: Rituximab (RTX) has been proven effective in managing refractory generalized myasthenia gravis (MG), and its use is increasing worldwide. MG stabilization may initially require oral corticosteroid (CS) therapy, but its long-term side effects require the shortest duration of treatment. We studied the clinical effectiveness and usefulness of corticosteroids associated with RTX compared to RTX alone on MG remission.

Methods: In a monocentric retrospective cohort in the Nice University Hospital, we compared naïve MG patients treated with RTX as first-line therapy alone (G1) or associated with CS (G2). After the RTX induction, we evaluated efficacy with the Osserman score (OS) and the requirement for any rescue therapy (IgIV or plasmapheresis).

Results: Sixty-eight patients were treated with RTX, of which 19 (27.94%) benefited from an association with at least 0.5 mg/kg of corticosteroids. RTX-CS patients were more severe than RTX alone (OS: G1: 74.1 and G2: 64.94, $p=0.044$). However, OS at three (83.44 and 83.12, $p=0.993$), six (88.69 and 86.36, $p=0.545$), nine (82.91 and 85.73, $p=0.563$), and twelve months (86.6 and 88.69, $p=0.761$) from the treatment induction were similar. Rescue therapy following RTX induction was significantly higher for the RTX-CS (20.41% and 47.37%, $p=0.037$). Regarding safety, adverse event rates were similar in the two groups (0% and 14.29%, $p=0.178$).

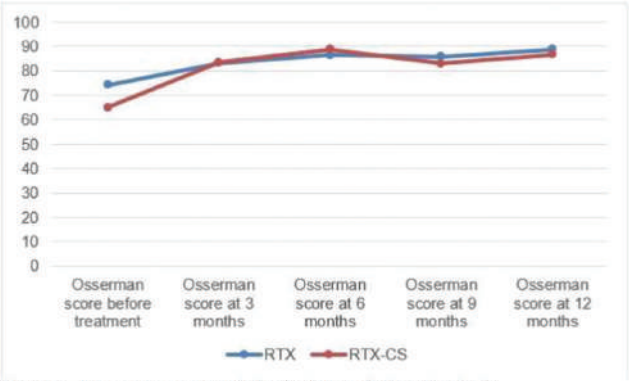

Figure 1 – Osserman score evolution before and after Rituximab

Conclusion: We suggest that RTX alone is as effective as RTX-CS in MG patients, indicating that avoiding steroids could reduce side effects, decrease rescue therapies, and not affect MG outcomes.

Disclosure: The authors have no conflict of interest to declare.

EPO-403 | Intensive care due to exacerbation of myasthenia gravis: Risk factors and prognosis

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Background and Aims: Exacerbation of myasthenia gravis (MG) with imminent respiratory failure requires intensive care. We studied the risk factors for intensive care and patients' prognosis thereafter.

Methods: This retrospective registry study covered Helsinki and Uusimaa hospital district from 2008 to 2021. Patients were identified using the ICD-10 code (G70.0) through a data repository search, followed by a chart review of patient medical records. The risk factors for intensive care (intensive care unit or intensive monitoring ward) were evaluated as compared with the patients never in need of in-hospital care for MG (outpatient group) and with those treated at a neurological ward for MG exacerbation. We compared the outcome between MG exacerbation and all reasons of intensive care.

Results: A total of 35 (9%) out of 386 MG patients required intensive care for MG exacerbation, within a median of 5.3 months from diagnosis. The intensive care group had a higher mean age at MG diagnosis and more comorbidities than the outpatient group. Thymoma (OR 4.8; $p = 0.028$) and female sex (OR 2.1; $p = 0.045$) were independent risk factors for intensive care due to MG exacerbation. High modified Rankin scale pre-hospitalization and late-onset MG (LOMG) were associated with prolonged intensive care stay and 6-month mortality (14.3%) was higher in patients with prolonged intensive care stay and older age.

Table 1. Demographic parameters of the study subgroups.

Characteristic	Intensive care group	Neurological ward group	*P*-value	Outpatient care group	*P*-value
N (% of total group)	35 (9.1%)	180 (46.6%)	-	171 (44.3%)	-
Female, n (%)	20 (57.1%)	84 (46.7%)	NS	95 (55.6%)	NS
Age at the diagnosis of MG, mean in years (±SD)	60.5 (±16.1)	53.4 (±20.8)	0.044	48.3 (±20.9)	<0.001
LOMG, n (%)	27 (77.1%)	105 (58.3%)	NS	88 (51.5%)	0.018*
AChR antibodies, n (% of cases with available antibody data)	24 (82.8%)	129 (80.6%)	NS	98 (81.7%)	NS
Thymectomy performed, n (%)	21 (60.0%)	112 (62.2%)	NS	77 (55.0%)	NS
Age at thymectomy, mean in years (±SD)	54.7 (±15.7)	48.2 (±19.5)	NS	39.9 (±18.1)	0.002
Thymoma, n (%)	4 (11.4%)	4 (2.2%)	0.026	2 (1.2%)	0.002
MG alone, n (%)	5 (14.3%)	26 (14.4%)	NS	58 (33.9%)	<0.001
MG with any comorbidity, n (%)	30 (85.7%)	154 (85.6%)	NS	113 (66.1%)	<0.001

Footnote to Table 1. AChR: acetylcholine receptor; AD: autoimmune disease; MG: myasthenia gravis; LOMG late-onset MG; NS: non-significant. P-values for statistically significant difference between the intensive care group and the other subgroups are shown.

Table 2. Data of MG patients in the intensive care group.

	MG patients in the intensive care group
Total number of patients	35
Age at admission (SD)	63.4 (16.9)
Time from diagnosis, median in months (range)	5.3 (-50.9-306.5)
Intensive care episode before MG diagnosis, n (%)	8 (22.9%)
Thymectomy done	21 (60%)
Time between thymectomy and the episode, median in months (range)	36.9 (-61.9-311.6)
First MG symptom	
Ocular	22.9%
Bulbar	54.3%
Weakness in limbs	14.3%
No MG medication before the episode	12 (34.3%)
Immunosuppressive medication before the episode	8 (22.9%)
Triggering factor of MG exacerbation, number of patients (%)†	
Infection	15 (42.9%)
Medications	5 (14.3%)
Surgery or anesthesia	5 (14.3%)
Poor compliance	2 (5.7%)
Unknown	9(25.7%)
Intensive care length of stay in days, median (range)	6 (1-34)
Mechanical or non-invasive ventilation, number of patients (%)	21 (51.4%)
Myasthenic crisis †† , number of patients (%)	25 (71%)
MG rescue therapy, number of patients (%)	
Plasmapheresis of immunoadsorption	21 (60%)
IVIG	3 (8.9%)
IVMP	5 (14.3%)
Immunosuppressive medication at next follow-up	18 (51.4%)
MGFA when entering hospital, median (range)	4 (1-5)
MGFA last follow-up, median (range)	2 (0-4)
Worst MGFA in intensive care, median (range)	5 (3-5)
MGFA next follow-up, median (range)	2 (0-4)
Medication enhancement in last follow-up	10 (33.3%)
Immunosuppression enhancement after the episode	18 (51.4%)
MGFA at 6 months, median (range)	2 (0-3)
mRS at 6 months	2 (0-6)
Age at death (n=17), mean in years (SD)	75.7 (11.9)
Potassium level (mmol/L) at the beginning of ICU episode, mean (SD) (all episodes, n=59)	3.8 (0.4)
Highest CRP level during the episode, mean (SD)	89.8 (84.4)
HUS hospital episode length, mean in days (SD)	22.6 (17.0)

Footnote to Table 2. CRP, C-reactive protein; HUS, the Hospital District of Helsinki and Uusimaa; IVIG, intravenous immunoglobulin; IVMP, intravenous methylprednisolone; MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America, only the numeral level is used; mRS, the Modified Rankin Scale; SD, standard deviation. Intensive care was defined as care given in units with individual patient monitoring and the possibility for respiratory support. †Some patients had more than one triggering factor. †† Myasthenic crisis was defined as an MG exacerbation requiring non-invasive ventilation, intubation, or a nasogastric tube.

Table 3. All episodes of intensive care during the study period and comparison of duration and mortality between MG exacerbation and acute exacerbation of asthma bronchiale treated in the intensive care.

	All intensive care episodes	Acute severe asthma	MG exacerbation
Number of patients	106910	142	35
Age, mean in years (±SD)	61.5 (18.5)	56.0 (20.5)	63.4 (17.2) *
Female, % (n)	43.1%	69.7% (99)	57.1% (20)
First intensive care episode in days, median (range)	1 (0-210)	1 (0-18)	6 (1-34) **
Duration of all intensive care episodes, days	382073	256	462
More than two intensive care episodes, n (%)	30400 (28.4%)	30 (21.1%)	4 (11.4%)
Mortality during intensive care episode, %	7.7% (in 10d)	4.9%	2.9%
Mortality in 6 months after intensive care episode, %	15.9%	7.7%	14.3%

Footnote to Table 3. MG, myasthenia gravis; SD, standard deviation. P-values indicating statistically significant differences between the studied subgroups of MG exacerbation and acute severe asthma are denoted with asterisks, and those not shown were insignificant. * $p = 0.04$, ** $p < 0.001$.

Conclusion: Our study shows an increased risk of intensive care for patients with LOMG or thymoma, occurring usually within six months from diagnosis. Special attention to early treatment choices should thus be given.

Disclosure: CM: received a grant from Maire Taponen Foundation; AT: travel expenses UCB Pharma, received research funding of the state of Finland governed through Helsinki University Hospital (project code Y223230047); SA: Nothing to disclose; SML: travel expenses

UCB Pharma, lecture fee Argenx, advisory fee UCB Pharma, Argenx, received research funding of the state of Finland governed through Helsinki University Hospital (project code TYH2023316).

EPO-404 | Clinical and genetic features of a cohort of patients with myoadenilate deaminase deficiency: A new mutation

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Background and Aims: Myoadenylate deaminase deficiency is the predominant metabolic disorder affecting skeletal muscles in the Caucasian population, involving approximately 2% of individuals. While the majority of those with the deficiency remain asymptomatic, some experience symptoms induced by exercise, suggesting a link between reduced enzyme activity and muscle function.
Methods: We conducted a cross-sectional analysis on 8 patients harboring mutations in AMPD1 and exhibiting a biochemical deficiency of myoadenylate deaminase (MAD) at histopathological analyses.
Results: Evaluated patients demonstrated a variable age of onset and a broad phenotypic spectrum, with most presenting exercise-induced myalgia and proximal weakness. Routine blood tests showed no significant abnormalities, except for persistent elevation in serum creatine kinase (CK). DNA analysis revealed the nonsense mutation c.34C>T (p.Q45*) in all patients, except for one with a novel compound heterozygous mutations p.Arg494Ser and p.Met511Val. These mutations located at a highly conserved position were predicted to be pathogenic by in silico tools. In comparison to other patients, the carrier of the novel mutation exhibited an earlier onset within the first months of life with primary dropped head syndrome and a more pronounced elevation of serum creatine kinase (CK) levels, which then progressed to proximal, limb-girdle type myopathy.
Conclusion: In conclusion, our work expands the genetic spectrum of MAD deficiency, disclosing a novel mutation and its related clinical effect, and provides a detailed description of the clinical features of a cohort of patients with AMPD1 mutations.
Disclosure: Nothing to disclose.

EPO-405 | Short-term and long-term prognoses in sub-very-late-onset and super-late-onset myasthenia gravis patients

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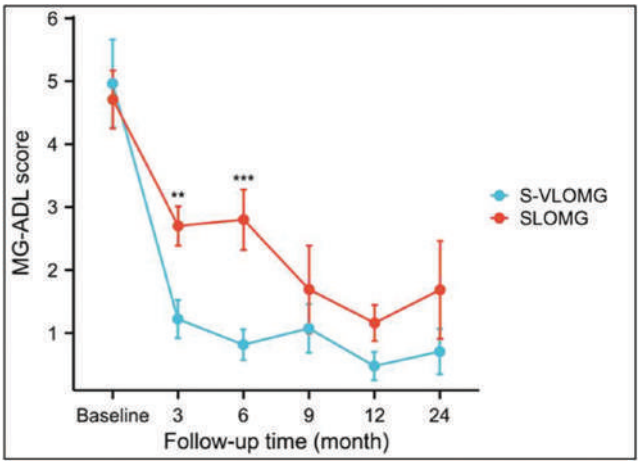
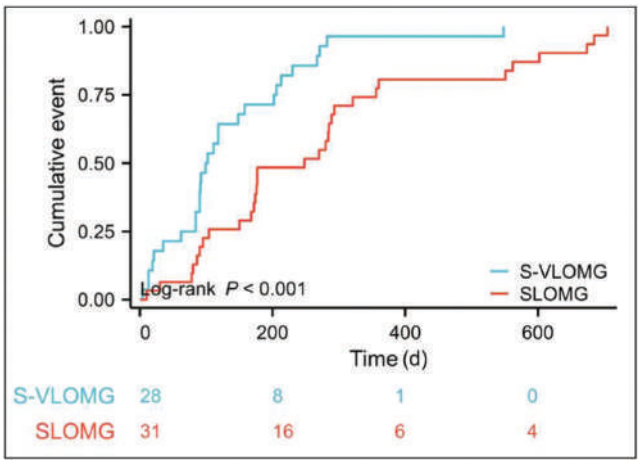
Background and Aims: To find the clinical factors that affect the short- and long-term prognosis of myasthenia gravis (MG) patients with onset age ≥65 years.
Methods: This was a retrospective, observational case-control study. Patients were classified into two age subgroups: sub-very-late-onset MG (S-VLOMG, onset age ≥65 and ≤69 years), and super-late-onset MG (SLOMG, onset age ≥70 years). The main outcome was the time to achieve minimal manifestations status (MMS) or better. We used the Cox proportional hazards model to identify factors influencing short- and long-term prognosis in all patients.
Results: A total of 59 patients were included, 28 of S-VLOMG and 31 of SLOMG. All patients reached MMS within 2 years, with a median time to MMS of 168.0 days. In S-VLOMG group, compared to SLOMG group, had lower MG-activities of daily living (MG-ADL) scores at 3rd and 6th months ($p=0.002$, $p=0.001$), and shorter time from treatment to MMS ($p=0.02$). In the COX proportional hazards model, we found that age at onset (≥65 to ≤69, HR=2.339, $p=0.022$), baseline MGFA classification (OMG, HR=2.534, $p=0.020$), baseline MG-ADL≤2 (HR=10.463, $p<0.0001$) and no limb weakness at baseline (HR=3.356, $p=0.004$) were associated with the 6th month prognosis (short-term). The factors affecting the prognosis of patients at 24th months (long-term) were like those at 6th months with the addition of changes of ΔMG-ADL at 6th months (HR=1.155, 95%CI=1.042-1.280, $p=0.006$).



Change in MG-ADL score in two groups over follow-up time. ** = $p \leq 0.01$; *** = $p \leq 0.001$.



Kaplan-Meier curve of the time from treatment to MMS between two groups.

Conclusion: The patients with S-VLOMG had a better short-term prognosis compared to SLOMG patients, while their long-term prognosis remains similar.
Disclosure: Nothing to disclose.

EPO-406 | Positive predictive value of acetylcholine receptor autoantibody testing by radioimmunoprecipitation assay

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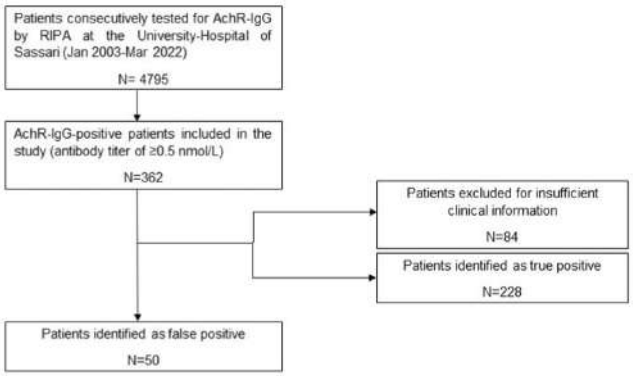
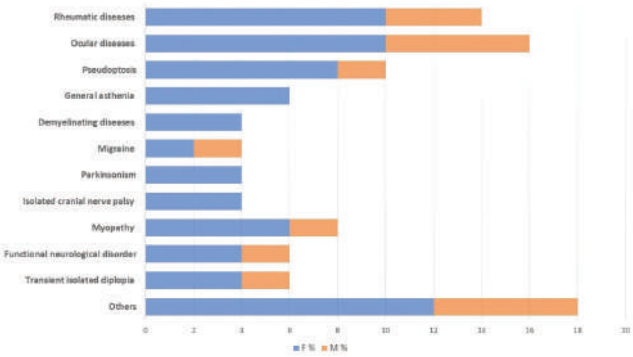
Background and Aims: Antibodies against the acetylcholine receptor (AChR-IgG) confirm a diagnosis of autoimmune myasthenia gravis (MG). Radioimmunoprecipitation assay (RIPA) is the gold standard for AChR-IgG detection with a reported specificity of ≈99%. However, its accuracy in large, unselected populations has not been fully elucidated. We determined the positive predictive value (PPV) and risk of false AChR-IgG positivity in a real-life setting.
Methods: The retrospective analysis included 4795 patients consecutively tested between 2003 and 2022. Medical records of patients with AChR-IgG positivity (antibody titer of ≥0.5 nmol/L) were reviewed to determine true vs false antibody positivity. AChR-IgG-positive patients with insufficient clinical information were excluded ($n=84$).
Results: Of 362 AChR-IgG-positive patients included in the study, 50 (13.8%) were designated as false positives. Specificity and PPV were 98.9% and 86.2%, respectively. Alternative diagnoses in patients with false AChR-IgG positivity included ocular diseases ($n=8$), rheumatic diseases ($n=7$), and others ($n=35$). Main reasons for antibody testing included isolated diplopia ($n=18$), nonspecific asthenia ($n=16$), or others. Compared to patients with true AChR-IgG positivity, false positive patients were younger, more frequently female and had a lower antibody titer. After stratification by AChR-IgG titers



The flow chart summarizes the steps towards identification of patient with false Ach-R IgG positivity.



The bar graph shows the percentage of alternative diagnoses.

AChR-IgG abtibody titer	Specificity	PPV
≥0.5 nmol/L	98.9% (95% CI, 98.5-99.2)	86.2% (95% CI, 82.2-89.6)
≥1 nmol/L	99.8% (95% CI, 99.6-99.9)	96.6% (95% CI, 94-98.3)

Variation of specificity and PPV after stratification.

of ≥1 nmol/L, specificity and PPV increased to 99.8% and 96.6%, respectively.
Conclusion: Despite the high specificity of AChR-IgG testing by RIPA, the risk of false antibody positivity is not negligible in clinical practice (14% in this study). Caution is needed when low titer AChR-IgG positivity (0.5-0.9 nmol/L) is detected in patients with symptoms that are nonspecific for MG.
Disclosure: Nothing to disclose.

EPO-407 | The safety and efficacy profile of eculizumab in myasthenic crisis: A prospective case series

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Background and Aims: Myasthenic crisis (MC) represents a severe exacerbation of myasthenia gravis. While eculizumab has shown promise in case reports, there is a lack of prospective data on its safety and efficacy. This study aims to investigate eculizumab as an adjunct therapy in refractory MC patients.
Methods: We conducted a prospective case series study over 12 weeks, targeting patients with acetylcholine receptor (AChR) subtype refractory MC. Participants were administered eculizumab as an add-on to standard therapy. Outcomes were measured using the MGFA-quantitative MG test (MGFA-QMG) and the MG-Activities of Daily Living (MG-ADL) scale, with additional monitoring of muscle strength across various domains. Additionally, serum anti-AChR antibody titers, CH50, C1q, C5a, and soluble C5b-9 (SC5b-9) levels were measured at the baseline and 12 weeks after eculizumab treatment.
Results: Patients exhibited significant improvements in both MGFA-QMG (baseline: 22.25±4.92, 12 weeks: 7.5±5.74) and MG-ADL (baseline: 18.25±2.5, 12 weeks: 2.75±4.86) scores from the 4-week mark onward. Muscle strength consistently increased across ocular, bulbar, respiratory, and limb/gross domains. One patient succumbed to cardiac failure at 16 weeks, but three cases remained in remission at 24 weeks. There were sustained declines in serum CH50 and soluble C5b-9 levels, with no significant changes in anti-AChR antibody titers, C1q and C5a. No significant side effects were reported.
Conclusion: Eculizumab was well-tolerated and effective in enhancing recovery and reducing disease activity in patients with MC. These findings support further large-scale prospective studies with extended follow-up to establish the safety and efficacy profile of eculizumab in a real-world setting.
Disclosure: Nothing to disclose.

EPO-408 | Real-world reduction in oral corticosteroid utilization following efgartigimod initiation

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Background and Aims: Reducing or tapering oral corticosteroids (OCS, prednisone equivalent), a common treatment used in generalised myasthenia gravis (gMG), can alleviate risk related to long-term OCS usage. The objective of this study was to evaluate OCS usage following efgartigimod initiation.
Methods: In this retrospective study, patients with gMG using OCS who initiated efgartigimod were identified from a United States medical and pharmacy claims database (based on information licenced from IQVIA: Longitudinal Access and Adjudication Data [LAAD] for the period April 2016–April 2023, reflecting estimates of real-world activity [all rights reserved]). Mean (SD) average daily dose (ADD) of OCS was evaluated during the 3-months prior to, and at 3- and 6-months post-efgartigimod initiation. Any patients enrolled in the "My VYVGART Path" patient support program that had baseline and follow-up myasthenia gravis activities of daily living (MG-ADL) scores available were identified to assess score change.
Results: Among 576 patients who initiated efgartigimod by September 30, 2022, and continued efgartigimod for ≥6 months, 231 (40%) were using OCS at baseline. Mean (SD) OCS ADD was significantly reduced at 3- (15.6 [14.8] mg/day, $p=0.0007$) and 6-months (14.5 [15.5] mg/day, $p=3.99x10\text{-}6$) post-efgartigimod initiation compared with baseline (19.0 [15.1] mg/day). A subset of 75 patients (32%) had MG-ADL scores available both before and during the 6-months following efgartigimod initiation. Among them, significant reduction was observed in best-follow up mean (SD) MG-ADL (from 8.7 [3.7] to 4.5 [3.3], $p=1.2x10\text{-}14$).
Conclusion: Early insights indicate that OCS usage was significantly reduced over 6 months post-efgartigimod initiation, while retaining MG-ADL response.
Disclosure: This research was funded by argenx US, Inc. (Boston, MA, USA). TR received honoraria and/or research support from Alexion, argenx, Biogen, Merck, Novartis and Roche. NG has received consulting fees from argenx, UCB, Janssen and Alexion, and grant support from argenx. CQ, DG, MJ, and GP are employees of argenx. JS has consulted for argenx on glucocorticoid toxicity. TBS, RRM and MS are employees of ZS Associates (Evanston, IL, USA) and serve as paid consultants for argenx.

EPO-409 | Steroid toxicity in adults with myasthenia gravis in the United States based on electronic health records

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Background and Aims: While benefits/risks of steroids in myasthenia gravis (MG) have been studied, quantifying steroid toxicity is challenging using real-world data.

Methods: Adults with MG (≥2 MG diagnoses 30-730 days apart between Jan 2014-Sep 2021) were identified in United States (US)-based Optum® de-identified Electronic Health Record data set (Optum® EHR) (Jan 2013-Dec 2022). Index dates were defined as first steroid prescription (for steroid initiators [MG-SI]) or assigned after age/gender match (for steroid-naïve [MG-SN]). Patients with available lab measures for main criteria of the Glucocorticoid Toxicity Index-Metabolic Domains (GTI-MD) were included. GTI-MD scores (Aggregate Improvement Score [AIS] and Cumulative Worsening Score [CWS], higher scores represent higher toxicity) were compared between MG-SI vs. MG-SN cohorts. Multivariate regression assessed the relationship of steroid usage, strength, and timing of follow-up assessment to GTI-MD.

Results: Among 27,157 patients with MG, 377 and 305 were included in the MG-SI and MG-SN cohorts, respectively. 30% of the MG-SI cohort had multiple steroid prescriptions and ≥20mg prescription at index. GTI-MD (SD) scores were higher in MG-SI compared with MG-SN (AIS: 4.9 [34.5] vs. 1.9 [34.3], $p = 0.27$; CWS: 22.6 [22.8] vs. 18.7 [21.2], $p = 0.023$). Regression results showed MG-SI patients with ≥2 records and ≥20mg at index had an average AIS 10.2 higher than MG-SN ($p = 0.01$). Each additional month of follow-up since index was associated with a decrease of 1.5 AIS ($p < 0.001$).

Conclusion: Our results demonstrated steroid toxicity is significantly higher in patients with higher strength and repeated steroid usage. Patients experienced consistent elevation in steroid toxicity over time.

Disclosure: This study was funded by argenx US, Inc. (Boston, MA, USA). TR received honoraria and/or research support from Alexion, Argenx, Biogen, Merck, Novartis and Roche. NG has served as a paid consultant for argenx, UCB, Janssen and Alexion, and has grant support from argenx. MH consults for argenx, Alexion, Janssen, UCB and Immunovant; received compensation as Guest Editor for Continuum Lifelong Learning in Neurology 2023; and is supported by UVM Medical Center grant for unrelated work. GP, CQ, and DG are employees of argenx. JHS has consulted for argenx on glucocorticoid toxicity; JHS's employer, the Massachusetts General Hospital, owns the intellectual property of the Glucocorticoid Toxicity Index (GTI). The intellectual property of the GTI-MD (Metabolic Domains) is co-owned by the Massachusetts General Hospital and Steritas, LLC. JHS co-founded Steritas and is the chair of the Scientific Advisory Board but has no fiduciary responsibility at the company. MS is an employee of Steritas. AC is a consultant to Steritas. DA, RK and AW are employees of ZS Associates (Evanston, IL, USA) and serve as paid consultants for argenx.

EPO-410 | Duchenne muscular dystrophy (DMD) patient vignettes development methodology

V. Merla[1]; P. Nathaniel[1]; O. Borecka[2]; S. Vincent[2]

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Background and Aims: Duchenne muscular dystrophy (DMD) is a severe, rare neuromuscular disease with wide-ranging impacts, therefore, accurately describing the quality of life (QoL) of people with DMD can be challenging. This study describes the methodology in the development and validation of DMD patient vignettes prepared for rating by neurologists using the 5-level EQ-5D (EQ-5D-5L) proxy version 1, to derive health-state utility values.

Methods: Eight vignettes representing DMD health states (based on Project HERCULES) were developed. The draft vignettes were developed through an extensive literature search. Following the development of the draft vignettes, two DMD PAG representatives with caregiver experience were interviewed to validate the vignettes. After incorporating PAG feedback, four specialist neurologists were recruited to review and score the vignettes using the EQ-5D-5L.

Results: The feedback obtained from PAG representatives on the draft vignettes was positive and confirmed their overall accuracy. The comments allowed for minor changes to some domains including requirements of 24-hour care in later non-ambulatory stages, a need for specialist equipment to assist with self-care and adjustments to mental health impacts, such as, additional wording around the patient feeling isolated and escalation of the severity descriptor of depression in the last health state.

Conclusion: Development of patient vignettes in rare conditions can be challenging; hence, PAG and specialist clinician feedback can play an important role in more accurately describing the QoL of people with DMD and other severe, rare diseases. The mental health impacts and the intensity of the care and assistance required by people with DMD should not be underestimated.

Disclosure: Val Merla and Nate Posner are employees of Pfizer Inc., and this study was funded by Pfizer Inc. Octavia Borecka and Sally Vincent are employees of Vitaccess Ltd.

EPO-411 | Early real-life experience of Zilucoplan in refractory generalized myasthenia gravis

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Background and Aims: Myasthenia gravis is a rare chronic autoimmune disease affecting the post-synaptic membrane of the muscle junction characterized by debilitating, and potentially fatal, muscle weakness. (1, 2). Treatment options available for generalized myasthenia gravis (gMG) have grown in recent years with the introduction of new drugs, such as the complement factor C5 inhibitors (2, 3). The objective of the Compassionate Use Program (GM0025IT) is to provide early access to Zilucoplan for gMG patients with a high unmet medical need and severe disease burden.

Methods: Zilucoplan was administered by daily subcutaneous self-injection as for protocol (2). Efficacy was assessed by using the MG-ADL scale and QMG. The patients' baseline therapy remained unchanged during the entire course of treatment.

Results: Three female patients (mean age 32 y) affected by AChR-seropositive gMG received Zilucoplan. A reduction in MG-ADL scores was observed in the first week from the first injection compared to baseline with a mean change of – 2.33 points (ranging from -4 to -1). The main change at one month was – 4.0 points. Regarding QMG, a reduction of -2 points was achieved in two patients at one month. All three patients reported a significant improvement in the quality of daily life. No safety issues were identified.

Conclusion: The decline in scores obtained testifies to the efficacy of treatment with Zilucoplan and the rapidity of its action onset. Also, Zilucoplan appears to be very easy to administer and has a favorable safety profile (2). Further data and longer observations are needed to confirm our data.

Disclosure: Vincenzo Di Stefano received compensation for speaking from Alexion, and Alnylam; he is SI in clinical trials for Alexion, Alnylam, Argenx, Dianthus, and Sanofi.

EPO-412 | A predictive nomogram for short-term outcomes of myasthenia gravis patients treated with low-dose rituximab

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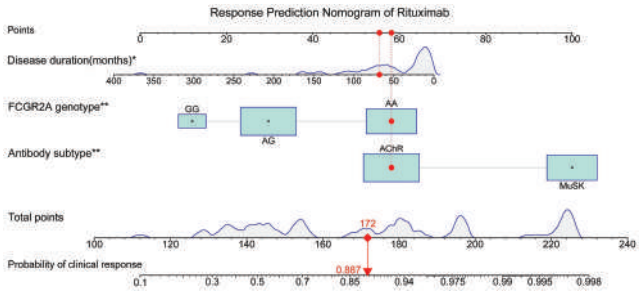
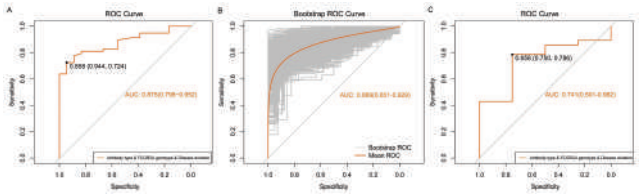
Background and Aims: This study aims to establish and validate a predictive nomogram for the short-term clinical outcomes of myasthenia gravis (MG) patients treated with low-dose rituximab.

Methods: We retrospectively reviewed 108 patients who received rituximab of 600 mg every six months in Huashan Hospital and Tangdu Hospital. Of them, 76 patients from Huashan Hospital were included in the derivation cohort to develop the predictive nomogram, which was externally validated using 32 patients from Tangdu Hospital. The clinical response is defined as a ≥3 points decrease in QMG score within 6 months. Both clinical and genetic characteristics were included to screen predictors via multivariate logistic regression. Discrimination and calibration were measured by the area under the receiver operating characteristic curve (AUC-ROC) and Hosmer-Lemeshow test, respectively.

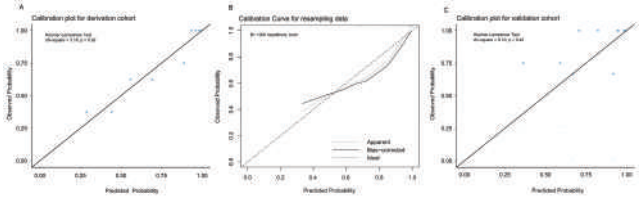
Results: Disease duration (OR = 0.987, $p = 0.032$), positive anti-muscle specific tyrosine kinase antibodies (OR = 19.8, $p = 0.007$), and genotypes in FCGR2A rs1801274 (AG: OR = 0.131, $p = 0.024$; GG: OR = 0.037, $p = 0.010$) were independently associated with clinical response of post-rituximab patients. The nomogram identified MG patients with clinical response with an AUC-ROC (95%CI) of 0.875 (0.798-0.952) in the derivation cohort and 0.741 (0.501-0.982) in the validation cohort. Hosmer-Lemeshow test showed a good calibration (derivation: chi-square = 3.181, $p = 0.923$; validation: chi-square = 8.098, $p = 0.424$).



Nomogram to estimate the probability of clinical response in MG patients after low-dose rituximab treatment.



ROC-AUC of nomogram A. Derivation cohort: ROC-AUC = 0.875, 95%CI: 0.798-0.952. B. Resampling: mean ROC-AUC = 0.889, 95%CI: 0.851-0.929. C. Validation cohort: ROC-AUC = 0.741, 95%CI: 0.501-0.982.



Model calibration of derivation cohort (A), resampling data using bootstrap (B), and validation cohort (C) The x- and y-axes in the graph represent the predicted and actual response probabilities from the nomogram, respectively.

Conclusion: The nomogram achieved an optimal prediction of short-term outcomes in patients treated with low-dose rituximab.
Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-413 | Response to single rituximab can predict a better outcome of multi-cycle treatment in refractory myasthenia gravis

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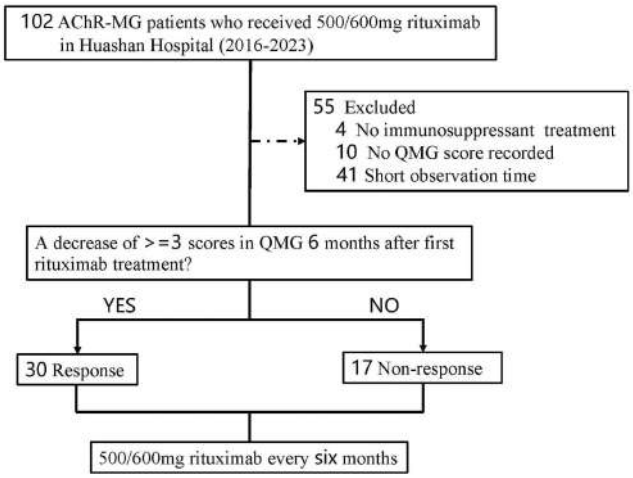
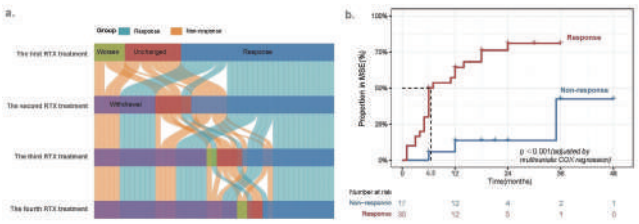
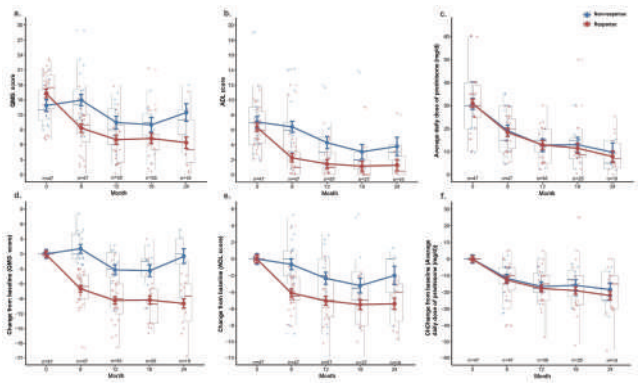
Background and Aims: This study aims to access the long-term clinical outcomes of myasthenia gravis (MG) patients treated with multi-cycle low-dose rituximab.
Methods: This retrospective cohort study with prospectively collected data involved 47 refractory patients who received 500/600 mg rituximab every six months in Huashan Hospital. We divided them into a response group ($n=30$) and a non-response group ($n=17$) based on a decrease of ≥3 scores in Quantitative Myasthenia Gravis (QMG) score 6 months after first rituximab treatment. We compared the change of QMG and Activities of Daily Living (ADL) scores and the time to minimal symptom expression (MSE, i.e., ADL 0-1 score) between the two groups.
Results: There were significant group×visit interactions for QMG score and ADL score. Six months after the fourth rituximab treatment, QMG score was lower for the response group (-6.07; $p=0.005$; 95%CI, -10.26 to -1.88) compared with the non-response group; the equivalent mean changes from baseline were -9.95 (95%CI, -11.78 to -8.12) and -0.45 (95%CI, -3.38 to 2.49), respectively. ADL score was lower for the response group (-2.84; $p=0.006$; 95%CI, -4.83 to -0.852) compared with the non-response group; the equivalent mean changes from baseline were -5.40 (95%CI, -6.74 to -4.05) and -1.99 (95%CI, -4.18 to 0.21), respectively. The median time to MSE was shorter in the response group (6.5 months versus not available; HR: 15.83; 95%CI,3.53-70.91; $p<0.001$).



Recruitment of patients with refractory generalized myasthenia gravis.



Post-treatment status (a) and time to MSE (b) after multi-cycle rituximab treatment in refractory generalized AChR-MG.



Clinical efficacy

Conclusion: The response to single low-dose rituximab can predict a better outcome of multi-cycle treatment in refractory MG.
Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Monday, July 01 2024

Ageing and dementia 3

EPO-414 | Exploring the interplay among neuroinflammation, neurodegeneration and mitochondrial damage in Alzheimer's disease

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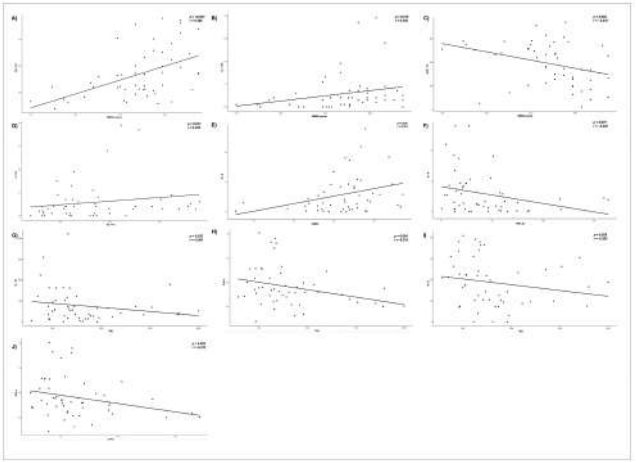
Background and Aims: This study aims to conduct a comprehensive assessment of various biomarkers related to different aspects of AD pathology. These aspects encompass neurodegeneration, glial activation, mitochondrial dysfunction, and immune response. The objective is to correlate these results among them and with the "classic" diagnostic AD biomarkers.
Methods: Neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP) and transactive response DNA binding protein (TDP-43) concentrations were assessed through the use of Simoa technology. Growth Differentiation Factor 15 (GDF-15) was assessed using ELISA. Concentrations of 11 selected cytokines were determined using a multiplex bead-based flow cytometry assay. Non-parametric statistical analyses were performed.
Results: CSF samples of the 52 AD patients were collected. Twenty-four patients were recruited in Genova and 28 patients in Siena. The median age was 74.3 years (25th–75th percentiles, 71.3–77.3) and 35% were male. MMSE score showed a positive correlation with the CSF Aβ1-42 concentrations ($r = 0.485$; $p < 0.001$), as well as with CSF interleukin (IL)-17A concentrations ($r = 0.34$; $p = 0.015$), and a negative correlation with CSF GDF-15 concentrations ($r = -0.418$; $p = 0.002$). CSF IL-17A concentrations also showed a positive correlation with CSF Aβ1-42 concentrations ($r = 0.302$; $p = 0.031$). CSF IL-6 concentrations showed a positive correlation with CSF NfL concentrations ($r = 0.312$; $p = 0.026$) and a negative correlation with CSF TDP-43 concentrations ($r = -0.322$; $p = 0.021$). CSF t-Tau concentrations were negatively correlated with CSF IL-10 ($r = -0.301$; $p = 0.032$;), IFN-gamma ($r = -0.315$; $p = 0.024$), and IL-8 concentrations ($r = -0.305$; p 0.029), CSF p-Tau concentrations were negatively correlated with CSF IFN-gamma concentrations ($r = -0.312$; p 0.026).



Partial correlation between A) MMSE and Aβ1-42; B) MMSE and IL-17A; C) MMSE and GDF-15; D) IL-17A and Aβ1-42; E) IL-6 and NfL; F) IL-17A and TDP-43; G) t-Tau and IL-10; H) t-Tau and IFN-g; I) t-Tau and IL-8; J) p-Tau and IFN-g; with age as control variable.

Conclusion: This ongoing study starts to cast light on the intricate interplay that exists among neuroinflammation, neurodegeneration, mitochondrial damage, and clinical disability in AD.
Disclosure: Nothing to disclose.

EPO-415 | Cholinesterase inhibitors and risk of epilepsy in Alzheimer's disease – Study on 32 121 patients from SveDem

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Background and Aims: Alzheimer's disease (AD) is the most common type of dementia and Cholinesterase inhibitors (ChEIs) are the first line symptomatic treatment. Given the increased incidence of epilepsy (EP) in AD, the question arises about whether ChEIs influences the risk of developing EP.
Methods: This cohort study was based on 32,121 patients with AD in the Swedish Dementia Registry SveDem with a study period of ten years. Incidence rates and Cox proportional hazard modeling were applied to the study outcomes epilepsy and mortality, for a total and PS-matched cohort, with ChEI use as the exposure. The primary aim was to explore a possible association between ChEI use and EP in AD. The secondary aim was to examine if ChEI use influences mortality.
Results: No association was found between ChEI use and EP, apart from in patients with a MMSE score above 25 who experienced a decreased EP risk of 30.5% when treated (HR 0.69; 95% CI: 0.49–0.99). A significant association was found between ChEI use and decreased mortality (HR 0.88; 95% CI: 0.85–0.92).
Conclusion: In line with existing research, this study has not identified a link between ChEI and increased EP risk. The association between ChEI use and decreased mortality is coherent with other studies. The decreased EP risk found in patients with early-stage dementia is understandable given disease characteristics and emerging research on an anti-epileptogenic ChEI element, such as the recently

outlined cholinergic anti-inflammatory pathway. Such an element could also constitute an explanation behind the decreased mortality.
Disclosure: None.

EPO-416 | Abstract withdrawn

EPO-417 | Development and use of cognition bolt-ons for the EQ-5D-3L and EQ-5D-5L: A systematic review

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Background and Aims: The widely used EQ-5D measures health-related quality of life across five dimensions. Cognition has been one of the earliest and most extensively applied additional dimensions ('bolt-on'). Our aim was to systematically review the literature on cognition bolt-ons for the EQ-5D, categorising existing items and their wordings across various populations.
Methods: We conducted a systematic literature search using PubMed, Web of Science and Google Scholar to identify publications that used cognition bolt-ons for the two adult versions of the EQ-5D (3L and 5L), following the PRISMA guidelines (PROSPERO CRD42023445567).
Results: The included 181 publications (1997-2023) from 137 studies revealed an increasing trend in using cognition bolt-ons. Cognition bolt-ons have been applied in 28 languages across 23 countries, with the Netherlands leading (64%). Overall, 71 different patient populations were included in these studies, with the most common being head or brain injury ($n=13$), dementia ($n=12$), depression ($n=5$), stroke, HIV and burn ($n=4$ each). We identified 52 different wordings (3L: $n=23$ and 5L: $n=29$). The most frequent descriptors, cognition (29%) and thinking ability (19%), included examples such as concentration (60%), memory (39%) and remembering (31%). Most bolt-on items lacked any qualitative input and they commonly deviated from the EQ-5D-format (e.g. extended dimension title, inappropriate examples or not severity-type response scale).
Conclusion: The growing and extensive use of cognition bolt-ons for the EQ-5D signals a demand from users for this bolt-on. The parallel existence of various wordings and the absence of proper development highlight the necessity for future bolt-on development and harmonisation efforts.
Disclosure: Funded by the EuroQol Research Foundation (ERF; EQ Project 1700-RA). FR, BM, APF and MFJ are members of the EuroQol Group. APF is employed by the ERF. Views expressed in the abstract are those of the authors and are not necessarily those of the ERF.

EPO-418 | Serum GFAP levels discriminate between AD and bvFTD but are influenced by renal function

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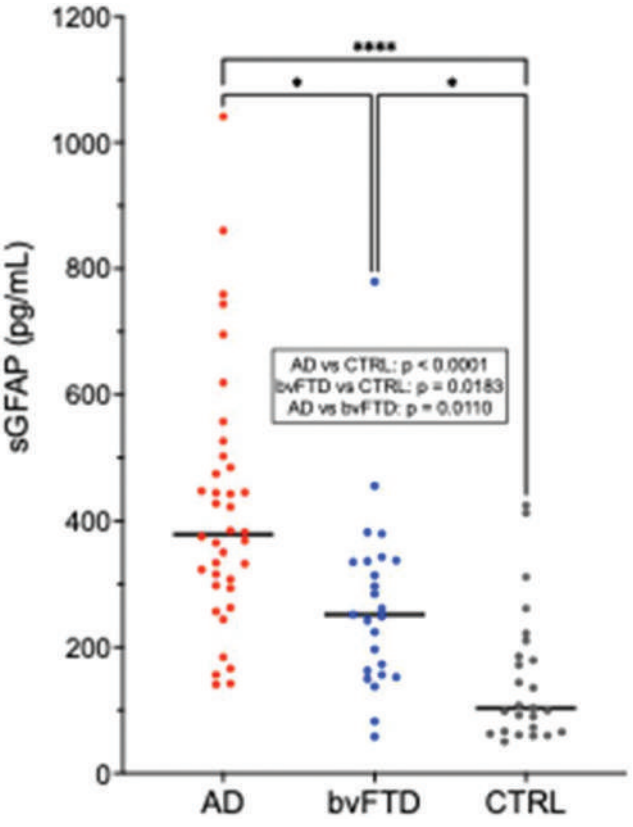
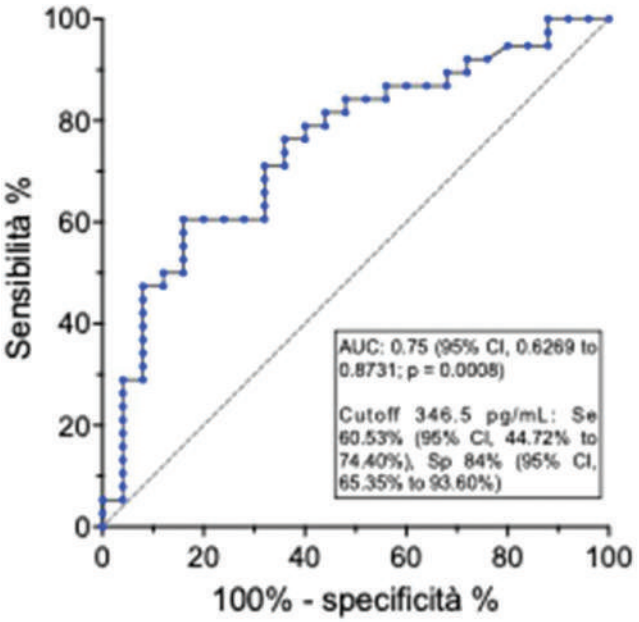
Background and Aims: Blood levels of GFAP are increased in Alzheimer's disease (AD).
Methods: We measured serum GFAP (sGFAP) in 38 patients with AD, 25 patients with the behavioural variant of FTD (bvFTD), and 25 neurologically healthy controls (NHCs).
Results: sGFAP was increased in AD compared to NHCs and to bvFTD, and in bvFTD compared to NHCs (all $p<0.05$). The ROC curves for the discrimination between AD and NHCs and between AD and bvFTD had AUCs of 0.9095 ($p<0.0001$) and 0.75 ($p=0.0008$), respectively. In (AD + bvFTD) ($N=51$), sGFAP correlated negatively with CSF Aβ42/40 ratio (r=-0.2931) and positively with P-tau181 (r=0.3973) and T-tau (r=0.3355) (all $p<0.05$). Accordingly, sGFAP was higher in neurochemically defined A+ vs. A-, T+ vs. T-, and N+ vs. N- patients (all $p<0.05$). In the whole cohort, sGFAP positively correlated with age (r=0.5111; $p<0.0001$). In (AD + bvFTD + CTRL), sGFAP negatively correlated with estimated glomerular filtration

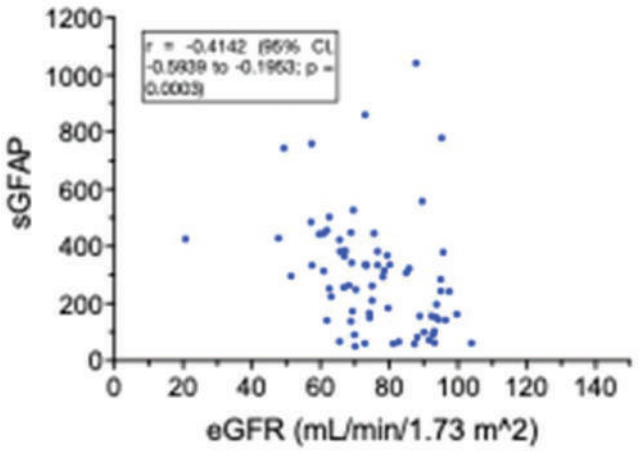


Serum GFAP levels in patients with AD, patients with bvFTD, and neurologically healthy controls.

rate (eGFR) (r = -0.4142; $p = 0.0003$; $N = 72$). Interestingly, in (AD + bvFTD), sGFAP also negatively correlated with the CSF/serum albumin ratio (Q-Alb) (r = -0.3557; $p = 0.0066$; $N = 57$).



ROC curve of serum GFAP for the discrimination between AD and bvFTD.



Negative correlation between serum GFAP and estimated glomerular filtration rate.

Conclusion: sGFAP is a promising biomarker for the discrimination between AD and bvFTD and is associated with neurochemical evidence of both Aβ and tau pathology. The negative correlation between sGFAP and eGFR may be practically important. The negative correlation with Q-Alb deserves further investigation.

Disclosure: Nothing to disclose.

EPO-419 | CSF synaptic proteins and monoaminergic systems in prodromal Alzheimer's disease: Insights from [18F]FDG PET correlations

F. Massa[1]; B. Orso[2]; V. Pelagotti[2]; M. Losa[2]; L. Argenti[2]; L. Lombardo[2]; P. Mattioli[1]; A. Brugnolo[1]; N. Girtler[1]; D. Arnaldi[1]; A. Chincarini[3]; S. Morbelli[4]; G. Sambuceti[5]; M. Pardini[1]

[1]*Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa, and IRCCS Ospedale Policlinico San Martino, Genoa, Italy*; [2]*Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genoa*; [3]*Istituto Nazionale di Fisica Nucleare (INFN), Genoa section, Italy*; [4]*Department of Medical Sciences, University of Turin, and Nuclear Medicine Unit, AOU Città Della Salute e Della Scienza di Torino, Turin, Italy*; [5]*Department of Health Sciences (DISSAL), University of Genoa, and IRCCS Ospedale Policlinico San Martino, Genoa, Italy*

Background and Aims: Understanding the interaction between molecular aberrations in prodromal Alzheimer's disease (AD) and diffuse projection systems may foster pharmacological intervention. With this aim, we assessed baseline [18F]FDG-PET metabolism colocalization with PET maps of monoaminergic systems and correlated with cerebrospinal fluid (CSF) biomarkers of AD pathology and synaptopathy in prodromal AD patients.

Methods: We retrospectively analyzed 49 MCI-AD patients with positive CSF AD biomarkers (Aβ42/40, pTau, t-Tau), then grouped by time until dementia (Early MCI,EMCI, $n = 34$ progressing within two years; late MCI,LMCI, $n = 15$ stable/progressing later). Using the JuSpace toolbox, [18F]FDG-PET images were compared voxel-wise against 40 matched healthy controls (HC) to generate hypometabolism maps. Spearman's correlation coefficients evaluated the colocalization strength between hypometabolism and neurotransmitter maps, with negative values signifying heightened disease involvement in cortical regions normally abundant in receptors/transmitters. Coefficients were correlated with CSF standard AD and synaptopathy biomarkers (NPTX2, Neurogranin) in MCI-AD and EMCI/LMCI subgroups.

Results: Voxel-wise analyses showed hypometabolism patterns in MCI-AD, primarily in the temporoparietal and precuneus/posterior cingulate cortices. CSF pTau negatively correlated with hypometabolism-5HT1B receptor colocalization in the MCI-AD group and EMCI (r = −.306, $p = 0.035$ and r = −.394, $p = 0.028$). In the LMCI subgroup, CSF NPTX2 and Neurogranin positively correlated with colocalization strength of hypometabolism with 5HT4- (r = .719, $p = .011$; r = .603, $p = 0.008$) and D1-receptor maps (r = .707, $p = 0.010$; r = .603, $p = 0.038$).

Conclusion: Reduced CSF synaptic biomarker levels in late MCI parallel hypometabolism in regions rich in dopaminergic and serotonergic terminals, consistent with their role in disease staging and suggesting an interplay between synaptopathy and diffuse projection system alterations.

Disclosure: Nothing to disclose.

EPO-420 | Creative thinking as a resource in pathology: A cognitive stimulation training for mild cognitive impairment patients

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Background and Aims: Considering the increase in life expectancy and the incidence rate of age-related chronic neurodegenerative diseases, non-pharmacological treatments are relevant to prevent and slow cognitive decline in prodromal stages of disease such as dementia. Creative thinking training has shown promising potential. The aim of the present research is to show the efficacy of a creativity-based training on cognitive and psychological variables in patients affected by Mild Cognitive Impairment (MCI).

Methods: An individual 10-sessions training (CREC, CReativity in Everyday life Challenges), based on exercises that stimulate divergent thinking, was administered to a sample of 30 patients with MCI (9 men; age: 77.57 ±3.51; education: 7.07 ±2.70). Other 16 MCI patients (3 men; age: 79.38 ±8.03; education: 5.75 ±1.34) were assigned to an active control group. Specific cognitive functions, divergent thinking abilities and psychological well-being were assessed before and after the training sessions.

Results: Although the study is still ongoing, the first results highlight a significant improvement in the experimental group compared to the control group in semantic fluency abilities. Moreover, both groups show improvement in praxic-constructive skills and in the perception of overall well-being, along with a reduction in anxious symptomatology.

Conclusion: CREC appears to be effective in promoting improvement in cognitive skills such as semantic abilities. These results suggest that creative thinking could be a useful resource against cognitive decline in patients with MCI, playing an important role in reducing or delaying progression of symptoms.

Disclosure: This research was funded by Fondazione Cariplo, grant no. 2018-0792. The authors declare no conflict of interest.

EPO-421 | Usability of tele-medicine and tele-rehabilitation applications in subjects with mild cognitive impairment

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Background and Aims: Tele-medicine and tele-rehabilitation systems are increasingly proposed approaches to improve or stabilize cognitive functions of patients with mild to moderate cognitive decline. The aim of the present project was to investigate the usability of tele-medicine and tele-rehabilitation systems designed for remote assistance and treatment of patients with mild cognitive impairment (MCI) and in their caregivers.

Methods: The project included two lines of intervention for which usability was analyzed: 1) a program of tele-rehabilitation for the MCI patients, using at home a dedicated software installed on a tablet (Neurotablet), for 4 consecutive weeks; 2) a program of visits in Tele-Medicine for educational and psychological support, for patients and caregivers, for 4 consecutive weeks. Ten Cognitive Disorders and Dementia Centers (CDCD), distributed throughout the Calabria region, in Italy, participated to the project. Usability was evaluated through the System Usability Scale (SUS) and measuring the patients performances using Neurotablet.

Results: All CDCDs consecutively recruited 134 patients with amnestic MCI (46.3% M/53.7% F; mean age 69.5 ±6.8 years; mean education: 9.6 ±3.7 years) and 131 caregivers (28.7% M/71.3% F; age strata (18-45 y): 36.2%, (45-65 y): 35%, (>65 y): 28.8%). As preliminary results on the usability of the system, SUS was good for patients (mean SUS score: 74.01) and excellent for caregivers (mean SUS score: 83.27). Other usability measurements analyses are currently ongoing.

Conclusion: The results of this project allow to highlight the strengths and the limitations of the use of tele-medicine and tele-rehabilitation in patients with MCI and in their caregivers.

Disclosure: This project was founded by the Alzheimer's and Dementia Fund 2021-2023 of the Italian Ministry of Health (Project Line #4) and coordinated by the Italian National Institute of Health.

EPO-422 | Correlation between alterations in rs-functional alterations of brain and CSF markers in patients with AD

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Background and Aims: The aim of this study was to explore the correlation between brain functional alterations and CSF pathological biomarkers in AD patients.
Methods: 23 AD patients and 16 control subjects were recruited. All subjects underwent CSF measurement and multimodal MRI scans. Independent component analysis was used to investigate the variations of FC by utilizing RS-fMRI data. Differences in ALFF and ReHo between the two groups were also calculated. Then correlation analyses were used to estimate the possible association between functional alterations and CSF biomarkers.
Results: In the AD group, ALFF decreased in the right Superior Frontal Gyrus, Middle Frontal Gyrus, left superior temporal gyrus, and increased in the right cerebellum anterior lobe, and caudate nucleus as compared to Non-AD CI group ($p<0.001$). In addition, ReHo decreased in the right insula and left middle temporal gyrus ($p<0.001$). Dynamic fluctuations of CSF Tau were observed to be associated with changes in FC between VN and PCC, FC of SMN, as well as the altered ReHo in the right insula and left middle temporal gyrus. Compared the AD group with the non-AD CI group, the aforementioned altered functional brain connectivity, with the exception of FC in the PCC and VN, was significantly associated with a decrease in CSF Aβ1-42.

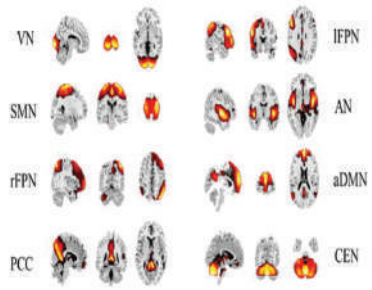

FIGURE.1. Ten ICs derived from the group ICA: anterior default mode network (aDMN), left frontoparietal network (lFPN), right frontoparietal network (rFPN), visual network (VN), sensory-motor network (SMN), posterior cingulate cortex (PCC), cerebellar network(CEN) and auditory network(AN).

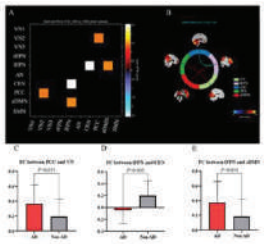

FIGURE.2. Inter-network functional connectivity changes: (A). Group averaged static functional connectivity matrix between nine ICs. (B). Group differences of FC strength in each network. Each square color represents one of the five networks. Blue lines represent decreased connectivity, while red lines represent increased functional connectivity in AD patients compared with controls. (P <0.05). (C). Compared with the control group, AD groups showed higher functional connectivity between the PCC and the VN. (D). Compared with the control group, AD groups showed lower functional connectivity between the lFPN and the celebellar. (E). Compared with the control group, AD groups showed higher functional connectivity between the lFPN and the aDMN.

Conclusion: These functional changes in AD patients are linked to the variations of Tau protein and Aβ1-42 in CSF, with Aβ1-42 having a particularly large impact on brain network function.
Disclosure: Nothing to disclose.

EPO-423 | Neuroinflammation biomarkers and clinical progression in amnestic mild cognitive impairment due to Alzheimer's disease

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Background and Aims: Ongoing Alzheimer's disease (AD) research has unveiled a promising range of fluid biomarkers with diagnostic and prognostic potential. In addition to established biomarkers of amyloidopathy (A), tauopathy (T), and neurodegeneration (N), novel biomarkers of inflammation (I) such as soluble Triggering receptor expressed on myeloid cells 2 (sTREM2), chitinase-3-like-1 protein (YKL-40), and glial fibrillary acidic protein (GFAP) are gaining attention. This study aims to investigate the role of "A", "T", "N" and "I" biomarkers in predicting clinical progression in mild cognitive impairment (MCI) due to AD.
Methods: Sixty subjects diagnosed with MCI due to AD underwent a comprehensive clinical evaluation, an extensive neuropsychological assessment, and CSF biomarkers analysis. CSF Aβ42/40 ratio, p-tau181, total-tau NfL, sTREM2, YKL-40 and GFAP were quantified using automated immunoassay systems. After a two-year follow-up, forty-nine subjects were re-evaluated and classified as "progressors" or "stable" based on clinical progression to dementia.
Results: Twenty-one subjects were classified as "progressors" and twenty-eight as "stable". The two groups exhibited no significant differences in terms of age, literacy and MMSE score at baseline. When comparing CSF biomarker levels between the cohorts, concentrations of p-tau181, t-tau, NfL and YKL-40 were significantly higher in the "progressors" group.
Conclusion: These results confirmed the importance of "T" and "N" biomarkers in predicting AD progression and identified YKL-40 as a novel potential predictor of cognitive decline since the early stages of AD. Future research should aim on validating these findings in larger cohorts, further exploring the potential role of inflammation biomarkers in refining diagnostics, prognostics, and treatment strategies.
Disclosure: Nothing to disclosure.

EPO-424 | A digitally supported lifestyle program to promote brain health among elderly (LETHE trial): Study design and progress

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Background and Aims: The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) multimodal lifestyle intervention yielded cognitive benefits in elderly at risk of dementia. The two-year multinational randomized controlled LETHE trial evaluates the feasibility of a digitally supported, adapted FINGER intervention among at-risk older adults.

Methods: The trial includes older adults (60–77 years) with digital readiness and increased dementia risk without substantial cognitive impairment. Participants are enrolled at four sites (Austria, Finland, Italy, Sweden). They were randomized in a 1:1 ratio to: 1) the intervention group (structured multimodal lifestyle program where in-person activities are supported with the LETHE App); or 2) the control group (self-guided program with simplified App and no personalized content). All participants wear smartwatches to gather passive data. Primary outcomes are retention/adherence and change in dementia risk scores. Secondary and exploratory outcomes include changes in lifestyle, cognition, stress, sleep, and dementia-related biomarkers. A sub-study explores the feasibility of novel interactive technology (audio glasses, social robot).

Results: Recruitment took place between September 2022 and June 2023. In total, 156 individuals were randomized (mean age 69 years, 65% women). Vascular/lifestyle risk factors were common (e.g., 65% with hypertension, 39% physically inactive). The trial will be completed by summer 2025. Retention until the first post-baseline visit (after 6 months) is high ($n=2$ discontinued).

Conclusion: LETHE provides crucial information about the feasibility of technology and a digitally supported FINGER program. Digital tools specifically designed for older adults could offer potential for large-scale, cost-effective prevention programs. The trial is registered at ClinicalTrials.gov (NCT05565170).

Disclosure: AR, HU, AG, MB, JB, BBS, RC, AD, DF, HH, SiH, TK, MK, JeL, VL, CT, StH, FM, PM, ES, and TN declare that they have no disclosures. MC and MP are employed by Innovation Grow. NK is employed by Kaasa Solution GmbH. JyL is employed by Combinostics Ltd. The LETHE project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no 101017405.

EPO-425 | Comparing oral anticoagulants for dementia risk in atrial fibrillation: A network meta-analysis

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Background and Aims: Atrial fibrillation (AF) is a potentially modifiable risk factor for dementia. Research has shown that oral anticoagulant (OAC) use may lower dementia risk in patients with AF. However, few studies have discussed dementia risk in patients with AF who receive different OACs.

Methods: This systematic review and network meta-analysis included randomized controlled trials (RCTs) and observational studies investigating the dementia risk in patients with AF, who were and were not administered OACs. We included studies in which patients received non-vitamin K antagonist oral anticoagulants (NOACs), warfarin, and non-OAC users. *p*-Scores were used to determine the ranking of the association between OAC use and dementia risk.

Results: We analyzed data from 1,096,125 patients (10 RCTs and nine cohort studies). The dementia risk was lower in patients administered NOACs (edoxaban, rivaroxaban, apixaban, dabigatran) and warfarin than in non-OAC users. When compared to warfarin, all NOACs (edoxaban 0.68, 95% CI: 0.54-0.87; rivaroxaban 0.77, 95% CI: 0.65-0.91; apixaban 0.80, 95% CI: 0.66-0.96; dabigatran 0.83, 95% CI: 0.71-0.98) exhibited a reduced dementia risk. NOACs did not show statistically significant intergroup differences. Edoxaban (*p*-score = 0.927) ranked highest in the association of reducing dementia risk in AF patients, followed by rivaroxaban, apixaban, and dabigatran.

Conclusion: The dementia risk was lower in NOAC and warfarin users than non-OAC users, and all NOACs outperformed warfarin. There were no statistically significant differences observed between different NOACs. These findings might highlight that NOAC (particularly edoxaban) administration may be preferred to minimize dementia risk in patients with AF.

Disclosure: Nothing to disclose.

EPO-426 | Effect of long-term exercise and lifestyle multidomain interventions on cognition in older adults: A meta-analysis

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Background and Aims: Emerging evidence suggests that multidomain lifestyle strategies including physical exercise may be effective the prevention of dementia. Observational data supports a protective role of physical activity in preserving cognition, yet randomized controlled trials (RCTs) examining physical exercise interventions provide unclear results, potentially due to short-term designs. We investigated the effect of long-term physical exercise and multidomain interventions on the global cognition of older adults.

Methods: Databases of Pubmed, WoS, CINAHL and PsychInfo were systematically searched from inception to May 1, 2023. RCTs enrolling non-demented, community-dwelling older adults (≥55 years) that assessed the effect of long-term (≥12 months) exercise or multidomain interventions on any validated global cognition measure were included. Random-effects inverse-variance meta-analysis with the Hartung-Knapp-Sidik-Jonkman adjustment was performed. Standardized mean differences (SMD) and 95% confidence intervals were calculated. Risk of bias and publication bias were assessed by the Cochrane Risk-of-Bias-2 tool, and Luis Furuya-Kanamori Index (LFKi), respectively. The certainty of the evidence was assessed with GRADE.

Results: We included 12 trials with 9,165 participants (mean age 73.3 [±4.3] years; 64.8% women). The overall risk of bias was low and minor presence of publication bias was observed for exercise (LFKi: 1.9) and multidomain interventions (LFKi: 2.0). Exercise interventions yielded a non-significant effect on global cognition, SMD = 0.05 (95% CI: -0.02 to 0.12, $p = 0.15$), while multidomain strategies had a small beneficial effect, SMD = 0.09 (95% CI: 0.01 to 0.17, $p = 0.04$).

Conclusion: Moderate certainty evidence supports a small impact of multidomain approaches inclusive of physical exercise for the prevention of cognitive decline in the older population.

Disclosure: Nothing to disclose.

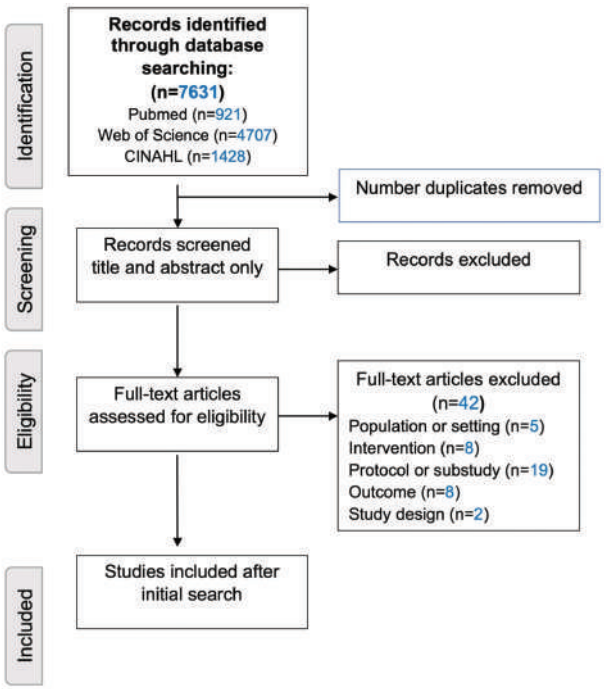
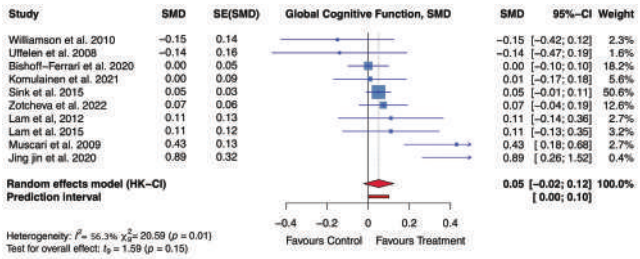
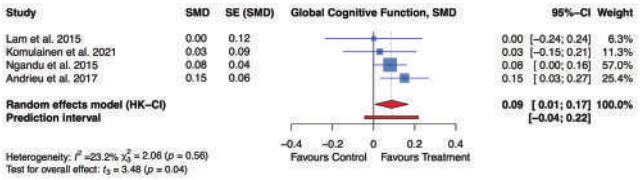


Figure 1. Flow chart of literature search.

Flow chart of the literature adapted from PRISMA guidelines.



Forest plot showing the effect of long-term physical exercise interventions on global cognitive function. SMD, Standardized Mean Difference. SE, Standard Error. HK-CI, Hartung-Knapp confidence intervals.



Forest plot showing the effect of long-term multidomain interventions on global cognitive function. SMD, Standardized Mean Difference. SE, Standard Error. HK-CI, Hartung-Knapp confidence intervals.

EPO-427 | Association between neuropsychiatric symptoms and biomarkers of Alzheimer's disease

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Background and Aims: Neuropsychiatric symptoms (NPS) are frequent in patients with Alzheimer's disease (AD). The association between AD pathophysiology and NPS remains unclear. Understanding the biological mechanisms of NPS in AD can expand our understanding and improve treatment. Aim: Evaluate the association between

NPS and the levels of AD biomarkers [CSF amyloid-β protein (Aβ42), total tau (t-tau) and phosphorylated-tau (p-tau)] and serum Neurofilament light chain (NfL) in patients with AD.

Methods: We performed a cross-sectional study, including patients with the diagnosis of AD, supported by CSF biomarkers. The presence of NPS was assessed with Neuropsychiatric Inventory (NPI) and Frontal Behavioral Inventory (FBI) through a structured interview with the patient and the caregiver. Global cognition was evaluated with Mini-Mental State Examination (MMSE).

Results: We included 60 patients (72.0% female). Average age of onset was of 64.3 (±6.8). Median education was 4.0 (IQR = 5.0). Aβ42 was correlated with NPI apathy (r = −0.56, $p = 0.001$), FBI loss of spontaneity (r = −0.54, $p = 0.003$), personal neglect (r = −0.44, $p = 0.019$), loss of insight (r = −0.48, $p = 0.010$) and incontinence (r = −0.51, $p = 0.005$). Aβ42/Aβ40 was correlated with indifference (r = 0.41, $p = 0.033$), personal neglect (r = 0.38, $p = 0.045$), disorganization (r = 0.38, $p = 0.045$), perseveration (r = 0.38, $p = 0.42$) and agitation (r = 0.39, $p = 0.039$). P-tau was correlated with NPI nocturnal behavior (r = 0.259; $p = 0.047$).

Conclusion: Lower levels of CSF Aβ42 were associated with the presence of apathy, loss of spontaneity, personal neglect and loss of insight. Differential relationships between Aβ42 and Aβ40 and some NPS may reflect the different rates of parenchymal vs vascular deposition, and comorbid cerebral amyloid angiopathy, meriting further studies.

Disclosure: Nothing to disclose.

EPO-428 | Plasma biomarkers profiles in Alzheimer's disease and Parkinson's disease

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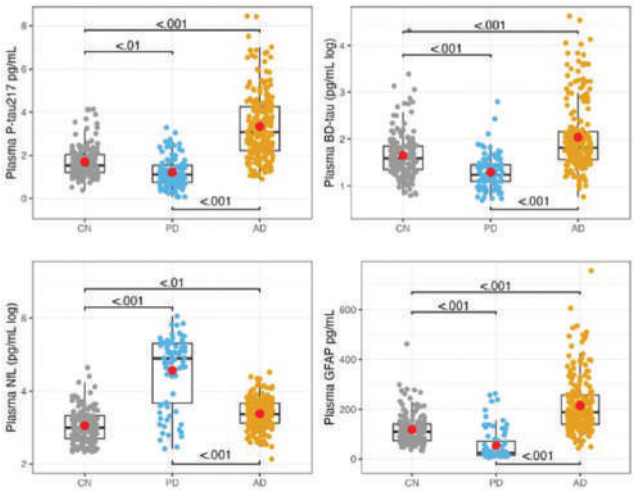
Background and Aims: Plasma biomarkers are accessible tools that are lacking in neurodegenerative diseases, especially in Parkinson's disease (PD). Biomarkers like phospho-tau217 (p-tau217) and brain-derived tau (BD-tau) have proven to be accurate and robust for Alzheimer's disease (AD) diagnosis. Similarly, glial fibrillary acidic protein (GFAP) and neurofilament light chain (NfL) have been proposed as biomarkers, predicting conversion to dementia and neuronal damage, respectively. To better characterize these biomarkers profiles and their relationship, our goal was to evaluate the levels of plasma p-tau217, BD-tau, NfL, and GFAP in PD and AD.

Methods: Plasma p-tau217, BD-tau, NfL, and GFAP were measured using SIMOA in patients with PD ($n = 108$) and AD ($n = 220$), as well as cognitively normal (NC) controls ($n = 157$).

Results: We found increased levels of p-tau217 and BD-tau in AD, and decreased levels in PD, compared to CN ($p < 0.001$). GFAP was increased in AD, compared to NC, but not in PD ($p < 0.001$). NfL was markedly increased in PD ($p < 0.001$), however with a large variability within the group, while being unchanged in AD, compared to NC. Correlations were found between p-tau217 and NfL, and the Trailmaking test part B (TMT-B) (r = 0.22, $p = 0.001$, r = 0.24, $p < 0.001$, respectively) in the AD, and NfL and Unified Parkinson's Disease Rating Scale (UPDRS) (r = 0.3, $p = 0.01$) in PD. Markers were also highly correlated between each other in both AD and PD.



Plasma p-tau217, BD-tau, NfL, and GFAP levels in CN, AD, and PD individuals.

Conclusion: We found that p-tau217, BD-tau and GFAP are increased in AD, while increased NfL levels were associated with PD, with associations with motor and cognitive impairment.

Disclosure: Nothing to disclose.

Motor neurone diseases

EPO-429 | Takotsubo syndrome in a Sardinian amyotrophic lateral sclerosis cohort

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Background and Aims: Amyotrophic lateral sclerosis (ALS) is known to be associated with varying degrees of autonomic and cardiovascular dysfunction. Recent case reports showed that ALS may be

linked to Takotsubo syndrome (TTS), an acute heart failure syndrome characterized by left ventricular dysfunction with a peculiar pattern, resulting in apical ballooning. Here we reported and described five ALS patients who developed TTS.

Methods: We retrospectively examined a ten-year incident ALS cohort (2010-2019), identified patients who developed TTS and described their clinical characteristics.

Results: Our Sardinian cohort included 344 ALS patients and five of them (1.45%) developed TTS. All were female and their median onset age was 71.5 years (IQR 62.75-77). No relevant genetic mutation was detected. Three patients had spinal and two bulbar onset, though all had bulbar involvement and were at an advanced stage of disease (ALSFRS ≤ 25, King's ≥3) at TTS diagnosis. We identified a potential physical and emotional TTS trigger in four patients (hospitalization for pneumonia, tracheostomy, PEG placement). Survival time was variable (up to 25 months after TTS).

Conclusion: TTS is not an infrequent condition in ALS and may influence these patients' prognosis. Female sex, bulbar involvement and later age of onset may be important risk factors for developing this cardiac condition and a physical or psychological trigger is often observed. Despite autonomic dysfunction in ALS has been demonstrated, the precise physiopathological mechanism underlying TTS needs to be furtherly clarified.

Disclosure: Nothing to disclose.

EPO-430 | Vitamin D levels and disease severity in ALS patients

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Background and Aims: The hypothesis that vitamin D may play a role in ALS disease mechanisms stems from pre-clinical studies and epidemiological findings in other neurological diseases. The objective of this study was to determine the levels of vitamin D in ALS patients compared with those in control subjects and correlate the levels of vitamin D with disease severity.

Methods: Vitamin D levels were measured in 45 ALS subjects and 45 controls. We estimated associations with ALSFRS-R scores by multivariate linear regression using data from baseline visit. As potential confounders were considered: age, gender, ethnicity, body mass index, smoking, history of performing physical exercise, vitamin D supplements, site of symptom onset, diagnostic delay, familial ALS cases.

Results: The majority of ALS subjects (73.3%) had levels below the recommended level of 30 ng/ml. Vitamin D levels in ALS patients were slightly lower than those in control subjects by a mean difference of −9.5 ng/ml; 95% CI (−15.0; −4.0). Demographics, body mass index, smoking, history of performing physical exercise, site of symptom onset, diagnostic delay did not differ across strata of baseline vitamin D level. The association between vitamin D and ALSFRS-R total scores did not appreciably change after adjusting for multiple baseline clinical characteristics.

Conclusion: We found that people with ALS had vitamin D levels below the recommended level in line with other reports in neurodegenerative disease. Worse severity score at baseline due to vitamin D deficiency, however, is unlikely based on our study.

Disclosure: Nothing to disclose.

EPO-431 | Ulnar CMAP and MUNE in adult SMA patients treated with nusinersen

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Background and Aims: Spinal muscular atrophy (SMA) is a progressive disease leading to motor neuron loss. Nusinersen treatment in adult patients can halt disease progression. Improvement of compound muscle action potential (CMAP) and estimation of the number of motor units (MUNE) in nusinersen-treated pediatric SMA patients were demonstrated by some authors.

Methods: 17 adult patients with SMA type 2 ($N=1$) or 3 ($N=16$) (35.3%F) treated with nusinersen were included in the study, 70.6% of patients were walkers. Sex- and age-matched healthy volunteers served as the control group (HC). All the patients were assessed at baseline, 6th, 14th months of treatment and consecutive infusions with functional scales (Hammersmith Functional Motor Scale Expanded-HFMSE or CHOP-INTEND and Revised Upper Limb Module-RULM) and CMAP, multipoint incremental MUNE, single motor unit potential (SMUP) of the abductor digiti minimi (ADM). The duration of observation was 30-50 months.

Results: CMAP and MUNE were significantly lower in SMA patients than in HC ($p<0.001$); SMUP was significantly higher in SMA patients than in HC ($p<0.001$). We have observed decrease in mean CMAP and MUNE in SMA patients at 6 months in the first year of treatment, since 14th month of treatment there was an increase and followed by stabilization of those parameters but there was no significant difference between baseline evaluation of CMAP and MUNE and evaluation at next infusions. Only SMUP value was significantly higher after six months in comparison with baseline value ($p=0.039$).

Conclusion: Nusinersen treatment stabilizes CMAP, MUNE and SMUP after 6 months of treatment in SMA adults with SMA2-3 observed for up to 50 months.

Disclosure: Anna Kostera-Pruszczyk - honoraria for advisory boards, speaking at educational events for Biogen, Novartis/AveXis, PTC and Roche, support for congress participation: Biogen, Roche, Novartis; institutional grant support from Biogen Anna Potulska-Chromik

- honoraria for speaking at educational events for Biogen, Abbvie, PTC and Roche, support for congress participation: Biogen, Novartis Anna Łusakowska - honoraria for speaking at educational events for Biogen, Roche, support for congress participation: Biogen, Roche Anna Frączek - honoraria for speaking at educational events for Biogen, Roche, support for congress participation: Biogen, Roche Karolina Aragon-Gawińska - - honoraria for speaking at educational events for Biogen, Roche, PTC, support for congress participation: Biogen, Roche, PTC Małgorzata Burlewicz, Zuzanna Gierlak-Wójcicka – speaker at the conferences and meetings organized by Biogen, Roche, support for congress participation: Biogen, Roche Ewa Sobieszczuk – nothing to disclose.

EPO-432 | Iron metabolism-genetic interplay in an ALS cohort: A single-center study

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Background and Aims: Impaired iron metabolism has been observed in ALS, but it is not known whether it is a cause or a consequence of the disease. The aim of our study is to investigate the interplay between iron homeostasis and ALS by analysing a panel of iron-related genes.

Methods: 20 ALS patients (male, $n=12$) were tested for common variants in iron-related genes, among which the p.Asp358Ala variant in the IL6R (interleukin 6-receptor) gene, known to increase soluble IL6-R levels. Patients were dichotomized into carriers (both heterozygous and homozygous) and non-carriers; all underwent blood sampling for measurement of iron-related molecules. Adjusted ANCOVA and correlation analysis and linear regression (with site of onset, sex, age and disease duration as independent variables) were performed.

Results: Median ferritin levels were 424.2 ng/ml in men (UNL: 400) and 192.4 ng/ml in women (UNL: 150), with 55% of patients having higher than normal levels. Higher ferritin levels were associated with the group of bulbar*fast progressor patients ($p=0.012$) and correlated with the disease progression rate [DPR] ($r=0.518$, $p=0.028$). The IL6R358Ala variant carriers had lower ferritin levels than non-carriers ($p=0.023$). In the multivariate analysis, this variant was found to be the only predictor of ferritin levels ($p=0.013$).

Conclusion: Our preliminary results may suggest a role of the IL6R358Ala variant in reducing ferritinemia. This could be explained by a kind of "buffering" system mediated by higher s-IL6-R levels, dampening the pro-inflammatory IL-6 signalling. These findings may help to better define the relationship between iron metabolism abnormalities and clinical features in ALS.

Disclosure: The authors have no potential conflict of interest to disclose.

EPO-433 | Evaluation of clinical effectiveness of edaravone in the treatment of amyotrophic lateral sclerosis in Uzbekistan

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Background and Aims: Amyotrophic lateral sclerosis (ALS) is a progressive, neurodegenerative disease of the central nervous system. Despite the positive outcome of clinical trial of edaravone for treatment of ALS, there are limitations which makes it difficult for clinicians to prescribe the drug with an expectation of efficacy. Our study aims to investigate the clinical efficacy of edaravone in the treatment of ALS in Uzbek patients.

Methods: We examined 36 patients with ALS, aged from 24 to 78 years, who were hospitalized between 2019 and 2023. Patients were divided into 2 groups: 1) main group: 25 (70%) patients who received Edaravone; 2) control group: 11 (30%) patients who received standard ALS treatment. All patients underwent a standard examinations: clinical and neurological examination; Electroneuromyography; ALS-FRS-Revised functional rating scale before and after treatment.

Results: The incidence of clinical symptoms in ALS before treatment with edaravone was reduced by 27% after the treatment of edaravone. The incidence of clinical symptoms in ALS before treatment with standard therapy was reduced by 15% after the treatment of standard therapy ($p<0.005$). According to ALS-FRS-R scale, scale index in the patients treated with edaravone significantly increased by 21% (40 +0.93) and the scale index in the patients treated with standard therapy increased by 11% (37+ 0.74), ($p<0.001$). According to ENMG parameters, the maximum amplitude of the M-response increased for all nerves in the edaravone group compared to the control group ($p<0.005$).

Conclusion: Our research showed that 60% of patients with ALS show positive dynamics in the initial stage of focal motor disorders in the treatment with edaravone. The use of edaravone in the therapy of ALS was highly effective, especially in the early stages of the disease, in cervico-thoracic and bulbar forms of ALS.

Disclosure: Nothing to disclose.

EPO-434 | Retrospective study of a cohort of patients with amyotrophic lateral sclerosis from the University of Pisa

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Background and Aims: Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder that involves upper and lower motor neurons. Different phenotypes are possible, with sometimes differences in survival. According to the epidemiological data, bulbar subtypes show a more rapid progression and shorter survival, compared to the spinal subtypes. The objective of our study was to analyze the survival of a cohort of patients with ALS across the different disease phenotypes.
Methods: All patients diagnosed, according to the Gold Coast Criteria, with ALS from January 2021 to January 2024 at our Center for Motor Neuron Disease were retrospectively evaluated. None had been excluded from the study, but 13 patients had been lost during follow-up, thus were excluded from the Kaplan-Meier analysis.
Results: A total of 99 patients were enrolled (median age: 65.1 ±11.5; 46.5% female). Among them, 73.8% had a spinal onset (57.4% male), 25.3% had a bulbar onset (64% female). The time hiatus between the disease onset and diagnosis was 18.6 ±18.7 months on average (14.2 ±12 months for bulbar onset, and 21.1 ±21.2 months for spinal onset). The number of dead patients was 25 (36% of bulbar onset; 22% of spinal onset). The disease duration was on average 34 ±23 months (28 ±15 months for the bulbar form, 37 ±25 months for the spinal form).
Conclusion: Our data are in line with those reported in literature. Patients stratification can help in identify prognostic factors and epidemiological data that may improve clinical, diagnostic, and therapeutic management of this complex disease.
Disclosure: Nothing to disclose.

EPO-435 | Lower Gas6 levels are associated with bulbar phenotype and faster disease progression in ALS patients

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Background and Aims: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder that primarily affects the motor neurons in the brain and spinal cord. While the exact cause of ALS is not fully understood, a combination of genetic and environmental factors is believed to contribute to its development. Research into the etiology and pathogenesis of ALS is ongoing, and we investigated the role of Growth Arrest-Specific 6 (Gas6) as a possible contributor. This vitamin K-dependent protein has been recognized to enhance survival of oligodendrocytes and neurons and, it has been associated with different kinds of (neuro) inflammatory conditions.
Methods: We conducted a prospective observational study including 65 ALS patients aimed to assess whether circulating serum levels of Gas6 and its soluble receptors (sAxl, sMer, sTyro-3) along with neurofilaments (NfLs) could represent a disease marker in ALS patients.
Results: In our ALS cohort, lower serum levels of Gas6, and concomitantly higher levels of NfL, were associated with a more aggressive disease, expressed with bulbar phenotype (*p*-value for Gas6: 0.03) and faster progression (*p*-value for Gas6: 0.03). Also, serum Gas6 can well distinguish (area under the curve, cut-off 13.70 ng/mL, sensitivity 69.57%, specificity 72.72%) between fast and slow progressors.
Conclusion: Due to neuroprotective properties, our data suggest that Gas6, could be an intriguing biomarker in ALS patients.
Disclosure: No disclosure.

EPO-436 | Validation of the Czech and Slovak versions of questionnaires used to monitor the clinical status of patients with ALS

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Background and Aims: This multicentre study aimed to validate Czech and Slovak versions of several questionnaires used to monitor patients with amyotrophic lateral sclerosis (ALS). The following scales and questionnaires were used: the ALS Functional Rating Scale – Revised (ALSFRS-R) and its extended version (ALSFRS-R-EX), the ALS Assessment Questionnaire - 40 items (ALSAQ-40), the Borg scale for breathlessness intensity, and the Dysphagia in ALS (DYALS) scale for dysphagia symptoms. Both the clinician-administered version of the ALSFRS-R and the self-administered version were compared.
Methods: All questionnaires and scales were translated using the forward-backward method. The first administration was made during clinical follow-up in four major Czech or Slovak neuromuscular centres (Brno, Prague, Bratislava, Martin), with a repeat administration by telephone after seven days. In both cases, the self-administered version of the ALSFRS-R was used. One week later, the ALSFRS-R+EX questionnaires were administered again by telephone in a non-self-administered version.
Results: The study involved 62 ALS patients (34 men) and showed excellent questionnaire comprehension in both languages. Statistical

analysis revealed no significant differences in scores between administrations, confirming excellent reproducibility and high internal consistency (Cronbach's alpha around 0.98). The intraclass correlation coefficient ranged from 0.905 to 0.994, indicating high agreement between different versions and/or administrations of the questionnaires.

Conclusion: The Czech and Slovak versions of all tested ALS-related questionnaires show high patient comprehensibility, internal consistency and reproducibility between repeated administrations, and excellent agreement between self-administered and clinician-administered versions of the ALSFRS-R questionnaire.

Disclosure: The authors declare no conflict of interest regarding this study.

EPO-437 | Analysis of C9orf72 repeat expansions in Georgian patients with amyotrophic lateral sclerosis

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Background and Aims: Amyotrophic lateral sclerosis (ALS) is a fatal progressive neurodegenerative disorder that affects the upper and lower motor neurons. Several genetic risk factors have been identified in the past decade with a hexanucleotide repeat expansion in the C9orf72 gene being the most significant. However, the presence of C9orf72 repeat expansion has not been examined in the Transcaucasian region, therefore we aimed to analyze its frequency in Georgian patients with ALS.

Methods: We included 74 self-reported Georgian patients with ALS from different parts of the country, fulfilling the Gold Coast criteria. To investigate the presence of an expanded GGGGCC hexanucleotide repeat in the non-coding region of the C9orf72 gene, we performed Repeat-Primed PCR (RP-PCR).

Results: In total, 74 sporadic and two familial ALS cases were identified. Patients were aged 26 to 84 years with a mean age of 58.3 years at disease onset. Bulbar onset was observed in 21.88%, upper limb onset in 34.38%, and lower limb onset in 43.75% of the patients. Frontotemporal dementia (FTD) fulfilling the Strong criteria was diagnosed in seven patients (10.94%). C9orf72 repeat expansion was detected in only one case using RP-PCR; the patient had a family history of dementia.

Conclusion: Our results indicate that C9orf72 hexanucleotide expansion does not belong to the major genetic risk factor of ALS in Georgian patients. Further genetic studies in a bigger study population are needed to reveal the genetic causes of ALS in the Transcaucasian population.

Disclosure: Nothing to disclose.

EPO-438 | Basal metabolism, myokine levels and disease severity in amyotrophic lateral sclerosis

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Background and Aims: Amyotrophic lateral sclerosis (ALS) can be considered as a multisystemic disease affecting metabolism and body composition. Abnormal resting energy expenditure (REE) has been reported in ALS patients and could be linked to variations in circulating myokine levels. The aim of this study is to investigate metabolic impairment and plasma myokine levels and their possible connection with disease progression.

Methods: ALS patients underwent ALS-functional rating scale-revised (ALS-FRS-R), MRC sum score and blood detection of myokines (irisin, IL-6) and 181pTau. Indirect calorimetry and dual-X-ray absorptiometry (DEXA) were performed on the same day to assess REE and body composition, respectively.

Results: We enrolled 10 patients and 10 healthy controls. At indirect calorimetry 8 patients were hypometabolic. REE, normalized with fat free mass, directly correlated with irisin levels. We found no correlations between either REE or irisin and functional scales of disease severity, whereas pTau levels were increased in patients ($p < 0.05$) and inversely correlated with MRC sum score ($p < 0.05$). IL-6 directly correlated with disease duration ($p < 0.05$) and inversely correlated with MRC sum score ($p < 0.05$).

Conclusion: Basal metabolism alterations are present in ALS and irisin can be linked to them, independently on disease severity. Conversely, pTau and IL-6 could be indicators of disease progression and severity. Further investigations are required to clarify whether metabolic abnormalities could have a role in ALS pathogenesis and disease progression or represent a consequence of secondary muscle wasting. Moreover, myokines such as irisin could be useful to investigate alterations of resting metabolic state.

Disclosure: Nothing to disclose.

EPO-439 | Study of anthropometric parameters in patients with amyotrophic lateral sclerosis (ALS)

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Background and Aims: Subclinical loss of muscle mass and subcutaneous fat in ALS patients is one of the reasons for the delayed diagnosis of latent protein-energy malnutrition (PEM).

Methods: The study included 49 ALS patients (13 (26%) men, 36 (74%) women), 62.0 [51.0; 67.0] years, BMI 25.2 [23.0; 28.0]. Me duration of the disease 13.2 [9.3; 19.7] months. Me of ALSFRS 46.0 [42.0; 47.0]. The control group 30 patients (10 (33%) men, 20 (67%) women) without neuromuscular pathology, 56.0 [47.0; 61.0] years, BMI 29.7 [25.5; 31.9]. There was no statistical difference in age, gender and BMI.

Results: Significant decreases in circumferences were found in ALS patients (Table 1). Almost all measured parameters among ALS patients were significantly lower (U, $p<0.05$) compared with the control group. No significant reduction in circumference above the ankle was revealed, that is probably due to the hidden edema in ALs patients, which is one of the clinical signs of PEM. The waist circumference in patients with ALS showed good quality of the diagnostic model, AUC=0.732±0.08 (95%CI0.575-0.856), $p=0.006$. The threshold value of waist circumference is ≤98 cm, sensitivity 80%, specificity 67% (Figure 1).

Table 1 – Circumferences in ALS patients in comparison with control group

Parameter, cm	ALS, n=49 Me[LQ;UQ]	Control, n=30 Me[LQ;UQ]	U, p
Chest circumference	96,0[88,0;101,0] *	104,5[97,0;111,00]	0,000177
Waist circumference	91,0[76,0;98,0] *	100,0[81,0;103,0]	0,009001
Buttock circumference	101,0[94,0;97,0] *	109,0[104,0;118,0]	0,000028
Arm circumference, D	30,0[28,0;33,0] *	36,0[32,0;38,5]	0,000002
Arm circumference, S	29,0[27,0;32,0] *	36,0[31,5;39,0]	0,000001
Forearm circumference, D	25,0[23,0;27,0] *	28,0[26,0;31,0]	0,000002
Forearm circumference, S	25,0[22,0;26,0] *	28,0[26,5;30,5]	0,000001
Wrist circumference, D	17,75[16,0;18,0]	18,0[17,0;19,0]	0,057517
Wrist circumference, S	17,0[16,0;18,0] *	18,0[17,5;19,0]	0,027901
Hip circumference, D	53,0[49,0;56,0] *	62,0[55,0;68,0]	0,000001
Hip circumference, S	52,0[46,5;54,0] *	61,0[54,0;66,0]	0,000001
Shin circumference, D	36,0[34,0;39,0] *	40,0[36,0;41,0]	0,001943
Shin circumference, S	36,0[35,0;38,0] *	40,0[36,0;42,0]	0,000383
Circumference above the ankle, D	23,0[22,0;25,0]	24,0[23,0;26,0]	0,186999
Circumference above the ankle, S	23,0[22,0;24,0]	23, 5[23,0;25,0]	0,175780

* - significant differences at p< 0.05 (according to the Mann-Whitney criterion). D – Dexter, S – Sinister.

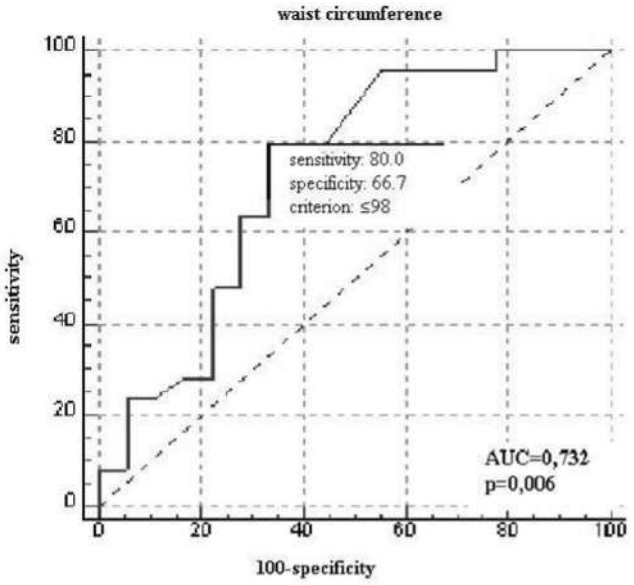

Figure 1 – ROC-waist circumference curve in patients with ALS

Conclusion: Despite the early stages of the disease, the preservation of functional capabilities significant decrease in circumferences were found, that indicates a progressive loss of muscle mass and subcutaneous fat in ALS patients. According to the ROC-analysis in ALS patients with an AUC value greater than 0.7, the threshold level of waist circumference sensitivity is over 80% and can be considered objective sign of PEM.

Disclosure: The authors have nothing to disclose.

EPO-440 | Early diagnosis of ALS using near-fiber EMG

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Background and Aims: Amyotrophic lateral sclerosis is characterized by rapid and progressive motor neuron lesions. The continuous process of denervation and reinnervation is manifested in EMG signals as changes in motor unit potential (MUP) size, temporal dispersion (complexity) and instability. Current methods to assess temporal dispersion and instability are either indirect (MUP turns, jiggle) or time-consuming (single fiber jitter). Near-Fiber EMG (NF-EMG) is a novel way to assess the size, temporal dispersion, and instability of routinely recorded MUPs directly and quantitatively in a semi-automated manner.

Methods: 1441 MUs in 60 muscles of 10 patients at the time of ALS diagnosis (Gold Coast criteria) were sampled using NF-EMG. MUP area and duration and NF-MUP dispersion and segment jitter were studied.

Results: On average, 49.1% of MUs showed increased NF-MUP dispersion and 53.7% exhibited increased NF-MUP segment jitter, whereas 31% of MUs had both increased NF-MUP dispersion and instability. Interestingly, 27% and 30% of MUs with normal sized MUPs had increased NF-MUP dispersion and segment jitter, respectively (3 and 2 times higher than in control subjects), indicating the capability of NF-EMG to detect electrophysiological abnormalities at early stages of the disease.

Muscle	MUPs (muscles)	% incr. NFM_SJ	% incr. NFM_SJ + Normal MUP size (area or dur)	% incr. NFM_Disp	% incr. NFM_Disp + Normal MUP size (area or dur)	% incr. NFM_SJ + NFM_Disp	% incr. NFM_SJ + NFM_Disp + Normal MUP size (area or dur)	% incr. NFM_SJ + Normal MUP size (area& dur)	% incr. NF_Disp + Normal MUP size (area& dur)	% incr. NFM_SJ + NF_Disp + Normal MUP size (area& dur)
Ext	353 (10)	49.0	29.6/37.5	51.0	33.3/40.7	31.2	17.0/22.1	26.1	30.0	14.2
FDI	379 (8)	38.2	20.6/68.2	52.0	31.3/44.7	41.3	22.9/34.1	49.7	30.7	23.8
VL	356 (16)	48.0	24.7/33.1	43.5	21.9/25.0	27.2	9.8/14.3	23.9	16.6	7.3
TA	419 (17)	51.6	33.7/39.6	53.1	33.7/38.9	32.9	19.8/23.9	30.1	28.9	16.7
MG	734 (9)	41.9	28.6/26.9	47.9	34.6/30.3	24.8	15.8/14.5	23.5	17.4	12.4
Total	1441(60)	53.7	33.4/41.1	49.1	30.5/35.9	31.5	14.5/21.9	30.3	26.7	14.5

TABLE 1 Percentage of MUs with increased temporal dispersion (NFM_Disp) and instability (NFM_SJ). Compared with control subjects, a significant percentage of MUs with normal sized MUPs showed increased NFM_Disp and/or increased NFM_SJ.

Conclusion: Near Fiber EMG can effectively characterize the functional status of a motor unit, by providing novel and useful information about the degree, stability, and course of denervation and/or reinnervation.

Disclosure: Nothing to disclose.

EPO-441 | Elevated serum MCP-2 and TARC are associated with increased risk of death in Guamanian ALS patients

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Background and Aims: This study explores the relationship between inflammation and longevity in post-WWII Guam amyotrophic lateral sclerosis (ALS). Characteristics of this focus include sudden high incidence and long lifespan in some cases. Understanding longevity in Guamanian ALS may help elucidate causal pathways and novel therapeutic targets. This research evaluates inflammation in biobanked Guamanian ALS patient serum to understand the relationship between immunoregulator levels and survival time.

Methods: Sera from 69 Guam ALS cases collected within early years of onset by NIH researchers from 1958-1990 were evaluated for 11 regulators of inflammation, using custom multiplex cytokine and single-plex CRP ELISA. Survival analysis with Cox proportional hazards models was used to determine factors associated with time to death.

Results: Factor 2 (MCP-2 and TARC) was associated with a 38% increase in risk of death (HR: 1·38, 95% CI [1·19, 1·65], *p*: 0·00). Individually, MCP-1 (HR: 1·03, 95% CI [1·004, 1·06], *p*: 0·02), MCP-2 (HR: 1·24, 95% CI [1·08, 1·44], *p*: 0·00), IFN-γ (HR: 2·34 95% CI [1·25, 4·36], *p*: 0·01), IP-10 (HR: 1·18, 95% CI [1·065, 1·312], *p*: 0·00), IL-6 (HR: 1·05, 95% CI [0·998, 1·108], *p*: 0·06), and TARC (HR: 1·03 95% CI [1·013, 1·044], *p*: 0·00), were also associated with increased risk of death.

Conclusion: Results suggest increased inflammation in Guamanian ALS is associated with shortened lifespan. Assessing serum levels of MCP-2 and TARC in early stages of disease may predict severity and duration in sporadic ALS. Research on the relationship between pathways associated with TARC, MCP-2 in ALS warrants further investigation.

Disclosure: Nothing to disclose with regard to conflicts of interest. Institutional Board Review (IRB) and Ethics disclosure: As all participant are deceased Binghamton University IRB has classified this as non-human subjects research, which does not require IRB approval.

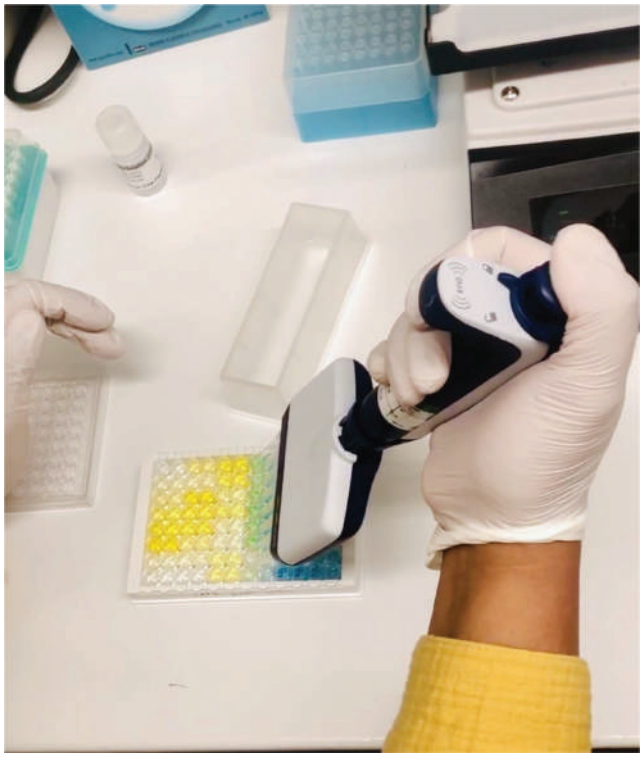

FIGURE 1 C-reactive Reactive Protein ELISA of Guamanian ALS sera.

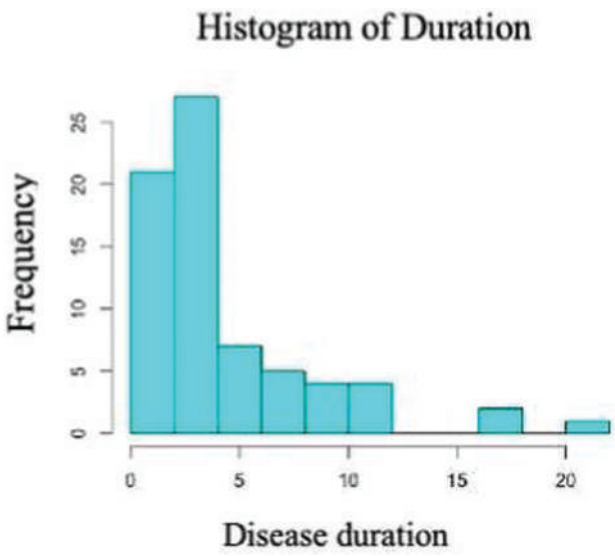

FIGURE 2 Distribution of disease duration: Cases represent a broad range of survival times (1-22 years, $n = 69$).

However, at time of collection, all specimens were obtained with informed written consent from patients following ethical standards set forth by the 1947 Nuremburg Code, the 1965 Declaration of Helsinki, and the 1974 Belmont Report. This research is consistent with the original use for which the samples were collected. All samples included in study were collected prior to 1985 when ALS was still highly prevalent on Guam.

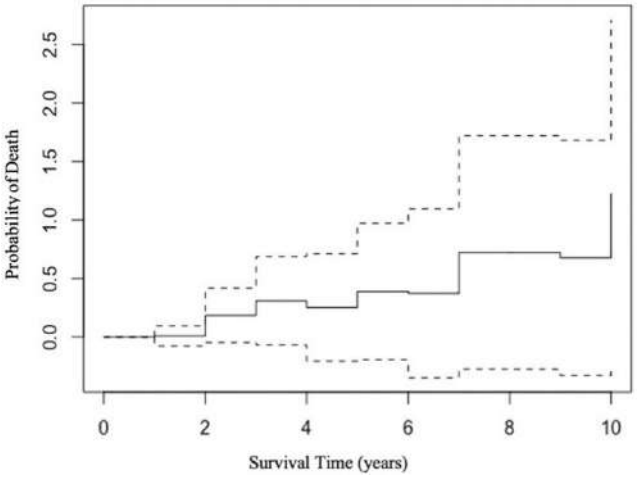

FIGURE 3 Increased probability of death with increase of Factor 2 (MCP-2 & TARC): Horizontal lines in Kaplan-Meier curve depict duration of survival; vertical lines depict change in probability of death; intermittent lines represent 95% confidence intervals.

EPO-442 | Exploring glymphatic system function in the ALS-FTD spectrum

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Background and Aims: Growing evidence suggests that glymphatic function is impaired in patients with several neurodegenerative diseases and neuroinflammation is thought to be entangled with glymphatic function. However, there are few available in vivo data about glymphatic function in patients with amyotrophic lateral sclerosis and/or frontotemporal dementia (ALS-FTD).

Methods: We measured serum levels of osteopontin, a neuroinflammatory biomarker which is thought to be produced by perivascular cells, in a cohort of patients with ALS and FTD, as well as in age-matched healthy controls, and correlated it to clinical features.

Results: Osteopontin serum levels correlated with age and were higher in ALS patients compared to healthy controls. Patients with higher osteopontin serum levels had a trend for a shorter survival.

Conclusion: We confirmed that osteopontin levels are higher in ALS patients compared to controls and correlate with a worse prognosis. Correlation with MRI data will provide information about 1) glymphatic function in patients with ALS-FTD and 2) osteopontin association with glymphatic function.

Disclosure: Nothing to disclose.

EPO-443 | Progression of cognitive impairment in ALS: Preliminary findings from a longitudinal monocentric study in Italy

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Background and Aims: The presence of cognitive and behavioral impairment in patients affected by Amyotrophic Lateral Sclerosis (ALS) is now well-established. However, there is no agreement about the worsening of cognitive deficits during disease progression, and the few longitudinal studies on the topic provided inconclusive results. This monocentric, longitudinal study aims at evaluating the cognition at the time of ALS diagnosis and after 12 months.

Methods: 62 Italian subjects (F:M = 0.44; age 63.51 ± 12.46y) with a diagnosis of ALS were subjected to a standardized neuropsychological evaluation at diagnosis through the Edinburgh Cognitive and Behavioral ALS Screen (ECAS) test, the Story-based Empathy Task (SET) test, and the Ekman 60-faces test. The evaluation was repeated after 12 months.

Results: In the overall study population, cognitive decline, as defined by ECAS abnormalities, was observed in 13 subjects (20.97%). Some alterations in emotions recognition emerged from Ekman test (mean 45.49, sd 6.88). Only 27 subjects could be assessed at the second time-point (F:M = 0.22; age 63.81, sd 12.99y). In this follow-up population, cognitive decline at ECAS was observed in 5 subjects at T0 (18.51%) and in 7 subjects at 12-months assessment (25.92%). Changes of ECAS, SET or Ekman test scores after 12 months were not statistically significant.

Conclusion: These preliminary results do not show progression of cognitive impairment. This could be influenced by the small sample size and by the attrition bias in the longitudinal study population (i.e. subjects with a better disease course being over-represented amongst the ones reaching the follow-up visit). More detailed data analysis is still ongoing.

Disclosure: Nothing to disclose.

Coma and chronic disorders of consciousness

EPO-444 | The functional communication measures for assessing communicative abilities in prolonged disorders of consciousness

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Background and Aims: The present cross-sectional study aimed to investigate the ability of the validated Italian version of the shortened Functional Communication Measures (sFCM) in assessing communication in individuals with severe Acquired Brain Injury (sABI) with and without prolonged Disorders of Consciousness (pDoC).
Methods: Participants: 17 sABI patients consecutively admitted to our sABI Rehabilitation Unit (males = 11; mean age = 60.4±15.3 years; pDoC = 7). Variables collected: i. demographic and anamnestic information at study entry; ii. Levels of Cognitive Functioning (LCF), Disability Rating Scale (DRS), Functional Oral Intake Scale (FOIS) scores, and Coma Recovery Scale-Revised (CRS-R) scores only in patients with pDoC; iii) sFCM scores administered independently by two blinded examiners.
Results: The sFCM inter-rater agreement ranged from perfect to substantial. The sFCM correlated significantly with LCF, DRS and FOIS scores (all $p < 0.05$). In the subgroup of patients with pDoC, the oral comprehension on sFCM correlated significantly with the CRS-R motor subscore ($\rho = .794$; $p = 0.017$). Specifically, patients with higher CRS-R motor subscore were classified by the sFCM as being able to execute simple commands or answer with a "yes/no" code to contextual questions with consistent and maximal facilitation, although they did not meet the CRS-R criteria for consistent command following.
Conclusion: We confirmed that sFCM are a solid and easy-to-administer tool for assessing communication abilities in fully conscious sABI patients. For the first time, we found that the sFCM are able to stratify patients with pDoC based on their language abilities more accurately than the CRS-R.
Disclosure: Nothing to disclose.

EPO-445 | Clinical improvements following transcutaneous auricular vagal nerve stimulation in acute disorders of consciousness

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Background and Aims: Patients with disorders of consciousness (DoC) are a challenging population lacking effective treatment options. Among neuromodulation techniques, trans-auricular vagal nerve stimulation (taVNS) may act through a bottom-up manner to modulate thalamo-cortical connectivity and promote the recovery of consciousness.
Methods: We are conducting the first randomized placebo-controlled double-blind clinical trial employing taVNS in 44 acute DoC. Patients randomly receive either 5 days of active bilateral vagal stimulation (45 min; 3mA; 200-300μs current width, 25Hz) or sham stimulation. Behavioural (Coma Recovery Scale-Revised, CRS-R) measures are collected at baseline and at the end of the treatment.
Results: Preliminary results on 30 patients show a significant difference in the behavioral score evolution (post vs pre) between the active and sham groups following the 5-day treatment period ($W = 150$; $p = 0.014$). Patients in the active taVNS group showed significantly increased CRS-R total scores post-treatment compared to baseline (median pre-treatment = 8 [5]; median post-treatment = 11 [12]; $V = 4.5$; $p = 0.021$), while patients from the sham group did not display such difference (median pre-treatment = 6.5 [6.25]; median post-treatment = 6.5 [3]; $V = 16$; $p = 0.83$). Moreover, in the active group ($n = 14$), 7 patients displayed a new sign of consciousness and 4 improved their diagnosis, among which 3 even emerged from DoC. In the placebo condition ($n = 16$), 2 patients improved and only one changed diagnosis.
Conclusion: Our results show that repeated taVNS might promote consciousness recovery in the early phase following severe brain injury. This study will contribute to define the role of taVNS for the treatment of these challenging conditions and identify patients' clusters for responses to treatment.
Disclosure: None.

EPO-446 | Rehabilitation of language and swallowing abilities in patients with severe brain injury: An online international survey

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Background and Aims: Patients with severe brain injury and disorders of consciousness (DoC) are unable to communicate and

frequently experience severe dysphagia. The DoC Special Interest Group of the International Brain Injury Association (IBIA) created a survey to identify the tools that are used by (speech-language) therapists, detect their needs and possibly identify new practices to improve language and swallowing rehabilitation in post-comatose patients.

Methods: The survey was developed based on the following structure: (1) Study presentation, (2) Socio-demographic information, (3) General questions regarding speech and language therapies (4) Swallowing assessment and management, (5) Language/communication assessment and management, and (6) Conclusion. The English questionnaire was then translated into 6 other languages, transferred to the Alchemer platform, and massively diffused.

Results: Preliminary data highlight the profile of therapists involved in the rehabilitation of language and swallowing abilities after coma, their degree of concern regarding the assessment and management of such abilities in this specific population, their recommendations as well as the tools they preferentially use in their practice.

Conclusion: This survey highlights the lack of guidelines for speech-therapy practice in patients with severe brain injury and DoC. Early and long-term assessment and management of both language and swallowing abilities should be improved, notably by providing (and/or adapting) new clinical tools.

Disclosure: Nothing to disclose.

EPO-447 | Hyperintense basal ganglia on T1-MRI in two patients with elevated serum manganese due to cirrhosis

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Background and Aims: Hepatic encephalopathy is a neuropsychiatric complication of acute or chronic liver disease with symptoms ranging from mild confusion to coma. The pathophysiology of hepatic encephalopathy is multifactorial, ammonia, manganese deposition and inflammation are thought to lead to astrocyte swelling and brain edema. Studies have shown that in patients with end-stage liver disease, increased serum manganese level causes manganese to accumulate in the basal ganglia.

Methods: Patient 1. A 68 -year -old female patient had a diagnosis of liver cirrhosis secondary to non- alcoholic steatohepatity and twice history of hepatic encephalopathy attacks. Neurological examination was unremarkable. The serum manganese level was high and the magnetic resonance images had T1 basal ganglion hyperintensity. Patient 2. A 65 -year -old male patient was detected amnesia, disorientation of time and space and psychomotor retardation. His serum manganese level was high and the magnetic resonance images had T1 basal ganglion hyperintensity. Liver cirrhosis was diagnosed after the investigations.

Results: Studies have shown a significant correlation between serum manganese levels and T1 basal ganglia hyperintensity seen on MRI, but no correlation between serum manganese and liver function or neurological findings has been demonstrated. Also, there is no correlation between T1 basal ganglia hyperintensity and neurological findings.

Conclusion: It would be useful to evaluate brain MRI and serum manganese levels in the hepatic encephalopathy clinic in patients with cirrhosis.

Disclosure: Nothing to disclose.

EPO-448 | Epileptic seizures in prolonged disorders of consciousness: Preliminary data of an Italian multicentre study

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Background and Aims: The occurrence of late-onset epileptic seizures (LES) and epileptiform abnormalities (EA) in prolonged Disorders of Consciousness (pDoC) was poorly and inconsistently reported across studies1. Our aim is to explore the LES/AE prevalence and their influence on consciousness recovery 3 months after admission to rehabilitation units (RUs) in pDoC.

Methods: This analysis was performed in the Italian multicentre PRABI study framework2 including only patients with a pDoC. At admission, the repeated Coma Recovery Scale-Revised-CRS-R and a standard electroencephalogram were performed3. The occurrence of LES was monitored during the RUs stay. The Disability Rating Scale-DRS, the Glasgow Outcome Scale Extended- GOSE and the CRS-R was performed at 3 months.

Results: One hundred eighty-six patients were enrolled (Table 1). At admission, patients presenting LES and/or EA were those with a higher Cumulative Illness Rating Severity Scale at admission ($p = 0.040$) and a higher Acute ES probability ($p = 0.008$). At 3 months, these patients reached lower scores of CRS-R ($p = 0.004$), DRS ($p < 0.001$), and less frequently a GOSE > 5 ($p = 0.03$)). The univariate and multivariate analyses showed the Minimally Conscious State instead of Unresponsive wakefulness syndrome, a lower time post onset, and the absence of LES during the RUs stay were associated with a higher probability to recover consciousness at 3 months (Table 3).

	Total sample	LES or EA at admission		
		No (64%)	Yes (36%)	p-value
Age	69 [21]	69 [24]	69 [19]	0.989
Sex (Female)	75 (40.3%)	42 (35.3%)	33 (49.3%)	0.062
Etiology				0.660
Traumatic	46 (24.7%)	29 (24.4%)	17 (25.4%)	
Anoxic	24 (12.9%)	15 (12.6%)	9 (13.4%)	
Vascular	109 (58.6%)	72 (60.5%)	37 (55.2%)	
Other	7 (3.8%)	3 (2.5%)	4 (6.0%)	
CIRS severity admission	0.77 [0.38]	**0.70 [0.38]**	**0.80 [0.53]**	**0.040**
CIRS comorbidity admission	2.0 [1.0]	2.0 [1.0]	2.0 [2.0]	0.088
TPO	41.5 [23]	40 [24]	45 [22]	0.536
Acute ES	23 (12.4%)	**9 (7.6%)**	**14 (20.9%)**	**0.008**
CRS-R (admission)	8 [7]	9 [7]	8 [6]	0.079
CRS-R (3 months)	15.5 [16]	**23 [13]**	**11.5 [17]**	**0.004**
DRS (3 months)	22 [6]	**20 [8]**	**24 [5]**	**<0.001**
GOSE≥5 (3 months)	12 (8.5%)	**11 (12.5%)**	**1 (1.9%)**	**0.030**

Legend: CIRS: Cumulative Illness Rating Scale; TPO: Time post-onset; ES: Epileptic Seizures; CRS-R: Coma Recovery Scale-Revised; DRS: Disability rating Scale; GOSE: Glasgow Outcome Scale Extended.

	B	E.S.	Wald	Sig.	Exp(B)	95%CI per Exp(B) Inf	Sup
Age	0.005	0.009	0.338	0.561	1.005	0.987	1.024
Sex	-0.252	0.306	0.678	0.410	0.777	0.427	1.416
Etiology (traumatic vs others)	-0.314	0.343	0.839	0.360	0.731	0.373	1.430
CRS-R admission	**0.294**	**0.050**	**34.450**	**<0.001**	**1.341**	**1.216**	**1.480**
MCS vs UWS	**1.920**	**0.343**	**31.379**	**<0.001**	**6.822**	**3.484**	**13.356**
TPO	**-0.017**	**0.008**	**4.498**	**0.034**	**0.983**	**0.967**	**0.999**
Acute ES	-0.266	0.455	0.340	0.560	0.767	0.314	1.872
LES	**-1.005**	**0.386**	**6.762**	**0.009**	**0.366**	**0.172**	**0.781**
EA (admission)	-0.292	0.373	0.611	0.434	0.747	0.359	1.552
Acute ES or LES or EA at admission	-0.534	0.306	3.041	0.081	0.586	0.322	1.068

Legend: CRS-R: Coma Recovery Scale-Revised; MCS: Minimally Conscious State; UWS: Unresponsive wakefulness syndrome; TPO: Time post-onset; ES: Epileptic Seizures; LES: Late-onset Epileptic seizures; EA: Epileptic Abnormalities; CIRS: Cumulative Illness Rat.

Model 1 R2=0.366	B	E.S.	Wald	Sig.	Exp(B)	95%CI per Exp(B) Inf	Sup
CRS-R score at admission	**0.301**	**0.052**	**33.641**	**0.000**	**1.352**	**1.221**	**1.497**
TPO	**-0.024**	**0.010**	**5.819**	**0.016**	**0.976**	**0.957**	**0.995**
LES	-0.648	0.437	2.197	0.138	0.523	0.222	1.232
Model 2 R2=0.297	B	E.S.	Wald	Sig.	Exp(B)	95%CI per Exp(B) Inf	Sup
MCS vs UWS	**1.966**	**0.355**	**30.588**	**0.000**	**7.140**	**3.558**	**14.329**
TPO	**-0.020**	**0.009**	**4.672**	**0.031**	**0.981**	**0.963**	**0.998**
LES	**-0.873**	**0.430**	**4.111**	**0.043**	**0.418**	**0.180**	**0.971**

Legend: CRS-R: Coma Recovery Scale-Revised; TPO: Time post-onset; LES: Late-onset Epileptic seizures; MCS: Minimally Conscious State; UWS: Unresponsive wakefulness syndrome.

Conclusion: The presence of late-onset epileptic seizures seems to negatively impact the short-term recovery of consciousness. References: 1 Lejeune, N et al. doi:10.1080/02699052.2021.1973104, 2 Hakiki, B. et al., 10.3389/358fneur.2022.711312, 3 Hirsh L. J. et al.,10.1097/WNP.0000000000000806

Disclosure: The authors report no disclosure.

EPO-449 | Prognostication after cardiac arrest: Which is more accurate EEG or ERPs?

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Background and Aims: Neurophysiological investigations (ERPs and EEG) occupy major place among the tools available for prognostication the patients resuscitated from CA (cardiac arrest). We tested the relationships between neurological outcome after CA (measured by GOS) and ERPs and EEG results measured in coma patient's state.
Methods: All 27 patients (17 men, 10 women, mean age 64 ± 15 years) were enrolled prospectively during the ICU admission after CA. Bedside EEG (standard 19/25 EEG channel system according to the 10-20 system) and ERPs – P3 (with patients own name as deviant stimulus) was recorded in the same day within 4-8 days of CA in unsedated patients who were still comatose during the examination. The resulting state was assessed between 30 - 64 days after arrest by GOS. The PPV, NPV, sensitivity and specificity of EEG (4 patterns) and ERPs – P3 own name (absence, presence) in relation to GOS were calculated.
Results: The presence of ERPs - P3 own name had a high specificity (81%) and sensitivity (67%) for GOS 4-5. Absence of P3 own name also had high specificity (67%) and sensitivity (81%) for GOS 1-2. EEG pattern burst suppression and low voltage pattern had high specificity (90%) but low sensitivity (43%) for GOS 1-2. The delta/theta EEG pattern had low sensitivity (33%) and specificity (33%) for GOS 1-2.
Conclusion: Therefore, ERPs – P3 own name appear to be more advantageous than EEG for prognostication of patients after CA.
Disclosure: Nothing to disclose.

EPO-450 | Quantum 123 pattern: A new quantum graph-based encephalopathy detection using EEG signals

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Background and Aims: The primary aim of our study is to explore the capability of machine learning in detecting encephalopathy through the analysis of electroencephalography (EEG) signals. To achieve this, we have introduced a novel quantum-inspired feature extractor and a self-organized feature engineering model.
Methods: In this investigation, we retrospectively gathered a substantial EEG signal dataset from Firat University Hospital. The dataset consists of two classes: (i) encephalopathy and (ii) no-findings/control. EEG signals were acquired from 54 participants using a multichannel EEG device and segmented into 15-second intervals. For automated encephalopathy detection, our proposed self-organized feature engineering model comprises four main phases: (1) Quantum 123 Pattern (Q123Pat) feature extraction, utilizing a graph resembling quantum circuits to select the most suitable feature extraction method based on the EEG signal structure; (2) feature selection with the neighborhood component analysis feature selector to identify the most informative features; (3) classification using k-nearest

neighbors and support vector machine classifiers; and (4) information fusion employing iterative majority voting and selecting the best outcome with a greedy algorithm. The Q123Pat-based self-organized model was applied to each EEG channel, and the results were used to generate a semantic cortex map.

Results: The proposed Q123Pat-based self-organized model achieved an impressive 97.96% classification accuracy, facilitating the identification of the most informative channels.

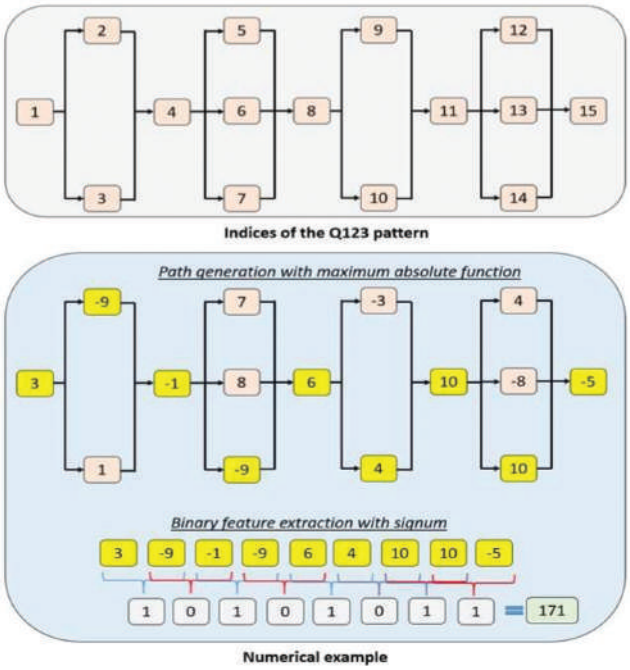

FIGURE 1 The proposed Q123 pattern. In this graph, there are 36 (=1×2×3×1×2×3) patterns, and the most suitable pattern has been selected using the maximum absolute function.

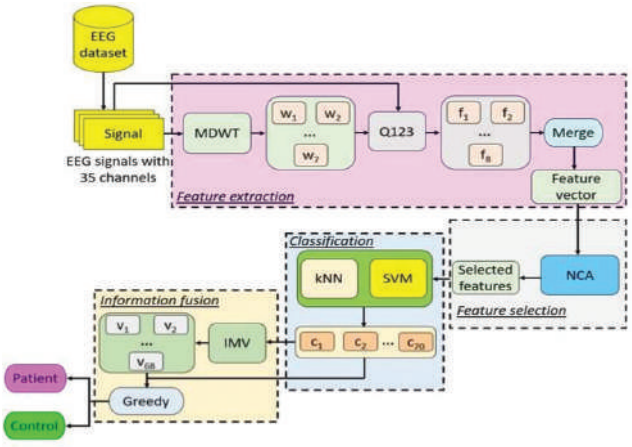

FIGURE 2 Graphical explanation of the proposed Q123-based model. Herein, MDWT: multilevel discrete wavelet transform, w: wavelet band, f: individual feature vector, NCA: neighborhood component analysis, kNN: k-nearest neighbors, SVM: support vector machine.

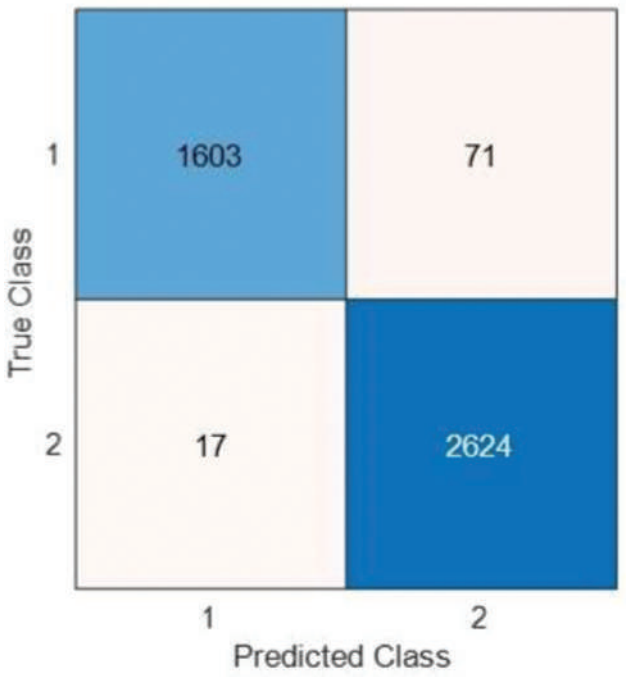

FIGURE 3 Confusion matrix of the final result. Herein, 1: Encephalopathy, 2: No-finding. Per this confusion matrix, the calculated classification performance metrics have been given follows. Accuracy: 97.96%, sensitivity: 95.76%, specificity: 99.36%, precision.

Conclusion: The computed classification performances unequivocally demonstrate the ability of machine learning models to detect encephalopathy using EEG signals. Furthermore, our model provides interpretable results about the cortex by generating a cortex map based on the classification performances of each channel.

Disclosure: Nothing to disclose.

EPO-451 | Exploring the neurophysiological effects of combined electrical and auditory stimulation in healthy subjects

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Background and Aims: Today, effective treatments for patients suffering from disorders of consciousness are lacking. Transcranial direct current stimulation (tDCS) and music have both shown promise in enhancing signs of consciousness. Given the potential for tDCS effects to be enhanced by complementary stimuli, this study aims to investigate its combination with music in a cohort of healthy participants at the cognitive and neurophysiological levels.

Methods: This randomized controlled double-blind crossover study involved four stimulation conditions: tDCS combined with music (tDCS/music) or white noise (tDCS/noise), and sham-tDCS with music (sham-tDCS/music) or white noise (sham-tDCS/noise), which were applied to 24 healthy human adults (<35 years old). Participants' performance (i.e., accuracy and time response) on Stroop and 3-back cognitive tests was measured before and after each condition. A 20-channel electroencephalogram explored the neurophysiological effects of the interventions.

Results: Cognitive performance (behavioral measures) and power spectral analyses revealed no significant differences between the interventions. A significant increase in global connectivity in the alpha band was found in post- compared to pre-intervention in music ($p=0.0026$) and tDCS/music ($p=0.0028$) conditions. The other conditions did not show any significant changes.

Conclusion: Overall, these findings suggest that a single tDCS session combined with music does not enhance cognitive functions in healthy subjects. However, music alone or combined with tDCS exhibited promise in increasing brain activity associated with cognitive performance. Further research, particularly involving multiple sessions of tDCS with or without music, is necessary to better understand the potential of these interventions, especially in patients with disorders of consciousness.

Disclosure: Nothing to disclose.

EPO-452 | A closed-loop EEG-tDCS approach to improve responsiveness of patients in minimally conscious state

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Background and Aims: Previous studies have reported mixed effects of transcranial direct current stimulation (tDCS) in patients in a minimally conscious state (MCS). Considering the potential impact of vigilance level on the effectiveness of stimulation, we aimed to compare the efficacy of closed-loop tDCS applied during high, low, and random levels of vigilance (based on online entropy measurements) in MCS patients.

Methods: In this double-blind randomized clinical trial, we aim to include 16 MCS patients. Each patient received three stimulation sessions (2mA for 20 minutes) over the left dorsolateral prefrontal cortex (DLPFC) at high, low, and random levels of vigilance, five days apart. Real-time analysis of spectral entropy was performed using a Starstim 20 EEG-tDCS closed-loop system which determined the triggering time of stimulation based on vigilance level. Patients were evaluated using the Coma Recovery Scale-Revised (CRS-R) before and after each session, together with a 15-minute EEG. Pre- and post-tDCS CRS-R scores were compared using Wilcoxon test.

Results: We included 13 MCS patients (mean age 48±18 years, 5 females). Median CRS-R score for high vigilance stimulation was 11 (8-15) before, and 12 (10-15.25) after stimulation ($p=0.037$). The median pre- and post-stimulation CRS-R scores were not significantly different for the low vigilance (11 [8-15] vs. 11 [8-16], $p=0.88$) and random vigilance groups (10 [8-15] vs. 11 [8-17], $p=0.33$).

Conclusion: These preliminary results suggest that stronger effects of tDCS over the left DLPFC in patients with MCS might be achieved if applied at high vigilance levels. This needs to be confirmed with the entire sample ($n=16$), where EEG data will also be analyzed.

Disclosure: MAN serves in the scientific advisory boards of Neuroelectrics and Precisis.

EPO-453 | Ketamine to treat disorders of consciousness: A feasibility study

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Background and Aims: Patients with post-comatose disorders of consciousness (DoC) have few treatment options, making the investigation for new ones fundamental. We present the results of a feasibility study using sub-anaesthetic doses of ketamine in DoC patients. Ketamine increases brain complexity, and this, according to several theories, should ameliorate DoC consciousness level.

Methods: We ran a double-blind, placebo-controlled, cross-over study (Figure 1) on 3 male patients with DoC (UWS, 32yo, TBI; MCS-, 50yo, subarachnoid haemorrhage; MCS+, 62yo, CO intoxication). We administered increasing concentration of ketamine or placebo intravenously (maximal concentration: 0.75 μg mL-1; steps of 0.15 μg mL-1) in two sessions within a week. Consciousness was assessed behaviourally using the Simplified Evaluation of CONsciousness Disorders (SECONDs). We tested spastic paresis with the Ashworth-Modified Scale (MAS) for two patients. Simultaneously, we recorded EEG (BrainVision, 128Ch) to measure whole-brain complexity with broadband Lempel-Ziv complexity (LZC).

Results: The UWS patient showed a response to a verbal command once during ketamine, which was not observed during placebo nor at baseline. All patients spent more time with eyes open. Spasticity decreased in all three patients after ketamine (Figure 2). No carry-over effects or adverse effects were observed. LZC increases during ketamine (Figure 3).

Conclusion: We demonstrated that ketamine can be safely administered to people with DoC, that it increases arousal and decreases spasticity. Other changes in behaviour should be investigated in a large-scale randomized controlled trial. Ketamine increases LZC in DoC, like what observed in healthy participants.

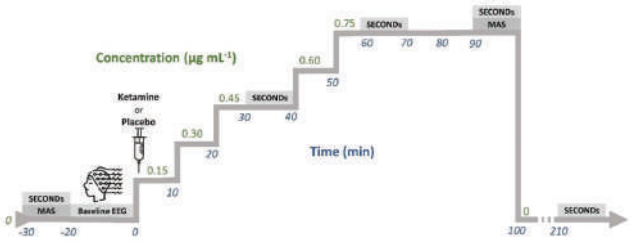

FIGURE 1 Protocol: Visual representation of one session. We assessed behavior via the SECONDs, and spastic paresis with the MAS. During the whole experiment, we recorded the brain activity using high-density EEG. The second session would take place with.

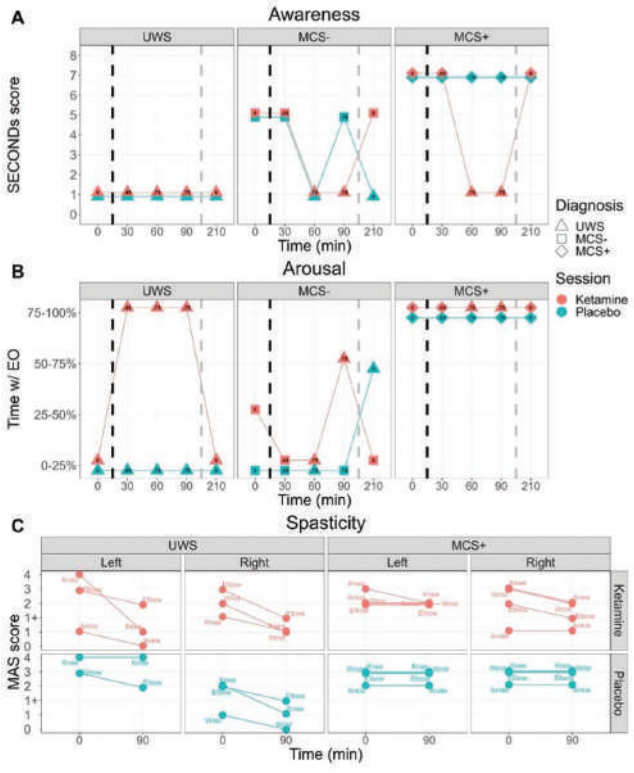

FIGURE 2 Behavioral results. A: SECONDs scores following infusion of ketamine and placebo. UWS scoring are represented as triangles, MCS- as squares, MCS+ as diamonds. For representational purposes, ketamine scores were increased by 0.1, and placebo ones.

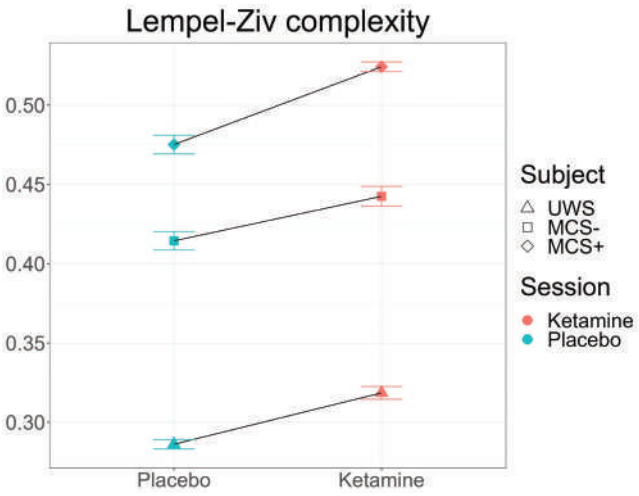

FIGURE 3 Brain Complexity: Distribution of brain complexity measured via whole-brain LZC shown for placebo and ketamine for each patient. Standard errors are calculated over electrodes.

Disclosure: VB has had financial relationships with Orion Pharma, Metronic, Elsevier, Edwards Medical, and Grunenthal. The other authors declare no conflict of interest.

EPO-454 | Reflex eye-opening response in brain death

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Background and Aims: The diagnostic criteria of brain death include unreactive coma with absent brainstem reflexes. Pain stimulation should not produce responses attributed to the cranial nerves.

Methods: We report the case of a brain-dead patient with bilateral, slow, partial eyelid opening driven by the autonomic sympathetic response to painful stimulation.

Results: A 41-year-old man was admitted to the ICU after a prolonged cardiorespiratory arrest due to a pulmonary thromboembolism. The neurological examination without sedation after 36 hours revealed a deep unreactive coma and absent brainstem reflexes. However, with bilateral painful nipple stimulation, the patient showed a slow bilateral, partial eyelid elevation, without pupillary size changes and a lack of any motor response. Brain-CT scan revealed extensive hypoxic-ischemic lesions, median nerve somatosensitive evoked potentials showed bilateral absence of thalamocortical responses and the EEG was isoelectric. The patient was diagnosed with brain death.

Conclusion: Eye-opening is determined by the combined action of voluntary and involuntary muscles, the eyelid elevator and the Muller's muscle respectively. The eyelid elevator is innervated by the third cranial nerve originating in the mesencephalon and so, its irrigation depends on the intracranial circulation. In contrast, Muller's

muscle is innervated by the sympathetic autonomic nervous system through the petrosal and viridian nerves originating in the superior cervical ganglion, which are irrigated by external carotid artery branches that do not depend on intracranial circulation. Therefore, slow eyelid elevation driven by Muller's muscle may occur in brain-dead patients due to a pain-induced activation of the sympathetic nervous system.

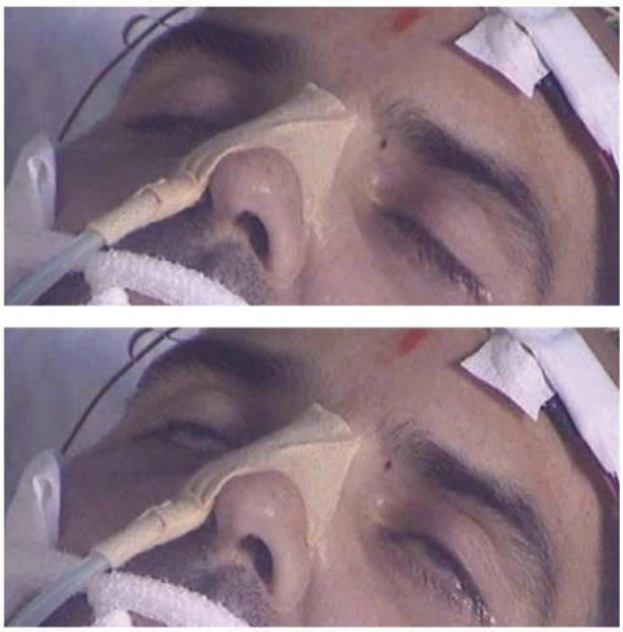
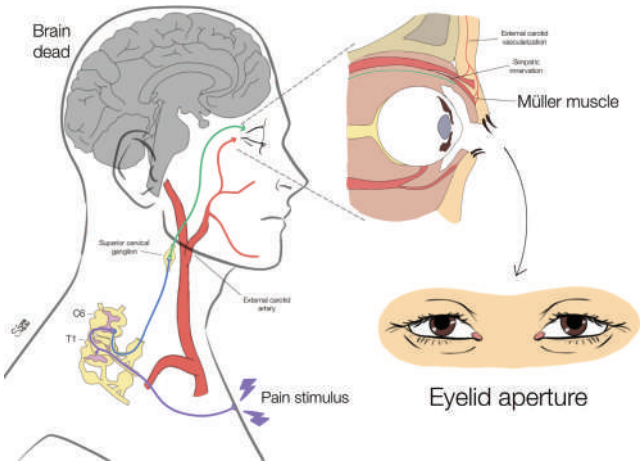


Image 1 and 2: Slow bilateral, partial eyelid elevation response to bilateral painful nipple stimulation.



Anatomy of the sympathetic pathway of Müller's muscle.

Disclosure: The authors have nothing to disclose.

EPO-455 | **Dynamic network analysis reveals lower temporal variability of functional connectivity at unconsciousness**

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Background and Aims: Severe Acquired Brain Injuries (sABI) may disrupt networks sustaining arousal and awareness, the two essential components of consciousness leading to atypical connectivity in such cortical/subcortical networks [1]. This study aims to use low-density EEG and its high temporal resolution to estimate the temporal variability of functional connectivity in prolonged Disorders of Consciousness (pDoC).

Methods: This analysis has been made in the framework of the PRABI study [2] including sABI patients in intensive rehabilitation unit. Consciousness was diagnosed with repetitive Coma Recovery Scale Revised assessments grouping patients between pDoC and emerged sABI patients. EEG was pre-processed following the PREP pipeline [3]. Debiased weighted Phase Lag Index was computed in the α, θ, and δ bands, at different connection (60%,70%,80%) and electrodes (6, 9, 15, and 19) densities. Burstiness, estimated via the coefficient of variation of the inter-contact times vector (i.e., temporal difference between two consecutive edges in a binarized adjacency matrix) was compared between groups (Mann-Whitney tests), Fig.1.

Results: Two-hundred seventeen sABI patients (median age of 62 years old [IQR = 17.6]; 79 (36.4%) females; 121 (46.4%) eMCS) were included (Tab.1). No significant differences were found for what concerns age, sex, and etiology between the two groups ($p > 0.05$). Burstiness was always found to be negative, leading to non-bursty TVGs. However, emerged patients showed larger periodic temporal

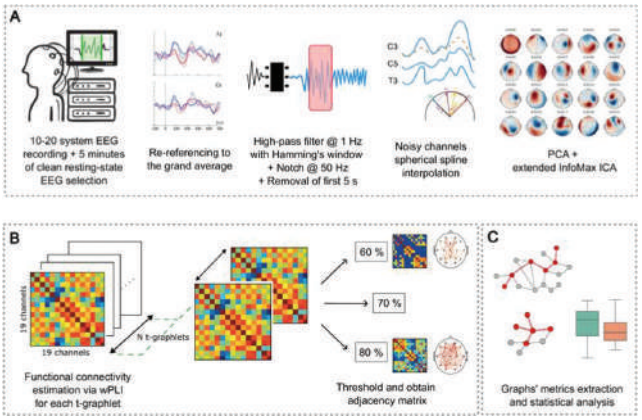

FIGURE 1 Work pipeline: (A) data collection and EEG preprocessing, (B) time-varying graphs (TVG) development and computation of adjacency matrixes (thresholding), (C) TVG metrics extraction and statistical comparison between pDoC and No-DoC.

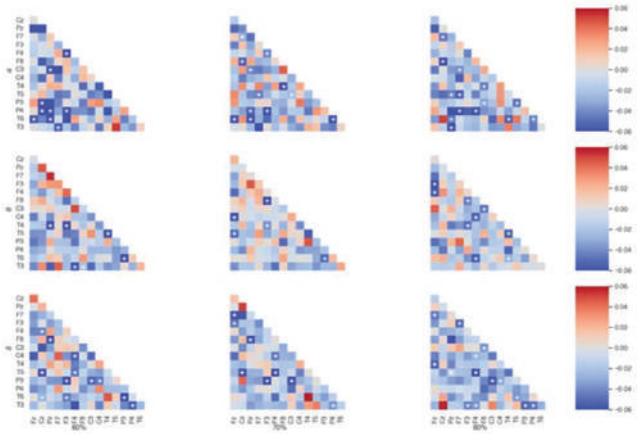

FIGURE 2 Difference in burstiness between the pDoC and the No-DoC patients for the 15-electrodes configuration. Each line refers to a bandwidth (α, θ, and δ) with significant differences ($p < 0.05$) marked with asterisks.

	sABI (N = 217)	Emerged (N = 121)	pDoC (N = 96)
Age, *years*	62 [17.6]	62 [17.2]	67 [18.1]
Gender, *females*	79 (36.4)	44 (36.4)	35 (36.5)
CRS-R, *points*	17 [6.9]	23 [2.0]	9.50 [4.7]
Etiology			
TBI	83 (38.2)	45 (37.2)	38 (36.9)
Anoxic	9 (4.1)	3 (2.5)	6 (6.2)
Ischemic	34 (15.7)	20 (16.5)	14 (6.5)
Hemorrhagic	81 (37.3)	46 (38.0)	35 (36.5)
Other etiologies	10 (4.6)	7 (5.8)	3 (3.1)
Affected area			
Right	42 (19.4)	24 (18.8)	18 (18.8)
Left	54 (24.9)	31 (25.6)	23 (24.0)
Bilateral	39 (18.8)	21 (17.4)	18 (18.8)
Subtentorial	33 (15.2)	23 (19.0)	10 (10.4)
DAI	13 (6.0)	6 (6.2)	7 (6.8)

TABLE 1 Population details. Data are presented as follows: numerical variables with median [interquartile range, in brackets], while categorical variables are reported as counts (percentages, in parenthesis).

connectivity pattern variability than pDoC (Fig.2), independently from the frequency band.

Conclusion: eMCS patients are confirmed to preserve at all frequencies a higher spatial connectivity patterns' irregularity than pDoC. Such capability calls for further investigations as a consciousness marker.

Disclosure: Nothing to disclose.

EPO-456 | CSF hydrodynamics in prolonged disorders of consciousness

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Background and Aims: Prolonged (i.e. >1 month) disorders of consciousness (PDOC) after brain injury is a major public health problem. Advances in intensive care allow patients to survive after brain injury, however, one third of patients do not regain consciousness. To date, no specific treatment has been shown to be effective in restoring consciousness. Brain imaging in PDOC patients often shows cerebral atrophy and ventriculomegaly, suggesting hydrocephalus due to impaired intracranial fluid circulation. Controversies remain about how to diagnose hydrocephalus in PDOC patients and whether to propose CSF diversion. We hypothesise that CSF hydrodynamics is relevant to better identify hydrocephalus in PDOC patients.

Methods: We retrospectively analysed 41 patients (26M/15W) with i) acute brain injury, ii) PDOC and iii) ventriculomegaly (i.e. Evan's ratio >0.3). These hydrocephalus-suspected PDOC patients were studied with a lumbar infusion test to measure CSF hydrodynamics using ICM+.

Results: Acute brain injury was related to: head trauma (17), subarachnoid haemorrhage (16), intracerebral haematoma (6), cardiopulmonary arrest (1), metabolic (1). The mean CSF outflow resistance (Rcsf) was increased (i.e. ≥12 mmHg/ml/min, see Table 1). 20 patients (49%) had increased Rcsf (i.e. ≥12 mmHg/ml/min above the dashed line) several months (up to 40 months) after brain injury (see Figure 1).

	Age (year)	Time between brain injury and insufion test (month)	ICP baseline (mmHg)	Pulsatility baseline (mmHg)	ICP plateau (mmHg)	Pulsatility plateau (mmHg)	Rcsf (mmHg/ml/min)
Mean	**53,7**	**12,8**	**9,59**	**0,65**	**25,26**	**2,34**	**16,26**
Median	**57,4**	**6,9**	**9,48**	**0,47**	**25,82**	**1,57**	**11,88**
SD	17,5	18,7	3,34	0,54	11,21	1,80	13,34
Min	17,2	0,8	2,66	0,04	1,65	0,11	0,80
Max	79,4	104,9	19,26	2,25	55,05	7,58	50,00

TABLE 1

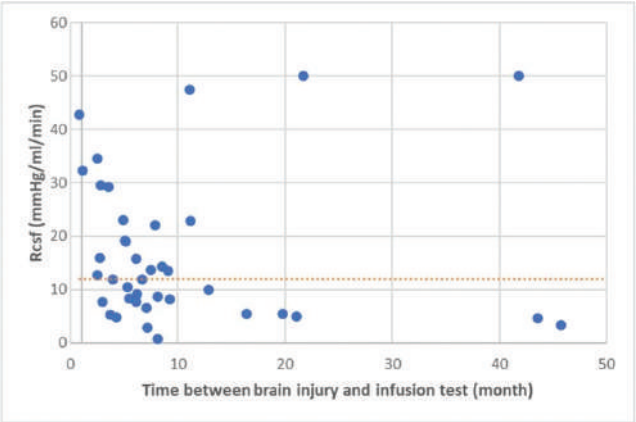

FIGURE 1

Conclusion: Half of the patients with PDOC and ventriculomegaly exhibit altered CSF hydrodynamics. Rcsf seems to be a useful metric that should be implemented in the management algorithm of PDOC patient to better advocate for CSF diversion when hydrocephalus is suspected, even months or years after brain injury.
Disclosure: None.

Infectious diseases

EPO-457 | Meningitis infection: Epidemiological analysis of the disease outcome among Brazilian regions

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[1]*Assis Gurgacz University Center – FAG, Cascavel, Paraná, Brazil;* [2]*São Lucas Hospital Center, Cascavel, Paraná, Brazil*

Background and Aims: A large number of pathogens cause Meningitis infection (MI), which accounts for more than 200,000 deaths and 2.5 million cases globally in 2019. After introducing the Meningococcal C vaccine into the national vaccination program (1975), Brazil's incidence and mortality rate has decreased over the years.
Methods: Data were available on the National Notifiable Diseases Information System (SINAN). The different outcomes and male/female rate (M/F) among Brazilian regions were searched from 2012-2023.
Results: MI total cases from 2012-2023 was 158,111, 58.83% male (M/F rate = 1.42). The Southeast region leads with 53.72% (*n* = 84,953), followed by the South, Northeast, North, and Central-West (% = 4.85). The M/F rate medium value was 1.45, highest in the Northeast (M/F = 1.5) and lowest in the Southeast (M/F = 1.93). The discharge rate was 0.85 (*n* = 134,633). Death by MI rate was 0.10 (*n* = 16,116), with an increase observed in the North (% = 15.64) and Central-West regions (% = 13.02), followed by the Northeast, Southeast, and South. Death with MI but by other causes rate was 0.04 (*n* = 7,362), of which 75.4% was distributed in the Southeast (% = 44.41) and South (% = 30.99).

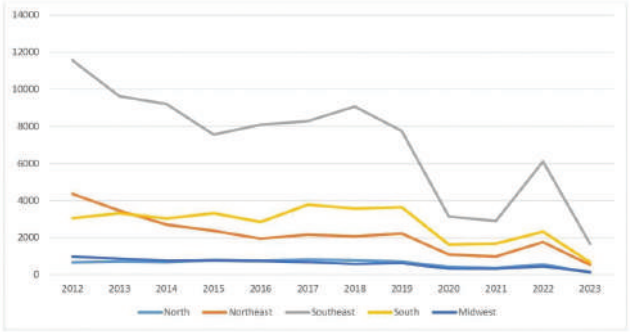

FIGURE 1 Total cases per year between regions.

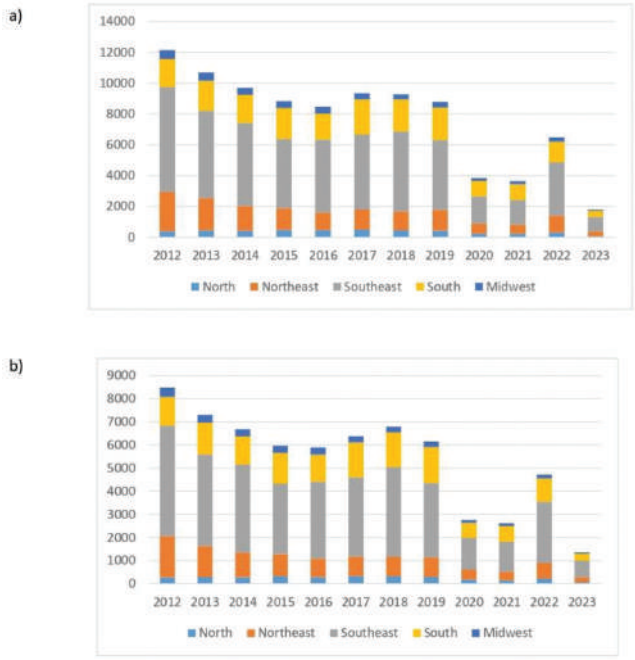

FIGURE 2 (a) Male cases between regions; (b) Female cases between regions.

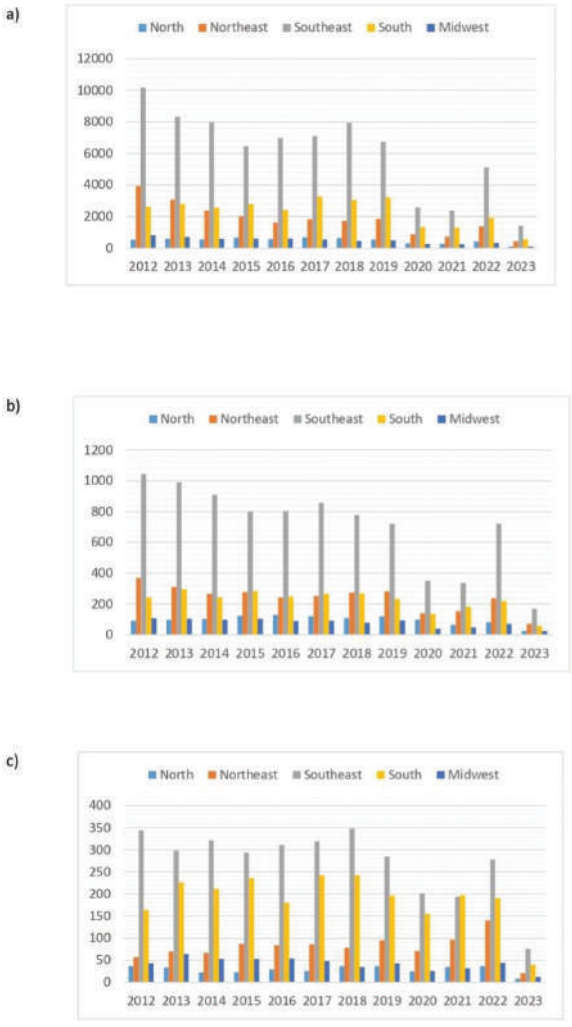

FIGURE 3 (a) Discharge cases between regions; (b) Death by MI between regions; (c) Death by other causes between regions.

Conclusion: A decrease in cases was observed in all regions. Whereas its largest population, the highest prevalence of cases and discharge rate was in the Southeast but it was not the same in the mortality rate, led by the neediest one, North.
Disclosure: Nothing to disclose.

EPO-458 | Dengue-induced acute cerebellitis

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[1]Assis Gurgacz University Center – FAG, Cascavel, Paraná, Brazil; [2]São Lucas Hospital Center, Cascavel, Paraná, Brazil

Background and Aims: The incidence of dengue has grown exponentially in recent years and has been associated with several neurological complications, with cerebellar involvement being one of the rarest of them, with few cases found in the literature.
Methods: We present an atypical case, occurring in the south of Brazil, of dengue fever, associated with cerebellar syndrome in a 10-year-old child.
Results: A 10-year-old child admitted due to a change in gait 3 days ago. Medical history of herpetic encephalitis associated with gait alteration, fever, and emesis 1 month ago, treated with IV Acyclovir for 15 days and with total clinical improvement. No comorbidities, medication, or allergies and no family history of neurological diseases. 15 days later, presented with fever and emesis, and after 2 days, gait alterations. Clinically stable on first assessment, complaining of mild headache and gait ataxia. No acute alterations on neuroaxis MRI and CSF. NS1 (Dengue) laboratory test was positive. After a neuropediatrician consult was suggested a post-infectious cerebellitis induced by the Dengue virus. After 5 days of Dexamethasone, analgesics, and antiemetics treatment, the patient had progressive improvement in both clinical and motor conditions and was discharged for follow-up care at an outpatient clinic.

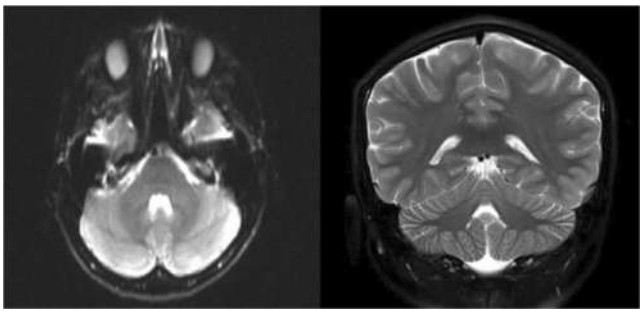

FIGURE 1 Magnetic resonance showing brain parenchyma with usual morphology and signal intensity for the age group.

Conclusion: Cerebellar syndrome in children after or during dengue fever is a rare case, being one of the first cases to be reported in the literature until this report was produced. Therefore, it is important to recognize atypical clinical conditions so that the best measures can be taken early without leaving consequences.
Disclosure: Nothing to disclose.

EPO-459 | Unveiling the Mimic: Progressive multifocal leukoencephalopathy presenting as acute ischemic stroke – A dual case report

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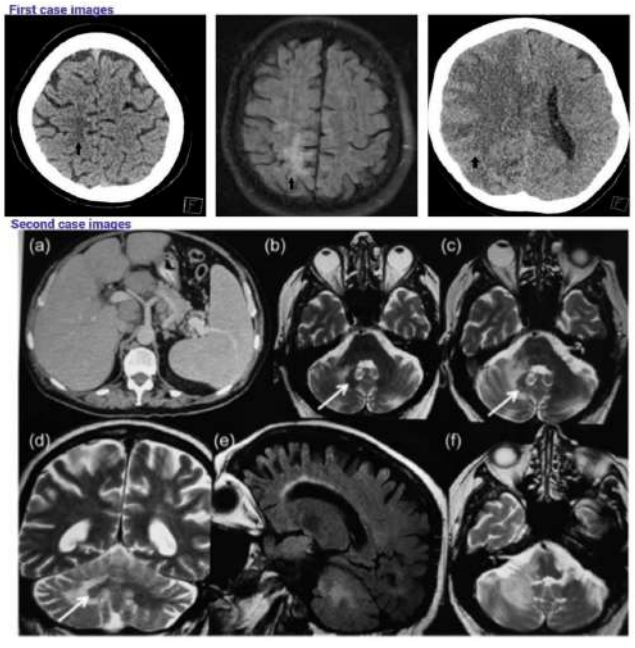
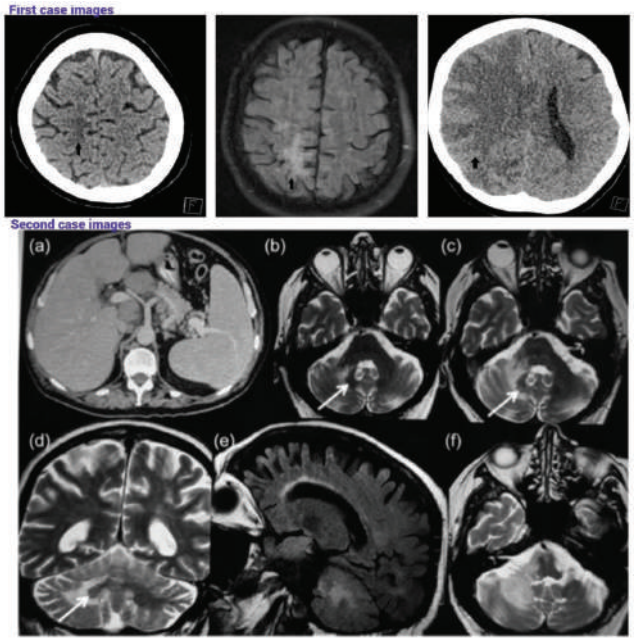
[1]Nottingham University Hospitals; [2]Sandwell and West Birmingham Hospitals; [3]Torbay and South Devon NHS Foundation Trust

Background and Aims: Progressive multifocal leukoencephalopathy, a demyelinating infectious disorder of the CNS, is seen in immunocompromised individuals with a history of AIDS, hematologic malignancies, or immunosuppressive drug therapy. We present two cases where patients initially diagnosed with acute ischemic stroke were later identified to have PML, as their symptoms mimicked stroke manifestations.
Methods: 1- A 56-year-old woman experienced left-sided numbness escalating to severe weakness in three days. Admission revealed an NIHSS score of 8 and imaging displayed enhancement along the right parietal gyrus. Whole-body CT raised suspicion of haematological malignancy. Inconclusive tumour marker assessment prompted a PML investigation, confirmed by JC Virus. Unexpectedly, HAART initiation led to IRIS, complicating the clinical course. Despite interventions, rapid deterioration ensued with IRIS-related complications. 2-A 79 a patient who present a stroke unit with symptoms that were consistent initially with a posterior circulation stroke. Prior chemotherapy with Rituximab, for a lymphoma, had predisposed the patient to infection with the JC virus.



CT scans and MRI findings



CT scans and MRI findings

Results: PML's subacute presentation can mimic a stroke, emphasizing the importance of understanding its background and potential complications, particularly in patients with HIV/AIDS or other immunocompromised conditions. Delayed diagnosis due to the absence of known immunocompromised status underscores the need for heightened awareness and early initiation of antiretroviral therapy.
Conclusion: In the complex realm of diagnoses, PML often masquerades as a stroke look-alike, demanding nuanced consideration in individuals with HIV/AIDS. Clinicians need a keen eye to distinguish between the two. Those undergoing Rituximab treatment should be made aware of the risk of opportunistic infections, including PML.
Disclosure: Nothing to disclose.

EPO-460 | Acute motor sensory axonal neuropathy as a presentation of Lyme disease

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Department of Neurology, Unidade Local Saude Arrabida EPE, Setubal, Portugal

Background and Aims: Neuroborreliosis affects up to 15% of patients with Lyme disease and usually presents as lymphocytic meningitis, facial nerve palsy or radiculoneuritis. Alternative neurological manifestations are possible, so this diagnosis may easily be overlooked.
Methods: A 36-year-old male, previously healthy, presented to the emergency room with abdominal pain radiating to the back, followed by speech changes, incoordination, diplopia, dysphagia, lower limb weakness, loss of sphincter control and respiratory failure needing invasive ventilatory support. Initial neurological assessment additionally revealed left peripheral facial palsy, flaccid areflexic quadriparesis (lower limbs MRC score 2, upper limbs score 4) and decreased pinprick on both feet. CSF analysis revealed 160 cells/μL (95% lymphocytes) and protein level of 268 mg/dL. Atypical Guillain-Barré Syndrome was assumed, and the patient was started on IV immunoglobulin therapy. Upon reassessment, on day 4 of IVIg, he was clinically worsened, quadriplegic and with ophthalmoparesis. Ceftriaxone was started empirically and then plasmapheresis, without clinical improvement.
Results: Laboratory workup revealed positive Borrelia burgdorferi antibodies in serum and CSF (IgG and IgM); EMG showed severe sensorimotor axonal polyneuropathy and spinal MRI presented with cauda equina roots and dorsal radicular emergences thickening and T1 enhancement following gadolinium administration. Neuroborreliosis was assumed and the patient completed a 4-week course of IV Ceftriaxone, with slow clinical improvement since.
Conclusion: Neuroborreliosis presents as a highly heterogenous, easily overlooked clinical entity, especially upon atypical manifestations. Awareness regarding this condition's many possible presentations is needed to prevent misdiagnoses and start prompt effective treatment, thus minimizing negative outcomes.
Disclosure: Nothing to disclose.

EPO-461 | Double doughnut over and above dengue dystonia

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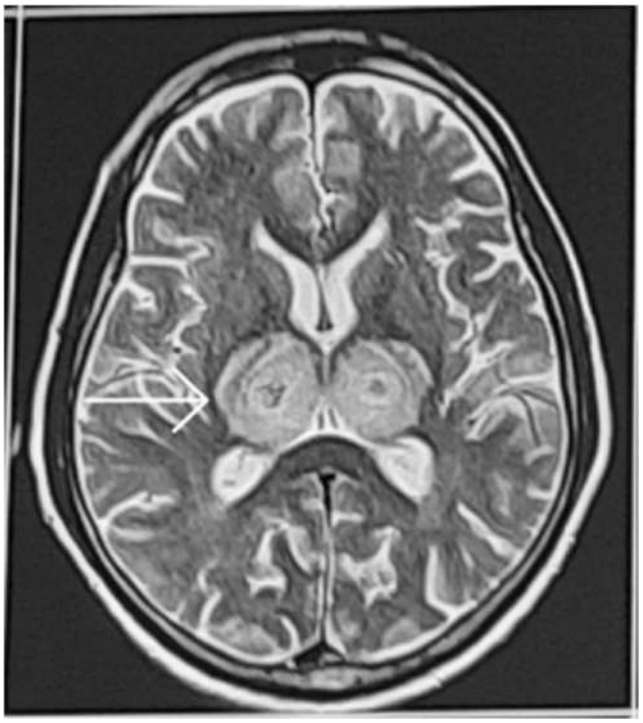
Background and Aims: The clinical manifestations of dengue range from mild febrile illness to severe dengue shock syndrome and dengue hemorrhagic fever. Recently, its various neurological manifestations have been reported. Dystonia as early presentation in dengue is very rare.
Methods: None.
Results: Results: A 60-year-old male presented with high-grade fever for 5 days associated with arthralgias and myalgias. For the past 3 days, the patient developed gradual deterioration in the sensorium such that he could not communicate although he could comprehend and was lethargic on presentation. On day 4 of admission, he was observed to have developed generalized dystonia. His fever profile was positive for NS1 the (Non-structural protein 1) antigen of Dengue virus. He had raised levels of aspartate aminotransferase alanine aminotransferase and thrombocytopenia. His magnetic resonance imaging showed bilateral thalamic involvement with a “double doughnut sign”. His CSF analysis showed 5 cells with protein 92 mg/dl and sugar 60 mg/dl and opening pressure of 8 cm of water. It was negative for gram stain, CBNAAT for mycobacterium tuberculosis, cryptococcal antigen, and other neurotropic viruses. He was managed with benzodiazepines, tetrabenazine, and pulse steroid therapy. Gradually his dystonia subsided and he could articulate and was discharged in stable condition.



MRI Brain: shows T2 weighted MRI image with double doughnut sign with bilateral thalamic involvement.

Conclusion: A high index of suspicion especially in highly endemic countries required to suspect dengue dystonia. Double doughnut sign in MRI brain will help in identification. Morbidity in dengue dystonia can be reduced by early and prompt treatment.
Disclosure: Nothing to disclose.

EPO-462 | Challenging diagnosis of Creutzfeldt-Jakob disease with atypical early symptoms: A case series

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Background and Aims: Creutzfeldt-Jakob disease (CJD) is a rapidly progressing neurodegenerative disorder whose classical presentation is characterized by the association of dementia, myoclonus and motor impairment in variable degree. However, atypical and non-specific presentations have been described, making the early clinical diagnosis difficult and challenging.
Methods: We present three cases admitted to a tertiary hospital after seeking emergency care for rapidly developing neurological abnormalities.
Results: The first patient experienced a decline in bilateral visual sharpness (Heidenhain variant). The second case showcased alien limb phenomenon, rigidity, cortical sensory loss and apraxia in the left upper limb, resembling a corticobasal syndrome. The third patient, upon examination, displayed restricted coordinated gaze, particularly in the vertical direction, accompanied by short steps and disrupted turns in walking, indicating a progressive supranuclear palsy. Diagnostic tests revealed: EEG findings consistent with paroxysmal focal activity, MRI with diffusion restriction in cortical áreas and fluid analysis showed positive 14-3-3 protein. These findings support the diagnosis of CJD.
Conclusion: The early manifestations of CJD with unusual symptoms are not extensively covered in scientific literature. Consequently, reviewing and underscoring the significance of promptly identifying these cases is essential for appropriate patient care. Results from additional tests may offer guidance in considering this prionic pathology.
Disclosure: Nothing to disclose.

EPO-463 | An atypical presentation of progressive multifocal leukoencephalopathy in a "well controlled" HIV patient

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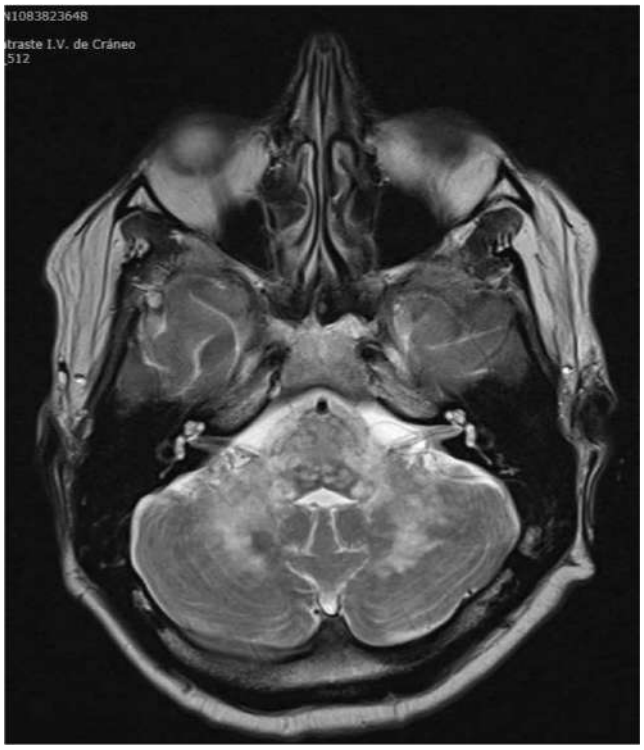
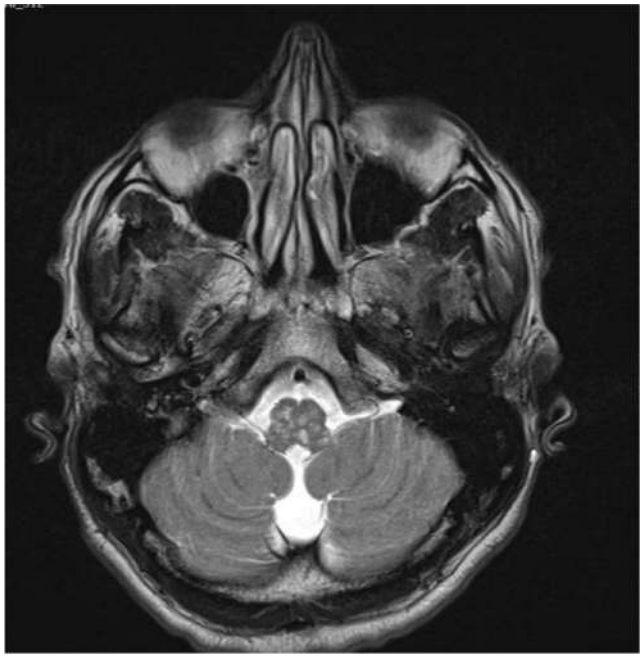
Background and Aims: Progressive Multifocal Leukoencephalopathy (PML) is a demyelinating disease of the central nervous system caused by JC virus, typically seen in inmunocompromised patients. It affects white matter, giving magnetic resonance (MRI) images predominantly involving supratentorial matter. We report a case of PML in an HIV-patient under combination antiretroviral therapy (cART) with an atypical clinical and radiologic presentation, with predominance involvement of the brainstem and cerebellum.
Methods: Case report.
Results: A 46-years old male, HIV well controlled with cART for years, consulted for dizziness, nausea, gait and speech disturbance, that were developed progressively in the last 5 months. Neurological exploration revealed nystagmus, mild paresis of the left hand, right hypoesthesia, exalted reflexes predominantly on the left with Babinski's sign, as well as bilateral dysmetria and gait ataxia. Brain MRI showed T2-hyperintense and T1-hypointense lesions in cerebellar peduncles and pons, with no restricted-diffusion; and a small similar lesion in frontal lobes. Blood tests were normal, CD4 count was preserved, but an inverted CD4/CD8 ratio was observed; and CSF-fluid showed hyperproteinorrachia, with Flow-cytometry, cultures and typical virus PCRs negative. The patient experienced a rapidly progressive course, dying two months later. In the necropsy was diagnosed as PML, with lesions involving brainstem, cerebellum, spinal cord, and supratentorial regions.



T2 hyperintense lesions involving pons and both cerebellar penduncles.



The described lesions extends to the medulla.

Conclusion: Although PML is usually seen in severe immunocompromised patients affecting the supratentorial regions, the clinical and radiological presentation can be unusual sometimes. Furthermore, the presence of an inverted CD4/CD8 ratio is noteworthy as a possible marker of immune dysfunction in an apparently well-controlled HIV patient.

Disclosure: The authors do not have any disclosure of interests.

EPO-464 | Headaches and fever: Disseminated cryptococcosis in an immunocompetent patient: A case report

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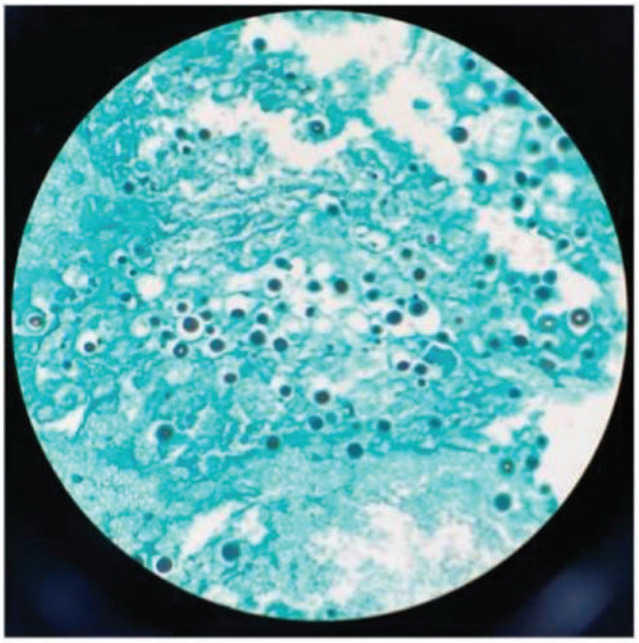
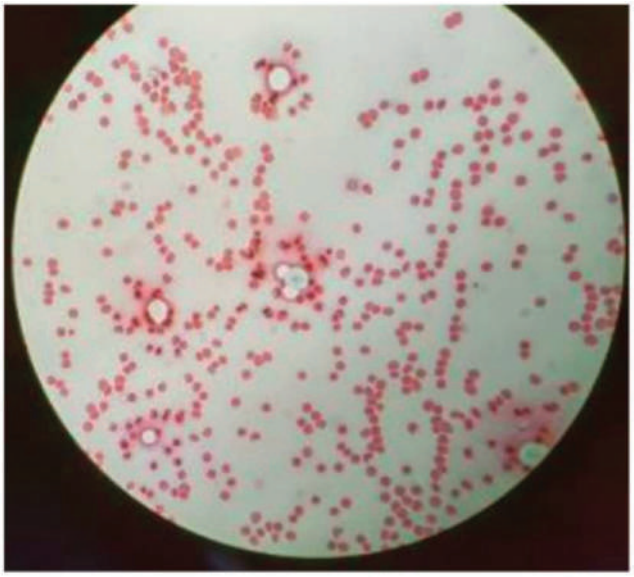
Background and Aims: Cryptococcosis is an opportunistic infection caused by encapsulated yeast Cryptococcus. The two species commonly infecting humans are C. neoformans and C. gatii and it commonly affects immunocompromised patients. Disseminated infection in immunocompetent is rare. In this study, we present a case of disseminated cryptococcus with lung and cerebral involvement in an immunocompetent patient.

Methods: The case is about a 28-year-old female from Marikina City who presented with fever, headaches and cough. Patient was initially treated as a case of Pulmonary Tuberculosis, but no improvement was noted during hospital stay. Further workup was done including chest and cranial CT scans which guided for definitive diagnosis. Cultures of CSF and lung mass biopsy were also done which revealed positive for cryptococcus infection. Patient was also tested for other immunodeficiency tests including HIV where she tested negative. Since the patient was confirmed with cryptococcus infection, patient was treated with systemic anti-fungal medications. Patient improved symptomatically and significantly hence was then discharged and advised follow up at OPD.

Results: Not applicable.



Grams stain of CSF for analysis.



H&E stain of CSF for analysis.

Conclusion: In this study, we present a rare case of disseminated cryptococcosis with lung and cerebral involvement in an apparent immunocompetent patient. Early recognition of the disease and treatment leads to better outcomes.
Disclosure: Nothing to disclose.

EPO-465 | Non-compressive myelopathy complicating acute community-acquired bacterial meningitis

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Background and Aims: Bacterial meningitis is a severe disease with high rates of complications and unfavourable outcome. Complications involving the spinal cord, such as myelitis or infarction, are infrequently reported.
Methods: Cases of non-compressive myelopathy were identified when included in a nationwide cohort study of adults with community-acquired bacterial meningitis in the Netherlands. Outcome was scored at discharge using the Glasgow Outcome Scale and a score of 1-4 was considered an unfavourable outcome. Subsequently, we reviewed the literature on non-compressive myelopathy as a complication of bacterial meningitis.
Results: Non-compressive myelopathy was reported in 5 of 3047 episodes of community-acquired bacterial meningitis (0.16%). The median age of these patients was 56 years (range 17-72). Causative pathogens were Streptococcus pneumoniae in 2, and Neisseria meningitidis, Haemophilus influenzae and Streptococcus agalactiae each in 1. Paresis of legs ($n=4$) or arms and legs ($n=1$) were the presenting symptoms during admission, occurring after a median duration of 13 days after admission (range 2-28). Spinal MRI showed T2-weighted abnormalities of the spinal cord in all patients. Outcome was unfavourable in all patients despite additional corticosteroid treatment in two. The literature review yielded 14 cases of non-compressive myelopathy in bacterial meningitis patients. The most reported causative pathogen was Neisseria meningitidis in 8 patients. Outcome was unfavourable in 12 of 14 of reported patients in literature (86%).
Conclusion: Non-compressive myelopathy is an uncommon but severe complication of bacterial meningitis. It is not constrained to one specific pathogen and is associated with high rates of unfavourable outcome.
Disclosure: Nothing to disclose.

EPO-466 | Even the smallest of organisms could change the course of life

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Background and Aims: Lumbosacral adhesive arachnoiditis is a serious and rare condition with multiple aetiologies, as it may be related to postoperative changes, inflammatory conditions, or secondary to previous infectious disease. In general, it presents as a polyradiculopathy, being uncommon its presentation as cauda equina syndrome, an entity that is associated with significant disability.
Methods: Case report.
Results: Female, 35 years old. History of fully recovered cytomegalovirus (CMV)-related polyradiculopathy secondary to stage 3 HIV the previous year. Progressive worsening of motor function started 2 months before hospital admission. Neurological examination: paresis of the left lower limb (2/5) and bilateral areflexia in lower extremities, without other alterations. Laboratory tests: CD4+ 226 cells/mm^3, undetectable HIV viral load. CSF: proteinorraquia, mild leukocytorrhea and oligoclonal bands with identical distribution in CSF and serum. Negative infectious and autoimmune panels. MRI of the lumbar spine showed thinning of the L1-2 nerve roots, hyperintensity and thickening of the L2 cauda equina and downward, narrow and adherent nerve roots that resembled an image of an empty L3-S1 thecal sac. The neurophysiological study evidenced active motor denervation, eminently of the distal left lower limb. The study was completed with a biopsy that confirmed focal fibrosis and chronic inflammation of the ligamentum flavum and the lumbar thecal sac.

Conclusion: The final diagnosis was postinfectious adhesive arachnoiditis. To our knowledge, this is the first case described following CMV-related polyradiculopathy. Diagnosis is based on clinical presentation, neuroimaging and biopsy. Pharmacological (e.g. immunoglobulins) and surgical treatments have been described, without clear benefit. Intensive physical rehabilitation is recommended.
Disclosure: Nothing to disclose.

EPO-467 | Neurovascular complications in patients with central nervous system infections

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Background and Aims: Neurovascular complications are common with nervous system infections, such as cerebral vascular insult, venous thrombosis, vasculitis and aneurysm formation. The aim of our study was to analyze clinical features of a group of patients with central nervous system (CNS) infection who developed neurovascular complication.
Methods: Prospective observational study collecting all the patients with CNS infections from a tertiary neurology center between 2007 and 2023 was made. Study sample consists of 265 patients with CNS infections and 42 (15.8%) with cerebrovascular complications.
Results: The mean age was 47.21 years, 57.1% men. The most common infections were meningitis (28.6%) and meningoencephalitis (42.9%). Neurovascular complications presented as: ischemic stroke (78.8%), multiple lesions (48%), cerebral vasculitis (30.9%), and cerebral venous thrombosis (31%). The most frequent predisposing factors were bronchopneumonia (52.4%), parameningeal infection (19.0%), and septicemia (16.7%). The pathogens were identified in 35.7% case, mostly cocci species. When compared to patients without neurovascular complications those with stroke presented higher blood sedimentation rate (41.00 vs 32.65mm/h, $p = 0.017$), CSF protein (4.17 g/l vs 1.62, $p < 0.05$), motor deficit (50% vs. 36.3%), seizures (9.5% vs 5.8%), and in-hospital mortality (28.6% vs 22.4%) but fever was less common (66.7% vs 76.7%). Logistic regression model shows that the presence of bronchopneumonia, smoking and pregnancy can predict the occurrence of the neurovascular complication with good probability (B = 1.67o, df = 1, $p = 0.00$, Exp B = 5.310).
Conclusion: Neurovascular complications in CNS infections affect mostly young patients and are more likely to manifest focal neurologic deficit and higher mortality rates.
Disclosure: Nothing to disclose.

EPO-468 | Exploring the neurological outcomes of Nipah virus: A narrative review of state from 1998 to 2023

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Background and Aims: Nipah virus (NiV) is an emerging zoonotic RNA virus causing severe respiratory and acute febrile encephalitic illness in humans. Pteropus fruit bats serve as reservoirs for the virus which led to human spread via consumption of food contaminated with bat secretion, contact with infected animals and human-to-human spread. This study aims to access the early, late-onset and long-term neurological outcomes of Nipah virus infection among affected individuals.
Methods: Articles from existing literature in PubMed, Medline and Google Scholar databases investigating Nipah virus-associated neurological outcomes were examined. 79 relevant articles were screened for this study using predefined inclusion and exclusion criteria.
Results: NiV infection in humans produces an encephalitic syndrome ranging from headache and pyrexia to brain stem abnormalities; and reduced level of consciousness (55% in Malaysia, 90% in Bangladesh) including tonic-clonic convulsions and segmental myoclonus. Fever with altered sensorium was the most common presentation in Siliguri, India (97%) and Bangladesh (90%), with a case fatality ratio (CFR) of about 40-100% in recent outbreaks. Residual neurological deficits were seen in 10-15% of survivors an average of 8 months after primary encephalitis. Brain MRI showed small discrete hyperintense lesions, widespread in the cortex, subcortical and deep white matter from microinfarctions due to underlying vasculitis of the cerebral blood vessels, seen in acute infections and patchy confluent hyperintense cortical lesions seen in relapsing NiV infections.
Conclusion: Proper education on good hygiene is important to prevent reemergence of the infection in affected areas. Effective neurorehabilitation is also necessary to reduce long-term neurological complications in NiV survivors.
Disclosure: Nothing to disclose.

EPO-469 | Diagnostic deadlock: A case of disseminated tuberculosis with neuroleptospirosis

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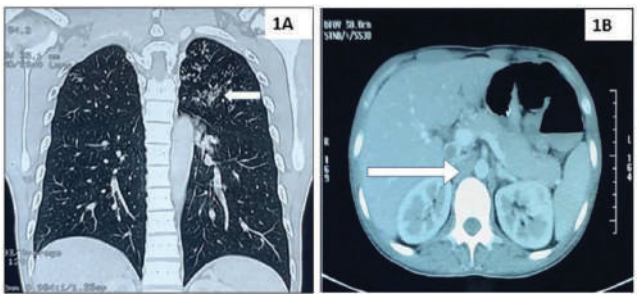
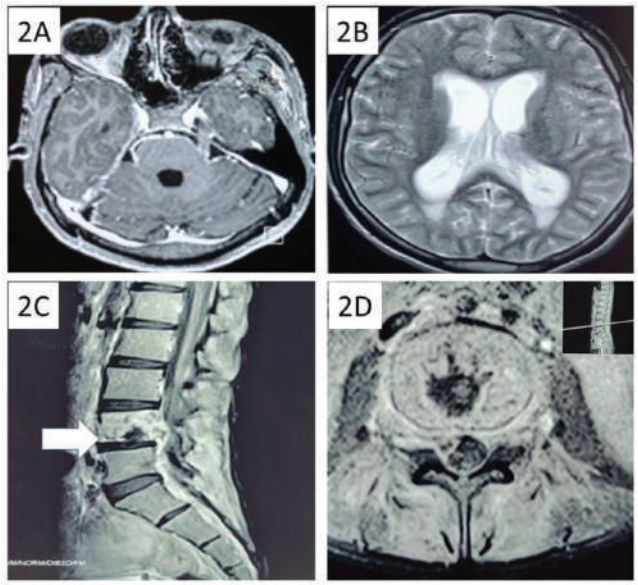
Background and Aims: Neuroleptospirosis may present with features like altered sensorium, GTCS, headache, and focal neurological deficit which are shared with other common neuro-infection like tuberculous meningitis. Coexistence of these two illnesses has not been yet reported.

Methods: A 19-years old male presented with high-grade fever, headache and vomiting for 4 days and right focal to bilateral tonic clonic seizures and altered sensorium for 3 days. On examination, he was febrile (101°F) and GCS score was E2V1M5. There was no papilledema and focal motor deficit. Signs of meningeal irritation were present.
Results: Serum IgM leptospira titre was high [26.4 Units (<9 units)] and creatine kinase [493 U/L (24-195 U/L)] was elevated. Patient received doxycycline with antiepileptic drugs (levetiracetam and lacosamide) for two weeks. There was improvement in sensorium and subsidence of seizure; however, high-grade fever persisted. CECT thorax, abdomen and pelvis revealed disseminated tuberculosis (Figure 1). MRI brain and spine with contrast revealed diffuse leptomeningeal enhancement and basal exudates with hydrocephalus and lytic lesion at L4 vertebrae suggestive of tuberculous meningitis and Pott's spine (Figure 2). Four drugs antitubercular therapy was started. Ventriculoperitoneal (VP) shunting was done. GCS improved to E3V3M5. However, he developed refractory status epilepticus, followed by ventilator associated pneumonia, septic shock and succumbed to the illness.



Contrast enhanced computed tomography of chest and abdomen revealing multiple centrilobular nodules in upper lobe of left lung parenchyma (1A) and multiple enlarged mediastinal, bilateral hilar and intraabdominal (arrow) lymph nodes (1B) suggestive of dis.



Contrast magnetic resonance imaging of brain showing leptomeningeal enhancement and basal exudates on T1W (2A) and hydrocephalus on T2W with periventricular ooze (2B) suggestive of tuberculous meningitis. Contrast magnetic resonance imaging of lumbosacral.

Conclusion: This is the first case report of coexistent neuroleptospirosis and disseminated tuberculosis creating diagnostic dilemma. One should revise his/her own diagnosis and work up plan once the anticipated therapeutic response is inadequate.
Disclosure: Nothing to disclose.

EPO-470 | Linking the unseen: Marchiafava-Bignami disease and tuberculous meningo-myelitis

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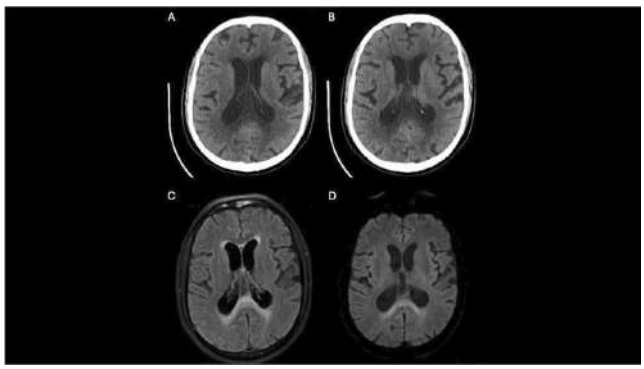
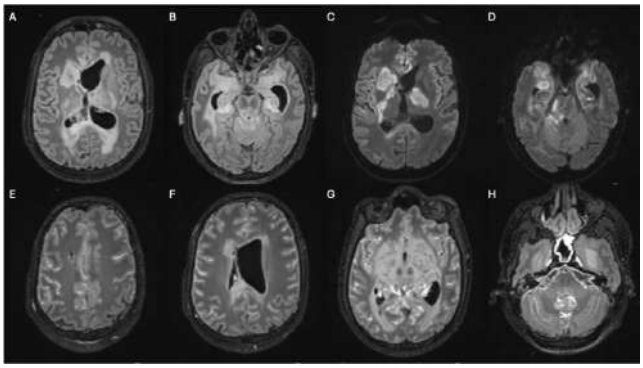
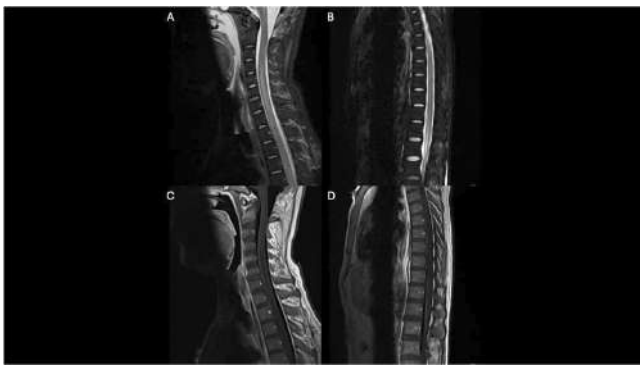
Background and Aims: This work reports the first-ever described case of tuberculous meningo-myelitis (TBMM) associated with Marchiafava-Bignami disease (MBD), complicated by communicating hydrocephalus, multiple acute ischemic strokes, and diabetes insipidus.
Methods: We present the case of a 33-year-old homeless Afghan male with a significant history of alcohol abuse, who presented to the Emergency Room with a recent-onset fever and a sudden and rapidly progressive impaired level of consciousness. Clinical manifestations included focal neurological deficits such as left motor facial and brachial sparing, flaccid paraplegia, sphincter release, and jerking movements.
Results: CT-scan and MRI revealed severe generalized cerebral atrophy with symmetrical hypodensity of the hemispheric white matter and splenium of the corpus callosum. EEG showed widespread slowing without epileptiform abnormalities. Laboratory results indicated electrolyte imbalances and diluted urine. Supportive therapy and vitaminic supplementation were initiated. A second CT-scan revealed communicating hydrocephalus with initial decompensation, necessitating immediate external ventricular drain insertion. CSF analysis showed lymphocytosis, elevated protein levels, decreased glucose levels, and positive cultures for Mycobacterium tuberculosis. A



CT scan: Splenium hypodensity in corpus callosum, suggestive of Marchiafava-Bignami; mild age-related ventricular and cerebral sulci enlargement (A,B). MRI FLAIR: Signal hyperintensity in splenium, supporting suspected Marchiafava-Bignami diagnosis (C,D).



MRI FLAIR: Hydrocephalus, periventricular hyperintensity (A). Mesencephalic and interpeduncular cistern hyperintensity suggests leptomeningitis (B). DWI: acute ischemia (C,D). Contrast-enhanced FLAIR: diffuse leptomeningeal enhancement (E,F,G,H).



MRI sagittal STIR: Hyperintensity in the spinal cord from C4 to C7 (A) and into the upper thoracic tract (B). Post-contrast T1-weighted sequences: Subtle enhancement along spinal cord margins (C,D). Findings suggest suspected myelitis.

second MRI with gadolinium unveiled multiple acute ischemic strokes and diffuse meningeal enhancement and a cervical-dorsal lesion consistent with TBMM. Despite antituberculous chemotherapy, the patient's condition deteriorated, culminating in coma and death.
Conclusion: Establishing a clear link between TBMM and MBD remains challenging. Speculation suggests a potential nutritional imbalance induced by TBMM's high metabolic demand in a multi-system disease, resembling a toxic-like state that can precipitate MBD. Both conditions require a high level of suspicion and prompt empiric treatment initiation in patients with behavioral and socioeconomic risk factors.
Disclosure: Nothing to disclose.

EPO-471 | Horner syndrome besides the obvious – *Pantoea* spp. as a rare cause of cervical spinal epidural abscess

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Background and Aims: Cervical spinal epidural abscess (CSEA) is an uncommon disease, associated with significant morbidity. Diagnosis can be elusive, especially if the classic triad of back pain, fever, and neurological deficit is not present. Horner syndrome (HS) is a rare but possible presentation. MRI with gadolinium is crucial for swift diagnosis and timely initiation of antimicrobial therapy. We present a case linked to the rare Pantoea spp, a group of plant pathogens that can cause human disease.
Methods: Case report.
Results: 53-year-old male, without relevant past medical history, was admitted to the ER after the acute onset of right eye ptosis and gait unsteadiness after osteopathic manipulation for neck and shoulder pain. Physical examination showed marked cervical neck tenderness. Neurological examination revealed a right HS and mild ataxia of the right leg. Brain CT angiography and cervical spine CT scans were normal. Markedly increased inflammatory markers in the workup prompted a lumbar puncture. CSF analysis revealed pleocytosis and hyperproteinorrachia. Empirical ceftriaxone IV 2g q12h was initiated. Spine MRI revealed septic arthritis at C7-D1 with an associated CSEA. Subsequent blood culture identified Pantoea spp, sensitive to ceftriaxone. After six weeks of treatment, there was clinical and radiological improvement.
Conclusion: We report an uncommon presentation of a rare entity caused by a very rare pathogen. This case is also unique because there was no direct inoculation or haematogenous spread, and the few cases of infection reported in the literature were on pediatric or immunocompromised adults. A prompt diagnosis and treatment is needed to achieve a good outcome.
Disclosure: Nothing to disclose.

Neuroimmunology 3

EPO-472 | Plasma proteomics and autoantibody screening: A tool for patient stratification and monitoring CIDP treatment responses

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[2]*Takeda Development Center Americas, Inc., Cambridge, MA, USA;*
[3]*Biognosys AG, Schlieren, Zürich, Switzerland*

Background and Aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an inflammatory neuropathy with heterogeneous presentation. Precise diagnosis and patient-tailored treatment decisions are hindered by lack of unbiased, quantifiable molecular markers. Although aberrant immune cell-mediated responses and circulating autoantibodies may accompany CIDP, underlying pathomechanisms remain elusive. We investigated correlation of clinically defined disease states with changes in plasma homeostasis in patients receiving immunoglobulin/placebo during remission versus relapse.
Methods: Plasma samples from patients with CIDP receiving hyaluronidase-facilitated subcutaneous immunoglobulin 10% (fSCIG 10%) or placebo during ADVANCE-CIDP 1 (NCT02549170) were analysed. Proteomic analysis (data-independent acquisition liquid

chromatography-mass spectrometry and Olink®) compared longitudinal samples from patients experiencing remission/relapse. A novel multiplex in-solution method to simultaneously detect autoantibodies against 32 CIDP-relevant antigens was also developed, potentially alleviating current technical hurdles associated with autoantibody detection in CIDP.

Results: For >1500 plasma proteins, concentration profiles differed significantly in patients with CIDP versus healthy controls. Identified CIDP profiles emphasized natural killer- and B-cell-mediated immune pathway involvement. When comparing remitting and relapsing patients, differences in profiles involved in extracellular matrix homeostasis, microtubule organization, tight junction assembly, and cytokine production were observed. fSCIG 10% progressively lowered proinflammatory cytokine levels versus placebo. Autoantibody profiling uncovered a CIDP signature for evaluation in larger cohorts.

Conclusion: Versus healthy controls, pronounced plasma protein dynamics were identified in patients with CIDP, providing a broad base for biomarker discovery. Combining plasma proteomics and autoantibody screening may identify unbiased, quantifiable biomarkers for patient stratification and/or monitoring pharmacodynamics following high-dose immunoglobulin administration. Study/writing support funders: Takeda Development Center Americas, Inc./Takeda Pharmaceuticals International AG.

Disclosure: AMC, IB, BG*: employees of Baxalta Innovations GmbH, a Takeda Company; IB: Takeda shareholder; MJC-D, LS: employees of Takeda Development Center Americas, Inc., and Takeda shareholders; JV: employee of Biognosys AG. *At the time of the study.

EPO-473 | The wide spectrum of Anti-Hu Paraneoplastic Neurological Syndromes (PNS): Case-series and review of the literature

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Background and Aims: PNS are autoimmune disorders arising from immune response to tumor antigens and they may precede cancer diagnosis for years. Anti-Hu neuronal autoantibodies are related to a wide and heterogeneous range of both Central and Peripheral Nervous System presentations.

Methods: We present four cases of Anti-Hu PNS, along with a systematic review of the literature. We searched MEDLINE for Anti-Hu case-series or case-reports, initially identifying 588 articles. Finally, 181 articles were included.

Results: Our case-series consists of 4 patients (1 Female, Mean Age 69 years). Two patients presented with Subacute Sensory Neuronopathy (SSN) and pronounced autonomic involvement, one patient with Limbic Encephalitis (LE) and one with Encephalomyelitis. Three patients had a concomitant small-cell lung cancer (SCLC), diagnosed after the PNS in two of them. Two patients died after 1 and 11 months, respectively. In our review, we found 1424 anti-Hu cases (Mean age: 63 years, 42% Women). The most common presentations were SSN (49%), LE (16%) and Encephalomyelitis (15%). In 1193 (84%) patients, a neoplasm (most commonly SCLC-84%) was identified and in 79% of them, PNS preceded cancer diagnosis. Immunosuppression along with neoplasm treatment were the preferable approaches in 52% and 51% of patients, respectively. 660 (55%) patients died during follow-up (Mean time to death: 13 months).

Conclusion: Anti-Hu PNS are rare but potentially treatable. They should always be included in the differential diagnosis of patients with compatible neurological syndromes, even without history of cancer. Thorough investigation to identify and treat an underlying neoplasm along with immunosuppressive agents may improve prognosis of these patients.

Disclosure: Nothing to disclose.

EPO-474 | Neurofilament light chain: The importance of plasma biomarkers in therapeutic decision-making in multiple sclerosis

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Background and Aims: Relapsing remitting Multiple Sclerosis (RRMS) is a subtype of MS, an autoimmune chronic inflammatory neurodegenerative disease. During the last decades MS has been remarkably impacted by the advances in knowledge on the pathophysiology, new therapeutic targets, early diagnosis criteria and monitoring of treatment response. Disease follow-up biomarkers as Neurofilament Light Chain (NfL) are not yet available in most locations, but since non-invasive techniques as SiMoA technique have been used to monitor progression and therapeutic response in RRMS, therapeutic decision making has been reviewed.

Methods: In this prospective study, SiMoA technique was used to assess NfL levels in RRMS classified as EDA, NEDA, naïve and patients that switched from first line therapy to moderate-high efficacy DMD.

Results: Sixty-six RRMS patients and 24 age-matched health controls were included. In EDA group, NfL mean level was 30.25 pg/mL, and 6.65 pg/mL for NEDA patients. Among patients without DMD and under first line therapy, NfL mean level were 13.98 pg/mL and 12.94 pg/mL, respectively. After therapy switch, or under moderate-high DMD, NfL levels significantly decreased (6.96 pg/mL; $p < 0.05$), similar to NEDA patients and healthy control (6.7 pg/mL).

Conclusion: The significant difference in NfL levels before and after moderate-high efficacy DMD showed the impact of new drugs in both efficacy and control of NFL levels. The role of NFL can contribute on treatment management, especially in the monitoring of the therapeutic failure beyond the usual outcomes as clinical relapsing and new lesions in MRI, aiming to early impact on the course of MS disability.

Disclosure: Nothing to disclose.

EPO-475 | Immune checkpoint inhibitor-related cerebellar toxicity and comparison with paraneoplastic cerebellar ataxia

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Background and Aims: Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy, and the association with immune-related adverse events (irAEs) is well-established. Our aim was (i) to characterize ICI-related cerebellar toxicity; (ii) to compare ICI-related cerebellar toxicity to paraneoplastic cerebellar ataxia (PCA).
Methods: Systematic review of the literature following PRISMA guidelines, with the addition of 8 original cases. We included adult patients developing new-onset, isolated or predominant cerebellar dysfunction within 12 months from the last ICI infusion. Such cases were compared with a consecutive cohort of patients with PCA.
Results: Thirty-five patients were included (males: 25/35 (71%), median age: 65 [range: 20-82]). The most frequent tumour was non-small cell lung cancer (12/35, 34%). Anti-PD1 were adopted in most cases (19/35, 54%). Symptoms developed a median of 11 weeks (range: 0.1-82) after ICI initiation; "isolated cerebellar ataxia" (gait and/or limb and/or trunk ataxia) prevailed at disease peak (13/35, 37%). Antibody positivity was detected in 15/31 patients tested (48%). Cerebrospinal fluid was inflammatory in 26/30 (87%). Magnetic resonance imaging showed cerebellar hyperintensities in 8/35 (23%). Immune-modulating therapy was applied in 33/35 cases (94%), and most patients showed neurological improvement with residual disability (17/35, 49%). When compared with PCA ($n = 15$), the ICI group was significantly associated with NSCLC, isolated ataxia, and a better neurological outcome.
Conclusion: We provided a characterization of ICI-related cerebellar toxicity. Compared to PCA, differences exist in terms of tumour association, clinical features, and outcome. Clinical presentation-antibody-tumor triad in the ICI group poorly reflects the typical associations of paraneoplastic disorders.
Disclosure: Nothing to disclose.

EPO-476 | Abstract withdrawn

EPO-477 | Novel approaches for immune-mediated chronic intestinal pseudo-obstruction: A case series

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Background and Aims: Neurologic autoimmune gastrointestinal dysmotility (nAGID) represents a significant contributor to gastrointestinal motility disorders, often leading to chronic intestinal pseudo-obstruction (CIPO). The response to immunotherapy varies based on the specific autoimmune disorder. Our goal is to describe the treatment responses of various drugs in 3 patients with CIPO.
Methods: Three consecutive cases diagnosed at a referral center for CIPO during 2023 are described. We collected baseline characteristics, clinical symptoms, radiologic tests, and histopathologic examination. The clinical and radiological response to treatment was used to measure outcome.
Results: All 3 patients had severe CIPO, refractory to previous treatments. Two patients underwent a full-thickness intestinal biopsy that detected lymphocytic myenteric ganglionitis. The first patient was a 35-year-old-male with myasthenia gravis associated to thymoma, who developed a nAGID without any serological marker of autoimmunity. He received vedolizumab with improvement of his digestive symptoms and nutritional status. The second patient was an 18 year old woman who had a non-paraneoplastic anti-Hu associated nAGID. She achieved clinical remission after rituximab. The third patient was a 60-year-old woman, with small cell lung cancer, who developed a paraneoplastic anti-Hu associated nAGID. She received cyclophosphamide, but did not improve and eventually died.
Conclusion: Our findings underscore the potential efficacy of rituximab and vedolizumab in the management of neurologic autoimmune gastrointestinal dysmotility with chronic intestinal pseudo-obstruction, particularly in refractory cases. Although a larger sample is needed, these interventions should be considered valuable options in the therapeutic landscape for such patients.
Disclosure: Nothing to disclose.

EPO-478 | Single fiber EMG in the diagnostic workup of diplopia and ptosis

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Background and Aims: Diplopia and ptosis are common neuro-ophthalmologic signs. Yet identifying the specific aetiology can be challenging due to the different possible causes. In this prospective study, we evaluated the reliability of the stimulated single fiber electromyography (SFEMG) in supporting the diagnosis of myasthenia gravis (MG) presenting with diplopia and ptosis.

Methods: We included 80 patients who presented with diplopia ($n=34$), ptosis ($n=16$), or both ($n=30$), and underwent SFEMG. Patients received a comprehensive diagnostic workup involving detailed history investigation, physical examination, orbital and brain imaging, thyroid function, antibody screening, orthoptic evaluation, ice pack test (when applicable) and repetitive nerve stimulation test (RNS).

Results: SFEMG yielded positive results in 29 of 80 (36.3%) patients of the cohort. Among the patients diagnosed with MG ($n=35$), SFEMG showed a sensitivity of 71.4% (95% CI: 0.55 – 0.84) and specificity of 91.1% (95% CI: 0.79 – 0.96) with a positive predictive value of 86.2% (95% CI: 0.69 – 0.95) and a negative predictive value of 80.3% (95% CI: 0.68 – 0.89). Notably, SFEMG was positive in 6 seronegative MG cases and in 14 cases with negative RNS. In the non-MG group (45/80 patients), SFEMG was negative in the majority (41 patients, 91.1%) of cases, further supporting its value in ruling out MG. A relevant proportion (21/45) of these cases remained undiagnosed.

Conclusion: Our findings suggest that SFEMG is a valuable tool in the diagnostic workup of diplopia and ptosis and in the differential diagnosis of MG, especially in seronegative MG cases and in those with negative RNS results.

Disclosure: Nothing to disclose.

EPO-479 | Difference between high-dose and moderate-dose vitamin D supplement in an animal model of progressive multiple sclerosis

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Background and Aims: Although many studies have found correlations between low vitamin D (VD) serum levels and the onset/progression of Multiple Sclerosis (MS), negative effects of VD supplementation are also reported. Uncritical intake of excessively high VD doses can lead to hypercalcemia and kidney damage. However, little is known about high dose effects on the central nervous system in neuroimmunological diseases. We developed an animal model that represents the cellular characteristics of progressive MS very well. In previous experiments we detected positive effects of moderate doses of VD in terms of alleviating brain pathology.

Methods: This work investigates whether high-dose VD (400IU/day; VD++) leads to histopathological differences compared to moderate doses (400IU/week; VD+) in our animal model. For this purpose, female rats ($n=20$) received VD (Fresenius-Kabi, Graz, Austria) accordingly from age 3 weeks on and underwent the standard procedure of our animal model (Ücal et al., 2017). Tissue was harvested on peak disease, and immunohistochemical evaluation was performed.

Results: Overall, there was no significant difference detectable between VD+ and VD++ with respect to preservation of myelin structures. However, microglial activation was significantly increased in the VD++ group on day 15 ($p=0.003$) and 30 ($p=0.002$). Furthermore, our preliminary data showed a lower number of apoptotic cells in the VD++ group, but at the same time increased neuronal cell loss.

Conclusion: We found no significant difference between VD+ and VD++ doses in preventing myelin damage but an increased microglial activation and neuronal loss in the VD++ group. Our data highlight the need for medically controlled VD supplementation.

Disclosure: This study was partially funded by Fresenius-Kabi (to Hochmeister S).

EPO-480 | Clinical impact of high dose corticosteroids on hospitalisations and complications in patients with Myasthenia Gravis

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Background and Aims: Oral corticosteroids (OCS) are medications for controlling symptoms in patients with Myasthenia Gravis (MG). While long-term use of high dose OCS is associated with serious side effects, the real-world clinical impact of high-dose OCS in patients with MG is not well understood.

Methods: A retrospective cohort study was performed using JMDC, a Japanese claims database. Patients with newly diagnosed MG were identified by standard disease codes and the first diagnosis date of MG was defined as the index date. Patients were stratified into two groups by OCS dose level (high OCS ≥7.5 mg/day; low OCS < 7.5mg/day). Patient characteristics, treatment patterns, long-term hospitalization (≥10 days), and clinical complications were compared between the two groups.

Results: We identified total 2,107 patients with a diagnosis of MG, 576 of whom were on OCS (high OCS, $n=210$; low OCS, $n=366$) during the follow-up period. There were no obvious differences in baseline comorbidities between high and low OCS groups. Intravenous immunoglobulin therapy was more frequent in the high OCS group versus the low OCS group (1.72 vs 1.30 courses/year). A significant increase in long-term hospitalization was observed in the high OCS group versus the low OCS group (odds ratio; 1.832, $p=0.007$). The

incidence of new complications such as diabetes, fracture or osteoporosis, neuropsychiatric disease, and sepsis was significantly higher with high OCS versus low OCS ($p=0.0015$, 0.0000, 0.0001 and 0.0022, respectively).

Conclusion: Use of high-dose OCS in patients with MG was associated with adverse outcomes including increased rates of long-term hospitalizations and clinical complications.

Disclosure: This study was funded by Alexion Pharma GK of which NN, TY and TY are employees. MW and TK are employees of AstraZeneca.

EPO-481 | Bio-markers profile in different types of encephalitis: Evidences from cerebrospinal fluid analyses

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Background and Aims: Encephalitis is defined by the presence of brain inflammation. This study was conducted to determine whether neuroinflammation, neuronal and neuroaxonal injury biomarkers could help to differentiate encephalitis and to improve diagnostic approach.

Methods: In this observational multicenter study, adult inpatients, with diagnosis of encephalitis were recruited. Clinical and laboratory features, inclusive of CSF inflammatory (IL-1β, IL-6, Il-8, TNF- α, CXCL-13), neuronal (NfL, p-Tau, aβ40, aβ42) and glial (GFAP, sTREM-2, YKL-40) damage biomarkers, were compared among the 4 groups through ANOVA and k2 test, were appropriate. Post-hoc analyses were performed using Bonferroni correction at $p=0.05$.

Results: One-hundred-fifty-eight encephalitis patients, namely 45 immune-mediated, 38 infectious, 69 not otherwise specified encephalitis (ENOS) and 63 HC entered the study. CSF cell count and protein levels were higher in the infectious group, compared to IE and ENOS. Infectious encephalitis showed higher inflammation parameters (IL-6, IL-8, TNF-α,) compared to HC and ENOS patients; whereas the chemokine CXCL13 was significant higher in both infectious ($p=0.012$) and immune-mediated ($p=0.013$) groups. Glial damage biomarkers were higher in the three different types of encephalitis compared to HC, excepted for sTREM-2, which showed higher values in both infectious ($p<0.001$) and immune-mediated ($p=0.004$) groups, compared to ENOS and HC.

Conclusion: This study indicates a different signature of encephalitis based on different etiologies. Inflammatory alteration was prominent in infectious encephalitis, whereas the B-cell–attracting CXCL13 was overexpressed in both infectious and immune-mediated patients, as for axonal damage biomarkers. Further studies are warranted to confirm and improve the diagnostic value of these biomarkers.

Disclosure: Nothing to disclose.

EPO-482 | Evaluating the effect of efgartigimod in myasthenia gravis crisis

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Background and Aims: In myasthenia gravis (MG) crisis, plasma exchange and immunoglobulin infusion are confirmed effective treatment options, but plasma exchange may not always be available in time, and the response rate to immunoglobulin is not always satisfactory. This study aims to investigate whether the addition of efgartigimod gain benefits for patients with MG crisis.

Methods: We enrolled MG crisis patients who were followed for one year in the NICU and were categorized into two groups: the traditional immunotherapy group and the additional efgartigimod treatment group. The efgartigimod treatment group received a regimen of 20mg/kg, administered on the first and fifth day. The primary endpoints were the duration of mechanical ventilation and the time of discharge.

Results: 19 patients were recruited. The median age at MG onset was 40.89 years. Plasma exchange was performed in 9/19 (47.3%) cases and intravenous immunoglobulin was performed in 15/19 (78.9%) cases. Six patients in the efgartigimod group had shorter hospital stays (16.8 ±8.7 days vs. 27.41 ±21.33 days, $p=0.03$) and mechanical ventilation durations (17.0 ±12.71 days vs. 18.25 ±15.17 days) compared to 13 patients in the conventional treatment group. Additionally, in the efgartigimod group, 66.7% of patients showed a 50% reduction in ADL score from baseline, compared to 38.46% in the conventional treatment group.

Conclusion: The efgartigimod group shows shorter hospital stays and mechanical ventilation durations and the potential to improve muscle weakness in the short term. The trend suggests that efgartigimod could potentially offer advantages in managing the MG crisis.

Disclosure: Nothing to disclose.

EPO-483 | Efgartigimod therapies in N-methyl-D-aspartate receptor encephalitis

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Background and Aims: N-methyl-D-aspartate receptor (NMDAR) encephalitis is the most common subtype of autoimmune encephalitis. Patients with NMDAR encephalitis develop an intrathecal immune response against NMDARs with antibodies. The therapeutic response to immunotherapy is often delayed and some patients develop complex neurologic and/or neuropsychiatric syndromes with prolonged course.
Methods: Efgartigimod, a human IgG1 antibody Fc fragment engineered to reduce pathogenic IgG autoantibody levels, was used in 5 patients with NMDAR encephalitis. The mean length of stay in these patients was more than 6 months before the use of efgartigimod.
Results: The patients had all used high-dose methylprednisolone, immunoglobulin, and rituximab, but they had not improved. Four of 5 patients showed a significant improvement in symptoms within a week after the use of efgartigimod. At the 3-month follow-up, they continued to improve without the addition of other medication.
Conclusion: Efgartigimod showed improvement in patient with NMDAR encephalitis with prolonged course.
Disclosure: Our study suggests that efgartigimod may have some potential in the treatment of long-standing autoimmune encephalitis.

EPO-484 | The therapeutic effect of efgartigimod in autoimmune encephalitis

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Background and Aims: In some cases of autoimmune encephalitis, patients may not respond to first-line treatments or may experience intolerable side effects of high-dose steroids or certain immunosuppressive agents, thereby limiting available treatment options. This study explores the therapeutic potential of efgartigimod, a fully humanized FcRn antagonist approved for generalized myasthenia gravis, for the treatment of anti-LGI1 encephalitis.
Methods: Two patients diagnosed with anti-LGI1 encephalitis were enrolled, who presenting seizures, cognitive impairment, and psychiatric disorders. Initial treatments with high-dose steroids and intravenous immunoglobulin showed no significant improvement. Efgartigimod was administered at 10mg/kg once a week for four doses.
Results: In the first 1-2 weeks of efgartigimod treatment, both patients exhibited notable alleviation of clinical symptoms. Antibody titers decreased, and no severe adverse reactions were observed. A 30-day follow-up indicated stable symptoms.
Conclusion: This study is the first to document the application of efgartigimod in treating autoimmune encephalitis. Efgartigimod shows promise as a safe and effective treatment for autoimmune encephalitis. This pioneering report highlights its potential as an innovative therapeutic option for this condition.
Disclosure: Nothing to disclose.

Sleep-wake disorders 1

EPO-485 | Sleep disorders in children with myotonic dystrophy type 1

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Background and Aims: Sleep disturbances are common in myotonic dystrophy type 1 (DM1), but most studies have focused on the prevalence of this symptomatology among adults. The purpose of the study was to evaluate the presence and nature of sleep disorders in children with DM1.
Methods: 9 children were examined: 5 girls, 4 boys, average age 11.7+2.7 years. Three patients (33%) had congenital DM1, six (67%) had childhood DM1. Patients underwent polysomnography (PSG) using a portable Somnolab2 PSG device (Loewenstein Medical (Weinmann), Germany).
Results: Changes in sleep architecture among children were similar to those previously described in adults: increased duration of stage 1 sleep, decreased stage 2 sleep, decreased sleep efficiency index. In 7 children (78%), according to PSG results, mild OSA was registered, in 3 (33%) - in combination with REM-dependent apnea, in 2 (22%) - with central apnea. No sleep disturbances were detected in 2 children (22%). In 87.5% of children, obstructive sleep apnea syndrome was observed in the absence of muscle weakness (8 children (89%) had 2 points on the MIRS scale, which corresponds to the presence of minimal muscle symptoms, 1 patient (11%) had 4 points).
Conclusion: The high incidence of obstructive sleep apnea syndrome in children with DM1 has been confirmed, which occurs even in the absence of significant muscle weakness. So it is advisable to conduct PSG in all patients for earlier diagnosis and treatment of breathing disorders during sleep.
Disclosure: Nothing to disclose.

EPO-486 | Dream experiences during intensive care unit stay: Prevalence, content, vividness, and associated factors

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Background and Aims: Vivid dream experiences in the Intensive Care Unit (ICU) are common, but poorly understood. We investigated the prevalence, vividness, content, emotional impact, and associated factors of dream experiences in the ICU.
Methods: Retrospective qualitative study with subjects ≥18 years, previously admitted to the ICU for ≥4 days and/or due to COVID-19, who were not sedated for ≥24 hours during their stay ($n=80$). Participants were interviewed by telephone. Clinical data were collected from patient files.
Results: Interviews were conducted a median of 9 months post-discharge. At the time of the interview, dream experiences were reported by 79%. Of patients with dream experiences, 73% reported "life-like" dreams, and 49% associated their dreams with negative emotions. Some participants (28.6%) continued to have similar dreams at home. The dream content was often related to the ICU admission. Younger age and longer length of stay were related to vivid dream experiences. Of participants with dream experiences 62.5% had experienced delirium during their ICU stay. Perceptual disturbances were also frequently reported by patients (50%) and only 45% could clearly distinguish them from dream experiences. There was an overlap between participants reporting perceptual disturbances and confirmed delirium (70%).
Conclusion: Life-like dream experiences are common in patients in the ICU and often have a negative emotional impact. To mitigate this impact, some participants suggest receiving information during their hospital stay about the potential for vivid dream experiences could be beneficial. Future studies should explore effective ways to distinguish dreams, delirium, and perceptual disturbances and how to reduce their impact.
Disclosure: Nothing to disclose.

EPO-487 | The burden of gender and depression on sleep inertia in central hypersomnias

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Background and Aims: Sleep inertia (SI) can be defined as difficulty becoming fully awake after sleep. We aimed to evaluate SI in patients affected by hypersomnias of central origin, including narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) and to study possible association with sex, age, depression, daytime somnolence and polysomnographic (PSG) parameters.
Methods: Patients with NT1, NT2 and IH underwent to nocturnal PSG recording, 5 naps Multi-sleep latency test (MSLT), Epworth Sleepiness Scale (ESS), Sleep Inertia Questionnaire (SIQ) and Beck Depression Inventory (BDI-II). SIQ total score and four SIQ subdomains (physiological, SIQ-P cognitive, SIQ-C, emotional, SIQ-E and responses to SI, SIQ-R) were assessed.
Results: 45 patients (27 females, 18 males, mean age 39.4±15 years) with diagnosis of NT1 ($n=11$), NT2 ($n=15$), IH ($n=19$). Mean SIQ total score didn't show differences among the three groups (NT1 53±21 vs NT2 56.9±21.4 vs IH 53.6±21.6, $p>0.05$), whereas was significantly higher in female (62.7±19.6 vs 42.3±16.9, $p<0.005$). Age, BDI, BMI, ESS were comparable in males and females. Strong positive correlation was observed between SIQ (total score and all SIQ subdomains) and BDI-II ($p<0.01$). SIQ-R negatively correlated with N3 ($p<0.01$), whereas was positively associated with Sleep Period Time and Total Sleep Time ($p<0.05$). Finally, SIQ does not correlate with age and ESS.
Conclusion: SI assessed by SIQ does not help in the differential diagnosis among hypersomnias of central origin, but appears to be strongly associated with female sex, depression and some polysomnographic parameters.
Disclosure: Nothing to disclose.

EPO-488 | Obstructive Sleep Apnea before and after CPAP titration: Can real-life data detect gender differences?

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Background and Aims: Since Obstructive Sleep Apnea (OSA) can have atypical features in women, our aim was to assess gender differences in OSA patients with an indication to use Continuous Positive Airway Pressure (CPAP) before and after treatment.
Methods: In this monocentric retrospective study, we recruited 199 OSA patients with an indication to use CPAP. We assessed gender differences in demographic, polygraphic and clinical features, and CPAP adherence.
Results: Median age was 59.5 (51.0-69.2) years, with 47 (23.6%) female patients. Median BMI was 31.0 (27.1-35.6) and apnea hypopnea index (AHI) 45.9 (31.9-66.0), indicating severe OSA. Twenty-seven patients (13.6%) suffered from insomnia. Thirty-eight patients (12.0%) refused CPAP treatment. After 6 (4-10) months, 85 patients underwent a follow-up visit showing a residual AHI of 3.3 (1.3-8.1) and 5.3 (4.4-6.3) hours of CPAP use. These variables did not show any gender differences. While snoring was the most reported symptom in both women and men (95.8%), women reported more nonrestorative sleep

(72.0% vs 55.9%, 0.046), less witnessed apneas (64.0% vs 73.1%, *p* 0.047) more insomnia (25.5% vs 9.9%, *p* 0.006) and hypothyroidism (15.0% vs 3.3.% *p* 0.005). Women with insomnia were older than those without (71 (64-72) vs 59 (51-67), *p* 0.012) and tended to use CPAP for less hours (5.4 (4.4-5.5) vs 6 (5.5-6.1), $p=0.072$).

Conclusion: In our sample women shared most of clinical features with men, probably due to the severity of OSA. However, women had more nonrestorative sleep and/or insomnia, possibly affecting CPAP adherence, showing it is crucial to take gender into account in clinical practice.

Disclosure: The authors declare no conflict of interest with regards to this paper.

EPO-489 | Heart rate response in spontaneous microarousals uncovers an autonomous nervous dysfunction in narcolepsy type 1

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Background and Aims: Narcolepsy type 1 (NT1) is characterized by the loss of hypothalamic orexin neurons important in the regulation of sleep-wake transitions. These cells have also been implicated in autonomous nervous system regulation and its disturbance has been recently suggested in NT1, although still unclear. This study aimed to assess heart rate (HR) response associated with spontaneous microarousals across sleep stages in NT1 compared to healthy controls.

Methods: Ten NT1 patients and 10 age-matched controls polysomnograpies were examined. Three to seven spontaneous microarousals in each sleep stage preceded by at least 30 seconds of stable sleep were randomly selected and analysed. The HR response was calculated based on the difference between the maximal and average HR during microarousal and average basal HR 10 seconds before the microarousal, and compared between groups.

Results: A total of 428 spontaneous microarousals were analysed (214 NT1 and 214 controls). The duration of spontaneous microarousals was significantly higher in NT1 for N1 (7.6 ±3.2vs5.8 ±1.6), N2 (7.0 ±2.2vs5.8 ±1.9) and N3 (7.1 ±2.6vs5.4 ±1.6). The difference between the average HR during and before microarousals was significantly higher in NT1 across all stages (N1 3.8 ±5vs0.5 ±4.3, N2 4 ±4.5vs0.5 ±3.9, N3 5.3 ±6.4vs2.3 ±4.3 and REM 3.9 ±6.1vs1 ±3.3). Considering the difference between maximal HR during and average basal HR before microarousals, a significantly higher variation was verified in N2 (11.5 ±6.9vs8.9 ±5.4) and REM (13.4 ±8.4vs9.2 ±6.7) for NT1.

Conclusion: The higher HR response in spontaneous microarousals during sleep points toward an enhanced sympathetic activity in the context of possible autonomic dysfunction. This reinforces the importance of looking for dysautonomia in NT1, given the associated morbimortality.

Disclosure: Nothing to disclose.

EPO-490 | REM without atonia index is inversely correlated with asymmetric nigrostriatal denervation in Dementia with Lewy Body

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Background and Aims: The clinical heterogeneity of alpha-synucleinopathies is supported by different pathways of Lewy body accumulation. REM sleep behavioural disorder (RBD) is held as clinical marker of "body-first" phenotype, while nigrostriatal denervation is thought to reflect a "brain-first" involvement in the context of Parkinson's disease. We investigated the associations between polysomnographic features and DAT-SPECT findings in a cohort of patients with Dementia with Lewy Bodies (DLB).

Methods: We enrolled 13 patients with DLB (69.71±8.39 years old) diagnosed according to McKeith 2017 criteria, who underwent clinical examination, polysomnography (PSG) - with evaluation of REM without atonia (RWA) index (%) (AASM criteria) - and DAT-SPECT. Quantitative analyses were performed with the DaT-QUANT software. We evaluated sleep features in DLB patients and used Pearson's analysis to correlate PSG findings with DaT-QUANT measures.

Results: In our cohort, 11/13 patients showed PSG-RWA, 11/13 had altered DAT-SPECT. We observed a positive correlation between sleep efficiency and Striatal Asymmetry ($r=0.866$, $p=0.001$) and a negative correlation between sleep latency and Putamen Asymmetry ($r=-0.608$. $p=0.036$). Moreover, Caudate Asymmetry correlated inversely with RWA index ($r=-0.690$, $p=0.019$) and positively with extrapyramidal motor symptoms measured with UPDRS ($r=-0.697$, $p=0.025$).

Conclusion: Asymmetry in nigrostriatal denervation points to brain-first involvement, due to prevalent ipsilateral connections in the connectome. Our results suggests that in DLB a higher RWA index is linked with more symmetric nigrostriatal impairment (body-first phenotype), while lower RWA is found in patients with more prominent motor symptoms and asymmetric DAT-SPECT alterations (brain-first), supporting the existence of two distinct phenotypes in the disease.

Disclosure: Nothing to disclose.

EPO-491 | Bright light therapy in myalgic encephalomyelitis/ chronic fatigue syndrome patients

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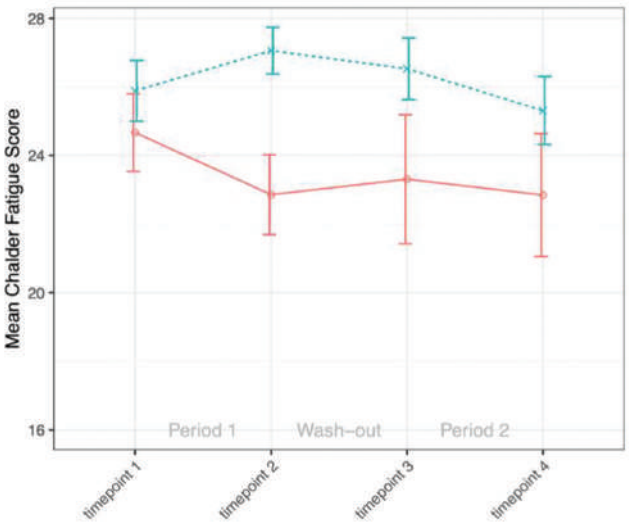
Background and Aims: Chronic Fatigue Syndrome (CFS), also referred to as Myalgic Encephalomyelitis (ME), is a chronic, debilitating

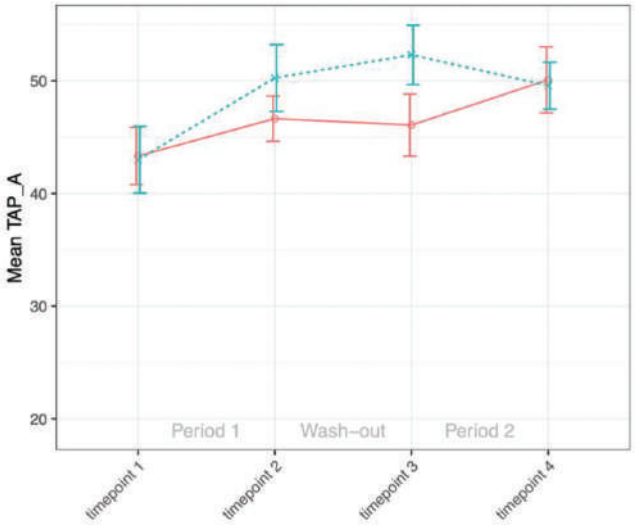
condition of unknown etiology and limited treatment options. Bright light therapy (BLT) has shown controversial results in studies with neurological patients experiencing fatigue symptoms. The aim of the current study was to test the effectiveness of BLT treatment on fatigue and cognitive function in patients with ME/CFS.

Methods: A randomized-controlled cross-over study design was chosen in order to provide all patients access to BLT treatment. 33 outpatients who met the diagnostic criteria according to the Institute of Medicine (2015) were randomly assigned to either start out with BLT or waitlist for the course of 2 weeks. After a 2-week wash-out phase, the assignment was reversed. Primary outcomes of the study were the Chalder Fatigue Score (CFQ) and the Test of Attentional Performance (TAP). A repeated measures ANOVA was performed to compare the effect of BLT on fatigue and cognitive function at baseline and the end of study.

Results: A statistically significant effect of BLT on subjective fatigue levels ($F(1,27) = 6.12$, $p = 0.02$) was found, irrespective of sequence of treatment/waitlist ($F(1,27) = 0.587$, $p = 0.45$). There was also a statistically significant effect of BLT on the domains Attention, ($F(1,26) = 11.96$, $p = 0.002$), irrespective of sequence of treatment/waitlist ($F(1,26) = 0.447$, $p = 0.51$). There was no statistically significant effect of BLT on the domains Divided Attention ($F(1,26) = 1.487$, $p = 0.23$) and Go-No Go ($F(1,27) = 1.93$, $p = 0.18$).



Rating of subjective fatigue with the Chalder Fatigue Score. Red line: group started with bright light therapy. Blue line: group started with waitlist.



Performance in the subdomain Attention of the standardized Test of Attentional Performance. Red line: group started with bright light therapy. Blue line: group started with waitlist.

Conclusion: These preliminary results suggest moderate effects of BLT on fatigue and cognition. Additional analyses accounting for possible placebo effects need to be considered.

Disclosure: Nothing to disclose.

EPO-492 | Periodic SREDA (subclinical rhythmic electrographic discharges of adults): A case report

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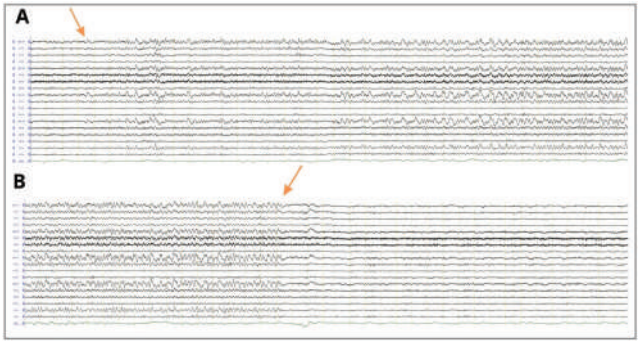
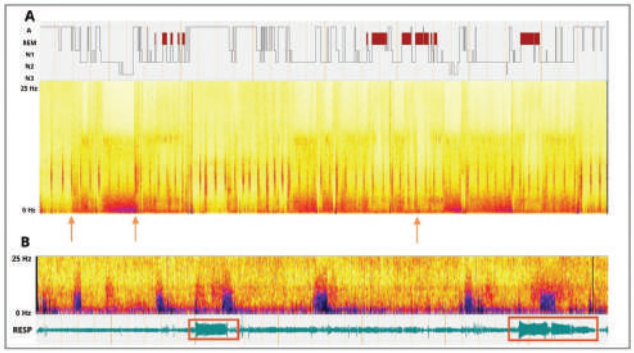
Background and Aims: SREDA (subclinical rhythmic electrographic discharges of adults) is a benign electroencephalographic (EEG) pattern, consisting of episodes during wakefulness of rhythmic theta activity in the frontoparietotemporal regions, without associated clinical findings. Atypical presentations with focal predominance, delta activity, or appearance during sleep have rarely been reported. It is important to recognize atypical SREDA patterns because they can mimic electrographic seizures.

Methods: We report a patient with atypical SREDA with a high number of episodes occurring periodically during sleep and wakefulness.

Results: A 70-year-old woman without past clinical history consulted because of chronic insomnia and nightmares. A nocturnal polysomnogram revealed a moderately reduced sleep efficiency with normal sleep architecture and 67 episodes of SREDA characterized by trains of moderate-high amplitude, diffuse theta-delta activity of anterior predominance, at 3-7 Hz, lasting 1-2 minutes, recurring every 8-9 minutes (range 2-15) throughout all phases of sleep and easily visible in the spectrogram (Figure 2A). A video-EEG during wakefulness revealed 7 episodes of SREDA (2 of them induced by hyperventilation which also increased their duration, figure 2B). The patient was able to talk, calculate, and perform simple and complex commands correctly.



An episode of SREDA starts in A (arrow) consisting of trains of theta-delta activity at 3-7 Hz, lasting 1-2 minutes, with an abrupt ending (arrow in B) and an immediate normalization of the record.



A) Hypnogram of 8 hr sleep recording and B) Daytime wake EEG showing more than 60 episodes of SREDA, indicated by the vertical red lines, appear periodically throughout all stages.

Conclusion: To our knowledge, this is the first report of a SREDA occurring periodically with a high frequency during wakefulness and all stages of sleep. Failure to recognize SREDA can lead to misdiagnoses and unnecessary and potentially harmful use of medication.
Disclosure: Nothing to disclose.

EPO-493 | The role of astrocytes in sleep and memory consolidation

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Background and Aims: Astrocytes are known to participate in homeostatic functions, such as the regulation of extracellular ions, stabilization of the environment surrounding synapses, and regulation of blood flow. Some studies have also indicated that astrocytes might play a role in the regulation of sleep and transitions between sleep states. In this study, our aim is to investigate the role of astrocytes in sleep and memory consolidation in the hippocampus.
Methods: We conducted experiments on 5 BL6 mice, in which we expressed genetically encoded calcium indicators (GCaMP6f) to monitor intracellular calcium levels in astrocytes. Additionally, we surgically inserted a window to the hippocampal CA1 region, as well as LFP and ECoG electrodes. Two-photon microscopy and electrophysiology recordings were utilized to examine astrocytic calcium signals throughout the sleep-wake cycle.
Results: Our findings revealed a reduction in astrocytic calcium signaling during sleep, with an increase shortly before awakening. Currently, we are analyzing the relationship between astrocytic calcium signals and various electrophysiological oscillations linked to memory consolidation. We hope to present these results at the conference this year.
Conclusion: Our findings support the hypothesis that astrocytes might be involved in regulation of the different sleep states, and potentially can facilitate EEG oscillations involved in memory consolidation.
Disclosure: None.

EPO-494 | Assessing Obstructive Sleep Apnoea Syndrome risk in Behçet Syndrome patients: An actigraphic approach

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Background and Aims: Previous studies found a higher risk of Obstructive Sleep Apnoea Syndrome (OSAS) in Behçet Syndrome (BS) patients compared to healthy controls (HCs). However, limited research with proper matching criteria assessed differences in OSAS risk between these populations. Furthermore, actigraphy has recently emerged as a valuable screening tool to estimate OSAS risk, with no studies used actigraphy to characterize BS patients' sleep. This cross-sectional study aimed at testing possible differences in both sleep parameters and actigraphic OSAS risk among BS patients and age-, BMI-, sex-, smoking habits-matched HCs.
Methods: Sleep parameters were evaluated through the Pittsburgh Sleep Quality Index and a 7-day actigraphic continuous monitoring. Actigraphic OSAS risk was estimated through a validated machine-learning algorithm, dividing participants into two classes of OSAS risk, i.e., high and non-high OSAS risk. Possible differences in sleep parameters and actigraphic OSAS risk were tested through nonparametric tests. A binomial logistic regression model with Firth bias reduction method was estimated to test possible predictors of high OSAS risk among participants, i.e., HCs group, age, sex, BMI, being a smoker and smoking intensity.

Results: 45 BS patients (Table 1) and 60 HCs were included in the study. Compared to HCs, BS patients showed significantly lower perceived sleep quality ($p < 0.001$), actigraphic sleep efficiency ($p < 0.044$), and OSAS risk ($p < 0.010$)(Table 2). In the regression model, high OSAS risk was significantly predicted only by the HCs group (beta = 3.16; $p < 0.025$).

TABLE 1: Behçet Syndrome patients' clinical data

Clinical Data[1]	N = 45[2]
Age	48 (42, 54)
BMI	23.9 (22.2, 27.6)
Sex	
Female	30 (67%)
Male	15 (33%)
Disease Duration	5 (4, 13)
BDCAF	0 (0, 2)
Active Disease	8 (18%)
Clinical Manifestations at the time of recruitment	
Mouth ulcers	13 (29%)
Genital ulcers	3 (6.7%)
Erythema nodosum	3 (6.7%)
Pseudofolliculitis	5 (11%)
Arthralgia	8 (18%)
Arthritis	2 (4.4%)
Uveitis	2 (4.4%)
Headache	1 (2.2%)
Diarrhea	5 (11%)
Superficial vein thrombosis	1 (2.2%)
Fibromyalgia	23 (51%)
HLAB*51 mutation	27 (60%)
Immunomodulatory and immunosuppressive treatment	
GC Treatment	18 (40%)
dGC	5.0 (5.0, 8.8)
One-year cumulative GC dose	104 (0, 1,400)
Colchicine	14 (33%)
Methotrexate	1 (2.3%)
Cyclosporine	1 (2.3%)
Azathioprine	9 (21%)
Biologic Agents	34 (76%)
Mood Disorders and Insomnia Treatment	
Mood Disorders and/or Insomnia Treatment	12 (27%)
Trazodone	3 (6.7%)
Zolpidem	1 (2.2%)
SSRIs	5 (11%)
SNRIs	1 (2.2%)
TCAs	2 (4.4%)
Mood stabilizers	3 (6.7%)
Gabapentinoids	4 (8.9%)

[1] BDCAF: Behcet Disease Current Activity Form - Interval Scale. Active Disease: BDCAF ≥ 3. HLAB*51: Human Leukocyte Antigens B51. GC: glucocorticoids. dGC: daily glucocorticoid dose (prednisone equivalents, mg). One-year cumulative GC dose: the sum of the total amount of GCs administered to a patient over the year before the recruitment (prednisone equivalents, mg). SSRIs: Selective Serotonine Reuptake Inhibitors. SNRIs: Serotonine and Noradrenaline Reuptake Inhibitors. TCAs: Tricyclic Antidepressants.
[2] Median (IQR); n (%)

TABLE 2: differences in matching variables, sleep parameters and actigraphic OSAS risk between BS patients and healthy controls

Variable[1]	BS Patients, N = 45[2]	Healthy Controls, N = 60[2]	p-value
Age	48 (42, 54)	49 (36, 58)	0.9[3]
BMI	23.9 (22.2, 27.6)	23.8 (22.3, 27.2)	0.9[3]
Sex			0.4[4]
Female	30 (67%)	35 (58%)	
Male	15 (33%)	25 (42%)	
Smoking intensity	0 (0, 0)	0 (0, 0)	0.2[3]
Smokers	4 (8.9%)	11 (18%)	0.4[4]
TST	6.88 (6.30, 7.63)	7.19 (6.51, 7.72)	0.4[3]
SE	92.4 (88.8, 94.8)	94.1 (90.5, 96.1)	**0.044**[3]
WASO	33 (24, 46)	28 (19, 45)	0.2[3]
SFI	6.7 (4.8, 9.8)	6.6 (5.1, 9.5)	>0.9[3]
SRI	77 (72, 83)	77 (66, 85)	0.9[3]
High actigraphic OSAS risk	0 (0%)	9 (15%)	**0.010**[4]
PSQI	8 (6, 11)	6 (3, 7)	**<0.001**[3]

[1] BS: Behçet Syndrome. BMI: Bodi Mass Index (kg/m^2). Smoking intensity: number of cigarettes per week. SE (Sleep Efficiency, %): the ratio of total sleep time to time in bed. TST: Total Sleep Time (hours). WASO (Wake After Sleep Onset, minutes): the period of wakefulness that occurs after a defined sleep onset. SFI (Sleep Fragmentation Index): the total number of awakenings divided by the total sleep time. SRI (Sleep Regularity Index, %): the likelihood of the same sleep-wake state occurring in epochs that are 24 hours apart. OSAS: Obstructive Sleep Apnea Syndrome. PSQI: Pittsburgh Sleep Quality Index.
[2] Median (IQR); n (%)
[3] Wilcoxon rank sum test
[4] Fisher's exact test

Conclusion: Compared to HCs, BS patients show lower perceived sleep quality, actigraphic sleep efficiency, and OSAS risk, irrespective of age, BMI, sex, and smoking habits.

Disclosure: Ugo Faraguna is President and co-founder of Sleepacta s.r.l., a University of Pisa spin-off private company, focused on sleep diagnostics.

EPO-495 | Utilizing transcranial direct current stimulation (tDCS) for insomnia

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Background and Aims: Transcranial direct current stimulation (tDCS) is acknowledged for its non-invasive modulation of neuronal activity in psychiatric disorders, with varied outcomes observed in insomnia research based on different tDCS types and patient conditions. Our primary goal is to elucidate the effectiveness of tDCS and reveal the underlying mechanisms in treating insomnia. We hypothesize that anodal prefrontal cortex stimulation activates glutamatergic projections from the infralimbic cortex (IL) to the ventrolateral preoptic area (VLPO), promoting sleep.

Methods: Electroencephalogram (EEG) electrodes were surgically implanted for sleep-wake data capture. The tDCS electrode was positioned over the infralimbic cortex on the skull, with the reference electrode using the EEG reference electrode. Designer receptors exclusively activated by designer drugs (DREADDs) selectively inhibited the IL-VLPO pathway, aiming to unveil its contribution to tDCS effects.

Results: Administering 0.06 mA of electrical currents for 8 minutes led to a significant increase in non-rapid eye movement (NREM) sleep in naive mice during the initial 3 hours post-stimulation, persisting up to 16-24 hours. In the insomnia group, tDCS enhanced NREM sleep bouts during acute stress response and improved both NREM and REM sleep duration in subsequent acute insomnia. NREM delta powers, assessing sleep quality, remained unchanged. Intervention in the IL-VLPO pathway using DREADDs with the cre-DIO system partially inhibited tDCS efficacy in improving sleep in stress-induced insomnia.

Conclusion: This research clarified that the activation of the IL-VLPO pathway mediates tDCS's impact on stress-induced insomnia, providing valuable insights for future investigations and clinical applications in sleep therapy.

Disclosure: Nothing to disclose.

EPO-496 | Screening restless leg syndrome in neuromyelitis optica and myelin oligodendrocyte glycoprotein-IgG associated disorder

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Background and Aims: Restless legs syndrome (RLS) is a sleep disorder which is diagnosed clinically, affecting 5.6% of Spanish population. Neuromyelitis optica spectrum disorder (NMOSD) and Myelin oligodendrocyte glycoprotein-IgG associated disorder (MOGAD) are immune-mediated inflammatory conditions of the central nervous system. To our knowledge, RLS in NMOSD or MOGAD had not been studied.

Methods: We designed an observational retrospective study. We reviewed data from 151 patients coded as "NMO", "MOGAD", "optic neuritis", "mielitis" or "isolated clinical syndrome". 12 met 2015 criteria for NMOSD and 11 met 2023 criteria for MOGAD. 1 met exclusion criteria and we were unable to contact 2. We administered the Cambridge–Hopkins RLS questionnaire by phone, with follow up open ended questions.

Results: In the NMOSD group, median age was 56 (39-80 y.o.), all female, median EDSS of 4 (0-8), 9/10 suffered spinal cord lesions. In the MOGAD group, median age was 46 (19-61 y.o.), 5 female, 5 male, median EDSS of 0 (0-2), 5/10 suffered spinal cord lesions. 7/10 NMOSD and 3/10 MOGAD had paresthesia, 4/10 NMOSD and 2/10 MOGAD had chronic neuropathic pain and 5/10 NMOSD and 2/10 MOGAD had leg cramps. 4/10 NMOSD and 1/10 MOGAD questionnaires were compatible with definite RLS. However, when asked open-ended questions 4 patients presented RLS-mimicks. Only 1 NMOSD patient was diagnosed with mild RLS.

Conclusion: Our work highlights the importance of validating RLS questionnaires in NMOSD and MOGAD patients, as RLS mimics are common. We did not find a higher-than-expected prevalence of RLS in these patients.

Disclosure: No disclosures.

EPO-497 | Prevalence of sleep disorders in the elderly: A questionnaire-based study

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Background and Aims: Several studies highlighted a high prevalence of sleep disorders in the elderly population: this could depend on different factors including neuropsychiatric comorbidities, medication use or circadian sleep-wake cycle alterations. The aim of the present study is to assess the prevalence of sleep disorders in geriatrics patients, according to sex and age, through validated screening questionnaires for sleep disorders, global cognition and depression.

Methods: This study included 58 subjects (58.6% women) with a mean age of 77.36 (SD = 6.07) admitted to the geriatrics clinic of the University Hospital of Rome "Tor Vergata". All participants were clinically evaluated and answered different questionnaires assessing sleep quality (Pittsburgh Sleep Quality Index-PSQI), insomnia (Insomnia Severity Index-ISI), sleep apnea risk (Berlin Questionnaire), excessive daytime sleepiness (Epworth sleepiness scale-ESS), restless legs syndrome (International RLS Study Group Scale-IRLSS), chronotype (Morningness-Eveningness Questionnaire-MEQ), depression (Geriatric Depression Scale-GDS) and global cognition (Mini-Mental Examination State-MMSE).

Results: We observed that the most frequent sleep-related complaint was worse quality of sleep measured through the PSQI (36.2%; $n = 21$), followed by sleep apnea risk (34.5%, $n = 20$), insomnia symptoms (25.9%, $n = 15$), EDS (15.5%, $n = 9$) and RLS (12.1%, $n = 7$). Insomnia symptoms, depression and worse sleep quality were more common in women than in men, while older patients (≥ 75 years) had more comorbidities and higher sleep apnea risk than the younger ones (<75 years).

Conclusion: Sleep disorders are frequent in the elderly and the screening through suitable questionnaires may facilitate their recognition and timely treatment.

Disclosure: Nothing to disclose.

EPO-498 | Nocturnal hypokinesia and sleep in Parkinson's disease

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Background and Aims: Bradykinesia is one of the main pillars in establishing the diagnosis of Parkinson's disease (PD). In addition to

affecting diurnal movement, hypokinesia can also occur during the night, affecting the quality of patients' sleep. Objective: Establishing the degree to which nocturnal hypokinesia impacts the sleep of PD patients.

Methods: The sleep of 131 PD patients was analysed using the Parkinson's Disease Sleep Scale (PDSS-2), Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI) and Athens Insomnia Scale (AIS).

Results: Based on the response to item 9 of the PDSS-2 ("Did you feel uncomfortable at night because you were unable to turn around in bed or move due to immobility?"), PD patients were grouped into two categories: with nocturnal hypokinesia (PD + hypokinesia), which included 97 (74.04%) participants and no nocturnal hypokinesia (PD – hypokinesia), which included 34 (25.95%) participants. PD + hypokinesia patients showed statistically significantly higher scores than PD - hypokinesia patients for the PSQI scales (10.42 $\pm$4.84 vs. 6.50 $\pm$4.22, $p<0.001$), PDSS-2 (27.14 $\pm$9.61 vs. 13.76 $\pm$8.44, $p<0.001$), ISI (12.23 $\pm$5.58 vs. 6.21 $\pm$4.73, $p<0.001$) and AIS (9.64 $\pm$4.59 vs. 4.68 $\pm$4.48, $p<0.001$).

Conclusion: The prevalence of nocturnal hypokinesia among PD patients is high, and the sleep quality of these patients is significantly lower, compared to those with normal mobility during the night. A higher degree of insomnia was also identified among this category.

Disclosure: Nothing to disclose.

EPO-499 | Self-reported sleep difficulties and potentially inappropriate z-hypnotic use among older adults in primary care

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Background and Aims: This study aims to assess prevalence and severity of sleep difficulties and potentially inappropriate z-hypnotic use in a General Practitioner (GP) population, and further to examine the association between potentially inappropriate z-hypnotics and self-reported sleep difficulties.

Methods: A cross-sectional study, including 687 older adults recruited through 31 GPs in south-east Norway. We defined z-hypnotics inappropriate use as use over four weeks, three times or more per week. Sleep difficulties were reported as yes/no/sometimes, type, and reasons. Descriptive statistics and logistic regression mixed effect models were conducted.

Results: Out of 687 patients included, 10% had potentially inappropriate z-hypnotic use. Among all the participants, 22% reported difficulty sleeping. The participants reported trouble falling asleep (12%), trouble staying asleep (24%), and 29% experienced both. They reported various reasons for sleep difficulties, including pain (9%), overthinking at bedtime (27%), and 20 % experienced both, including bereavement in close relations. Patients experiencing difficulty sleeping, problems with falling asleep and staying asleep, and experiencing pain and overthinking at bedtime, had higher odds of being users of potentially inappropriate z-hypnotics, than patients without these experiences.

Conclusion: Older adults in primary care have a high prevalence of self-reported sleeping problems and a high proportion of potentially inappropriate z-hypnotics use. GPs need to be aware of patients sleeping problems and their appropriate treatments.

Disclosure: C.L had support for clinical studies (Lundbeck pharma) and received lecture honoraria. All other authors have nothing to disclose.

Neuroimaging 1

EPO-500 | Evidence for hypometabolism in epileptic focus and GABA alterations in drug-resistant MRI-negative TLE

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Background and Aims: Increasing evidence suggests that the hypometabolism of the epileptogenic focus affects the treatment prognosis of temporal lobe epilepsy (TLE). Epileptic seizures involve neurotransmitter synthesis and consumption, accompanied by central nervous system energy substance depletion. Therefore, we attempted to investigate the metabolic levels of the epileptogenic focus through single-voxel MRS to provide more evidence for the correlation between hypometabolism of the epileptogenic focus and drug-resistant epilepsy in MRI-negative TLE.

Methods: 47 patients of MRI-negative TLE were divided into a drug-resistant group ($n=9$) and a drug-responsive group ($n=38$) based on their response to medication. Brain metabolite concentrations were quantitatively analyzed by using LCModel. MRS data were compared with those of 20 age- and gender-matched healthy controls, analyzing differences in epileptic focus indicated by video-EEG metabolite changes among different groups.

Results: GABA (gamma-aminobutyric acid) ($p=0.048$), Glu ($p=0.039$), NAA ($p=0.002$), NAAG ($p<0.001$), Cho ($p=0.004$), Cr ($p=0.046$) concentrations on the epileptic side were significantly lower than contralateral in patients. Interestingly, the difference was most evident in patients with drug-resistant epilepsy. GABA was significantly different between the drug-resistant, drug-responsive, and healthy controls group ($p=0.019$).

Conclusion: GABA and Glu levels are significantly reduced on the epileptic side. These metabolite levels were even lower in drug-resistant epilepsy. Cho and Cr are important substances for brain energy regulation and supply, the reduction of them also affects neurotransmitter synthesis, thereby influencing neuronal excitability. This study supports the correlation between hypometabolism of the epileptic focus and poor prognosis in drug-resistant MRI-negative TLE.

Disclosure: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EPO-501 | Before and after: Favorable radiological evolution in a pseudotumoral form of multiple sclerosis treated with rituximab

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Background and Aims: Pseudotumoral lesions are an unusual demyelinating disease that could be related to multiple sclerosis and may simulate brain tumors, being necessary an appropriate differential diagnosis, even including brain biopsy. We report a case of a relapsing and progressive pseudotumoral form of multiple sclerosis (PFMS) in a patient controlled due to Rituximab.

Methods: Medical history review of a previously healthy 31-year-old man who developed ten days of progressive left hemiparesis.

Results: A brain magnetic resonance imaging (MRI) verified a T1 hypointense, T2/FLAIR hyperintense right centrum semiovale lesion with restricted diffusion and incomplete ring enhancement, and another similar left parietooccipital lesion (Fig.1). Cerebrospinal fluid (CSF) analysis showed hyperproteinorrachia, absence of IgG oligoclonal bands, negative anti-AQP4 and anti-MOG antibodies and positive HHV-6 PCR. He was treated with dexamethasone and ganciclovir with full recovery. Nine months later he presented a sudden right homonymous hemianopsia. A brain MRI revealed a new occipitotemporal lesion with the same radiological behaviour (Fig.1). CFS analysis without changes except negativization of HHV-6. He received five days of intravenous methylprednisolone with full recovery in the visual field. A new control brain MRI few months later manifested an asymptomatic left frontal injury and consequently a brain biopsy was performed. Pathological findings confirmed demyelination and the diagnosis of PFMS (Fig.2). He started biannual rituximab with good tolerability, remaining clinically stable and next brain MRIs didn't manifest progression (Fig.3).

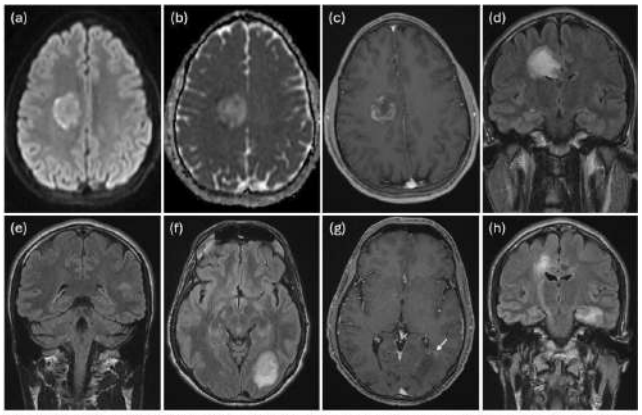

Fig. 1: In (a) and (b) restricted pattern in diffusion and in (c) an incomplete ring enhancement of right centrum semiovale lesion. In (d) hyperintense right centrum semiovale lesion. In (e) hyperintense left parietooccipital lesion. In (f) hyperintense left occipital lesion. In (g) incomplete ring enhancement of left occipital lesion. In (h) hyperintense Wallerian degeneration of the right corticospinal tract, right centrum semiovale and left temporal lesions.

FIGURE 1 Brain MRI: (a) DWI in axial plane. (b) ADC in axial plane. (c) post-gadolinium T1 in axial plane. (d) and (e) FLAIR in coronal plane. 9 months later: (f) FLAIR in axial plane. (g) post-gadolinium T1 in axial plane. (h) FLAIR in coronal plane.

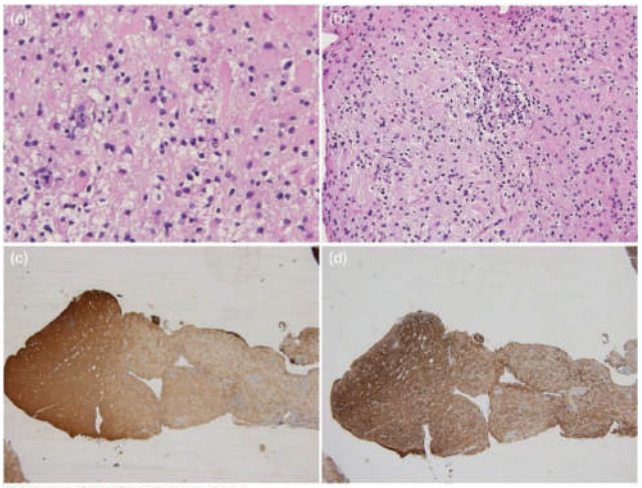

Fig. 2. Left frontal lesion's pathological findings.

FIGURE 2 (a) Astrogliosis and infiltration by macrophages. Hematoxylin-eosin (HE). (b) Perivascular inflammatory infiltrates. HE. (c) demyelinating areas. Luxol and staining for myelin. (d) Neurofilaments.

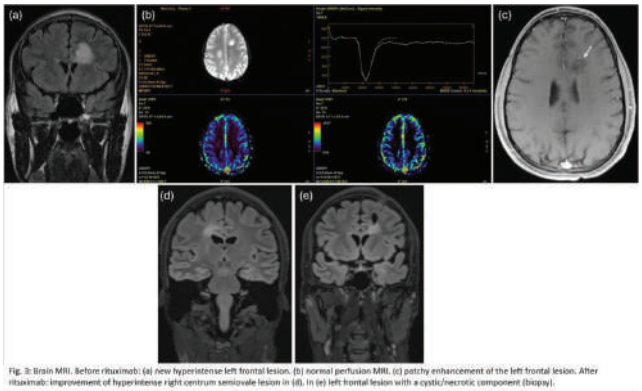

Fig. 3: Brain MRI. Before rituximab: (a) new hyperintense left frontal lesion. (b) normal perfusion MRI. (c) patchy enhancement of the left frontal lesion. After rituximab: improvement of hyperintense right centrum semiovale lesion in (d). In (e) left frontal lesion with a cystic/necrotic component (biopsy).

Conclusion: Sometimes the PFMS's diagnosis and treatment are delayed. Further studies and guidelines are required in this field to establish optimal treatment strategies.
Disclosure: Nothing to disclose.

EPO-502 | Unveiling the hippocampal subfield changes across the Alzheimer's disease continuum: a systematic review

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Background and aims: Studies exploring the hippocampal subregional changes in Alzheimer's disease (AD) have shown contradictory results. This review aims to disentangle such heterogeneity by systematically investigating the dynamic changes of hippocampal subfields across the AD continuum, from the asymptomatic to the dementia stage.
Methods: We systematically searched the PubMed and EMBASE databases for case-control studies. Selected studies included investigations of biomarker-based amyloid status and reported data on hippocampal subfield atrophy using advanced neuroimaging techniques. We assessed the quality of the studies using the Joanna Briggs Institute (JBI) Collaboration's ten-item checklist for case-control studies.
Results: We systematically searched the PubMed and EMBASE databases for case-control studies. Selected studies included investigations of biomarker-based amyloid status and reported data on hippocampal subfield atrophy using advanced neuroimaging techniques. We assessed the quality of the studies using the Joanna Briggs Institute (JBI) Collaboration's ten-item checklist for case-control studies.

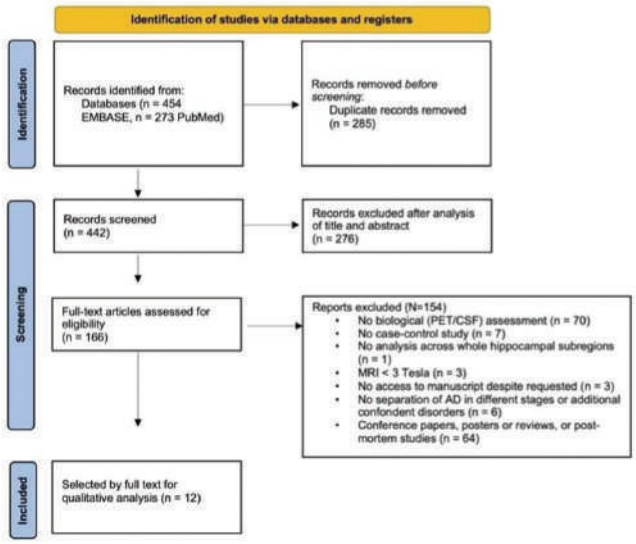

TABLE 1 Modified version of the PRISMA flow chart (Page et al., 2021).

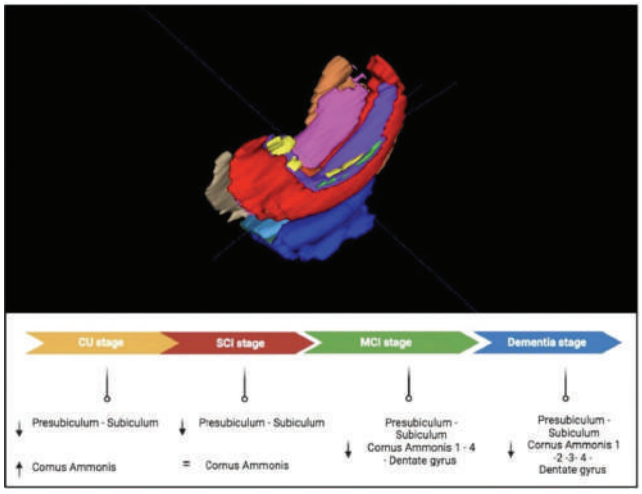

FIGURE 1 An example of hippocampal subfield segmentation with 3D reconstruction obtained using the Automated Segmentation of Hippocampal Subfields software on a high-resolution T2 coronal sequence, along with an exploration of the dynamic changes in hippoca.

Conclusion: A distinguishable pattern of involvement of hippocampal subfields can be recognized from the cognitively unimpaired phase to the dementia stage, shedding light on hippocampal changes with disease progression, as well as the functional role of hippocampal subregions.
Disclosure: Nothing to disclose.

EPO-503 | Right temporal variant frontotemporal dementia: A multimodal MRI analysis of a new emerging syndrome

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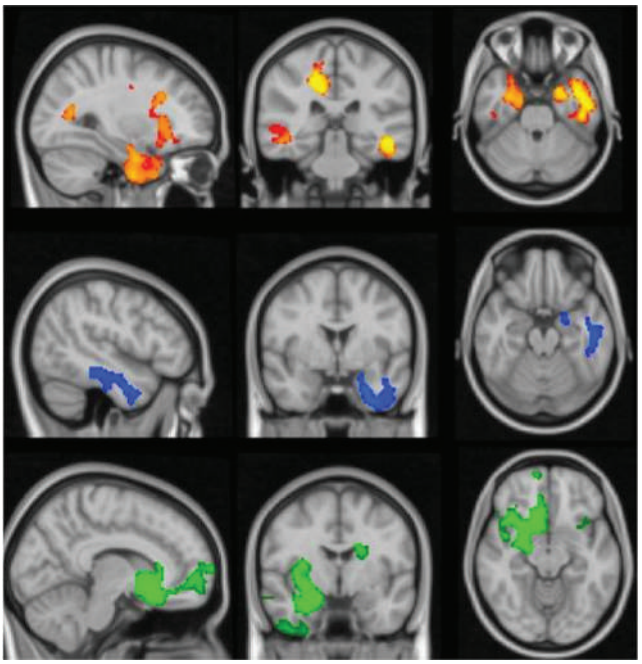
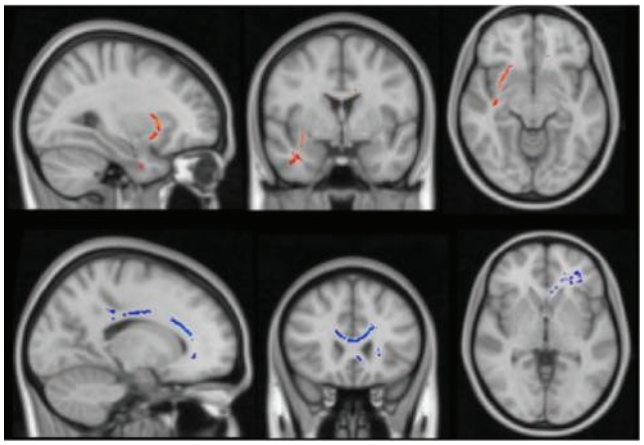
Background and Aims: Right-temporal-variant frontotemporal dementia (rtvFTD) is characterized by right anterior temporal lobe (rATL) atrophy and peculiar clinical presentation. Clinical diagnosis is challenging since rtvFTD shares features with both behavioral-variant FTD (bvFTD) and semantic-variant primary progressive aphasia (svPPA). Few studies investigated patterns of gray matter (GM) atrophy. Even less is known about white matter (WM) involvement. We conducted a preliminary-MRI-study on the rtvFTD neuroimaging features.
Methods: We compared GM volume and WM microstructural integrity in rtvFTD and svPPA patients and healthy controls, using voxel-based morphometry (VBM) and tract-based spatial statistics (TBSS), considering age and disease duration as covariates of no interest.
Results: SvPPA patients showed GM atrophy in the left temporal structures relative to HC. rtvFTD patients compared to HC showed GM atrophy in the right fronto-temporal structures, but also in insula

bilaterally and in left temporal and orbitofrontal cortices. RtvFTD were more atrophic than svPPA patients in fronto-temporal regions bilaterally. Moreover, rtvFTD patients had less WM integrity than controls in corpus callosum, right inferior fronto-occipital, inferior longitudinal and uncinate fasciculi. SvPPA patients had decreased WM integrity in corpus callosum and left inferior fronto-occipital fasciculus.



Results of VBM analysis. In red-yellow, regions of rtvFTD patients' GM atrophy compared to controls. In blue svPPA patients' GM atrophy compared to controls. In green regions of rtvFTD patients' GM volume greater reduction in comparison to svPPA patients.



Results of TBSS analysis. In red-yellow, regions of rtvFTD patients' decreased WM integrity compared to controls. In blue-light blue regions of svPPA patients' decreased WM integrity compared to controls.

Conclusion: RtvFTD patients show greater atrophy compared to svPPA patients in both hemisphere, independently of disease duration, suggesting that rtvFTD and svPPA do not mirror each other in GM loss and that a neurodegenerative process starting in the right hemisphere must be more widespread to become clinically evident. Moreover rtvFTD patients show WM disruption in fasciculi which have been implicated in face recognition, emotion processing and language functions.

Disclosure: Nothing to disclose.

EPO-504 | In-vivo PET study of mitochondrial complex 1, sigma-1, & synaptic vesicle 2A in amyotrophic lateral sclerosis patients

E. de Natale[1] ; J. Verghese[1]; A. Terry[1]; H. Wilson[1]; P. Khosropanah[1]; H. Wright[1]; L. Passamonti[2]; K. Evans[2]; R. Comley[3]; H. Tsukada[4]; J. Passchie[5]; G. Searle[5]; E. Pererva[5]; R. Gunn[5]; E. Rabiner[5]; M. Politis[1]; MIND-MAPS Consortium

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Background and Aims: This study investigates the potential link between mitochondrial energy dysfunction and synaptic impairment that may contribute to neurodegeneration in Amyotrophic Lateral Sclerosis (ALS). We present preliminary findings from an ongoing longitudinal in-vivo imaging study of mitochondrial complex-1 (MC1), synaptic vesicle protein-2A (SV2A), and sigma-1 receptor (S1R), in ALS patients.

Methods: Nine patients with sporadic ALS (mean age: 59.1±9.7 years, King's staging: 2.42±1.08), and nine matched healthy controls (HC, mean age: 54.2±13.7 years), underwent clinical evaluation, a 3T MRI, and PET/CT scans using [18F]BCPP-EF for MC1, [11C]UCB-J for SV2A, and [11C]SA-4503 for S1R. Analysis deployed the Clinical Imaging Centre atlas for cortical and subcortical Region of Interest (ROI). Volume of distribution (VT) was the primary outcome measure for each tracer. Additional measures included VT corrected for plasma free fraction (VT/fp), and Distribution Volume Ratio minus 1 (DVR-1), using the Centrum Semiovale as reference. Due to notable volumetric differences between ALS and HC in cortical and subcortical ROIs, partial volume correction was applied.

Results: The ALS cohort had a mean ALSFRS of 41.44±4.5. Trends of lower [18F]BCPP-EF VT was observed in ALS patients, with significant difference in the amygdala (-16.4%, $p=0.026$). Conversely, [11C]UCB-J VT was significantly greater in the posterior cingulate (+11.2%, $p=0.036$) in ALS. No significant differences were detected in [11C]SA-4503 binding.

Conclusion: These preliminary, cross-sectional findings, provide initial evidence of altered MC1 and SV2A expression in ALS patients, compared with healthy controls. Collection of clinical and imaging data for up to 16 ALS patients, at baseline and at follow-up, is ongoing.

Disclosure: This research was conducted with support from Invicro, a Konica Minolta Company and the MIND-MAPS Consortium, incorporating AbbVie, Inc., Biogen, Inc., Celgene, Inc., Pfizer, Inc., and Takeda, Inc. EAR is an employee of Invicro, KCE was an employee and stock-holder of Biogen at the time the study was conducted. RAC is an employee and shareholder of AbbVie Inc.

EPO-505 | Synaptic density loss in patients with multiple system atrophy: An in-vivo [11C]UCB-J PET molecular imaging study

H. Wilson[1]; E. de Natale[1]; A. Terry[1]; J. Verghese[1]; G. Pagano[1]; P. Khosropanah[1]; L. Passamonti[2]; R. Hutchison[2]; K. Evans[2]; H. Wright[1]; M. Howard[1]; L. Cashmore[1]; Y. Lewis[3]; E. Rabiner[3]; M. Politis[1]

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Background and Aims: This study represents an initial in-vivo investigation of pre-synaptic terminal density in patients with Multiple System Atrophy (MSA), using the synaptic vesicle glycoprotein 2A (SV2A) selective PET radioligand [11C]UCB-J.

Methods: Ten MSA patients classified according to the 2022 Movement Disorders Society diagnostic criteria ($n=5$ MSA-P; $n=5$ MSA-C, age: 61.6±5.7), underwent a [11C]UCB-J PET scan with arterial blood collection. For comparison, [11C]UCB-J PET previously acquired from 11 Parkinson's disease (PD, age: 59.0±9.0) and 16 healthy controls (HCs, age: 61.4±12.5). We employed a one tissue-compartment model to calculate total volumes of distribution (VT) for each a priori defined region-of-interest, and subsequently calculated a regional distribution volume ratio parameter (VTROI/ VTCSO=DVR-1) using the centrum semiovale (CSO) as a pseudo-reference region.

Results: [11C]UCB-J DVR-1 was significantly decreased in MSA compared to HCs in the putamen (-17%; $p=0.001$), brainstem (-39%; $p=0.022$) and cerebellum (-22%; $p=0.003$). MSA-P exhibited a reduction in [11C]UCB-J DVR-1 in the putamen compared with HCs (-27%; $p<0.001$) and PD (-20%; $p=0.05$), and additionally in the brainstem (-42%; $p=0.03$) and cerebellum (-26%; $p<0.001$) compared to HCs. MSA-C showed decreased [11C]UCB-J DVR-1 in the cerebellum (-18%; $p=0.053$) compared to HCs. [11C]UCB-J DVR-1 in the putamen was lower in MSA-P compared to MSA-C (-28%; $p=0.014$). Alternative outcome parameters (VT and VT/plasma free fraction) showed similar patterns of reduction.

Conclusion: Our initial findings show evidence of reduced SV2A density in brain regions known to be affected by MSA pathology. Baseline and longitudinal follow-up data collection is ongoing to assess if [11C]UCB-J PET can effectively track disease progression.

Disclosure: This research was conducted with support from Invicro, a Konica Minolta Company and the MIND-MAPS Consortium, incorporating AbbVie, Inc., Biogen, Inc., Celgene, Inc., Pfizer, Inc., and Takeda, Inc. EAR is an employee of Invicro, KCE was an employee and stock-holder of Biogen at the time the study was conducted.

EPO-506 | Abstract withdrawn

EPO-507 | Functional connectivity and microstructural integrity changes in Amyotrophic Lateral Sclerosis

P. Khosropanah[1]; H. Wilson[1]; E. Rosario de Natale[1]; J. Verghese[1]; A. Terry[1]; L. Passamonti[2]; K. Evans[2]; C. Bishop[3]; J. O'Callaghan[3]; E. Rabiner[3]; M. Politis[1]

[1]Neurodegeneration Imaging Group, University of Exeter Medical School, UK; [2]Biogen, Cambridge, MA, USA; [3]Invicro Centre for Imaging Sciences, Hammersmith Hospital, London UK

Background and aims: This study aims to provide a comprehensive analysis, integrating structural, microstructural, and functional aspects, to understand brain changes and functional reorganization in Amyotrophic Lateral Sclerosis (ALS) through Magnetic Resonance Imaging (MRI). This differs from prior research focusing on individual MRI aspects.

Methods: We conducted 3-Tesla MRI scan on twelve ALS patients (age=56±12.3) and sixteen healthy (age=56±15.8) individuals. The sequences included diffusion tensor imaging, resting-state functional MRI, and structural-MRI. We analysed fractional anisotropy (FA), local functional connectivity, and cortical thickness using Tract-Based Spatial Statistics, Regional Homogeneity (ReHo), and surface-based methodologies, respectively.

Results: ALS patients exhibited significant atrophy in the bilateral precentral gyrus, left temporal pole, right-caudal-middle frontal gyrus, and pars-opercularis ($p<0.01$). Left precentral atrophy correlated with King's scale-staging (r=-0.67, $p=0.022$). Compared to controls, ALS showed altered local signal coherence (ReHo) in multiple regions (pAlphaSim<0.05, cluster-size >45 voxels), including frontal lobes, occipital, hippocampal areas, fusiform gyrus, and cingulum. ReHo was decreased in regions displaying significant atrophy ($p<0.05$), except for increased coherence in the right precentral. Reduced ReHo in the right middle frontal gyrus correlated with worse executive function on ECAS (r=0.73, $p=0.009$). FA was reduced in ALS in the bilateral posterior thalamic radiation, superior longitudinal fasciculus, posterior and anterior limb of internal capsule, corona radiata, cerebral peduncle, corpus callosum (body and splenium), motor fibers, fornix, and sagittal stratum ($p<0.05$).

Conclusion: Our multiparametric MRI study highlights complex compensatory mechanisms in ALS brain. Cortical atrophic areas, especially precentral, showed increased local functional connectivity. This underscores the intricate interplay between structural and functional changes in ALS.

Disclosure: This research was conducted with support from Invicro, a Konica Minolta Company and the MIND-MAPS Consortium, incorporating AbbVie, Inc., Biogen, Inc., Celgene, Inc., Pfizer, Inc., and Takeda, Inc. EAR is an employee of Invicro, KCE was an employee and stock-holder of Biogen at the time the study was conducted.

EPO-508 | Lipopolysaccharide induced microglial activation in Parkinson's disease patients: An in vivo PET study

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Background and Aims: Neuroinflammation plays a critical role in Parkinson's disease (PD) pathophysiology, but the exact underlying mechanisms are still unclear. We present preliminary data of an in vivo Positron Emission Tomography (PET) study with [11C]PBR28 and a pharmacological challenge with Lipopolysaccharide (LPS), aiming to visualise acute translocator protein (TSPO) changes reflecting microglial activation in PD.
Methods: Four people with Parkinson's (PwP), three with early disease (mean age 63.3±15 years) and one with MCI (age 61 years), and three healthy controls (mean age 61.33±10.41 years), underwent a PET/MR scan with [11C]PBR28 before, and four hours after intravenous injection of LPS (dose: 1ng/Kg). Percentage change of volume distribution (VT) in cortical and subcortical regions of interest was calculated with the formula %ΔVT = [(VTpostLPS/VTpreLPS) −1] x 100.
Results: PwP with early disease showed higher post-LPS TSPO levels compared to controls, more marked in frontal cortex (42.6% vs 32.1%), temporal cortex (45.4% vs 34.0%), hippocampus (34.3% vs 21.8%), amygdala (48.1% vs 13.6%), thalamus (48.8% vs 32.9%) and midbrain (38.8% vs 18.7%). The PwP with MCI showed smaller change of TSPO levels after LPS challenge in frontal cortex (15.2%), temporal cortex (13.4%), hippocampus (13.5%), amygdala (8.6%), thalamus (15.1%), and midbrain (15.0%).
Conclusion: These preliminary data show a trend for the differential widespread expression of microglial activation of PwP and healthy controls following a challenge with LPS which may provide valuable insights in the understanding of innate immune response. The process of gathering more data from additional PwP and healthy control subjects is currently in progress.
Disclosure: G.P., A.E.T., B.Z., and V.M. are full-time employees and shareholders of F.Hoffmann-La Roche Ltd.

EPO-509 | MRI–based radiomics features to predict post-stroke cognitive impairment: A pilot study

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Background and Aims: Post-stroke cognitive impairment (PSCI) occurs in about 20% of acute ischemic stroke (AIS) patients within the first months and is associated with poor long-term prognosis. MRI radiomics surpasses standard MRI in assessing the heterogeneity of AIS lesions and the subtle regional changes. This study aimed to develop a predictive model incorporating MRI radiomics features and clinical factors to accurately predict PSCI six months after AIS.
Methods: Data were collected from 40 patients with first-ever symptomatic supratentorial AIS confirmed by brain MRI without a history of cognitive impairment or dementia. AIS lesions were segmented using ADC and FLAIR images. First- and second-order statistics radiomics features were extracted using PyRadiomics software. Neuropsychological assessments consisting of the Montreal Cognitive Assessment test, Digit Symbol, Digit Backward, Stroop Color-Word Test, and Rey Auditory Verbal Learning test were performed one and six months after AIS.
Results: Baseline modified Rankin scale, National Institutes of Health Stroke Scale (NIHSS) score and radiomics score were independent predictors of PSCI. The area under the ROC curve of the clinical-radiomics model was 0.84 in the training cohort and 0.87 in the validation cohort.
Conclusion: The clinical-radiomics models outperformed individual clinical or radiomics models and seem to be a useful tool in predicting PSCI.
Disclosure: Nothing to disclose.

EPO-510 | New Year, new headache: A case report of spontaneous intracranial hypotension following a fall on New Year's Eve

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Background and Aims: Spontaneous intracranial hypotension (SIH) is characterised by postural headache and is usually associated with cerebrospinal fluid (CSF) leaks. The main reasons for CSF leaks include dural tears and meningeal diverticula [1]. Tarlov cysts, CSF filled perineural cysts, constitute a very cause of SIH.
Methods: A 26-year-old female presented to the emergency department with postural headaches following a fall on New Year's Eve. Spinal magnetic resonance imaging (MRI) revealed a large sacral Tarlov cyst, as well as fluid accumulation along the S1 nerve root and free fluid in the presacral area. Cerebral MRI disclosed bilateral subdural hygromas. Digital subtraction myelography (DSM) and postmyelographic CT revealed a communication between the Tarlov cyst, the epidural and intrathecal spaces as well as a pathologic contrast distribution pattern beyond the cyst. Conservative management, encompassing bed rest, analgesics, caffeine, and intravenous fluids, was initiated.
Results: After ten days of conservative treatment, the patient achieved sufficient symptom control, even after discontinuation of all analgesics. Gradual mobilization was successful, leading to discharge after a total of 14 days.

Conclusion: Clinical and imaging findings indicated spontaneous intracranial hypotension, triggered by a traumatic rupture of an unusually large Tarlov cyst. The success of conservative management in this case suggests that, even with traumatic dural tears, a watchful waiting strategy may be considered before opting for more invasive interventions such as autologous blood patch or surgical treatment.
Disclosure: Nothing to disclose.

EPO-511 | Nerve ultrasound versus MR-Neurography monitoring disease course in chronic inflammatory demyelinating polyneuropathy

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Background and Aims: We evaluated nerve ultrasound (NUS) and magnetic resonance neurography (MRN) for the longitudinal assessment of patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).
Methods: Twelve CIDP patients, who had received an initial MRN and NUS examination in 2016, were re-examined six years later in 2022. The cross-sectional area (CSA) of all peripheral nerves were evaluated with NUS bilaterally. The lumbosacral plexus, and sciatic, tibial and fibular nerves were evaluated using MRN (T2 weighted imaging and diffusion tensor imaging (DTI)). Imaging parameters were compared between time-points in correlation to clinical assessment.
Results: Over six years, nerve CSA of CIDP patients decreased at the lumbosacral plexus in MRN ($p = 0.015$) and remained stable in NUS. Comparison of the MRN values of the tibial nerve and fibular nerve at the popliteal fossa with a Bland-Altman analysis showed of bias of 2.195 and − 1.903 respectively. Longitudinally, changes in CSA of the lumbosacral plexus (MRN) and tibial nerve (MRN and NUS) correlated with changes in the inflammatory neuropathy cause and treatment validated overall disability sum score (INCAT/ODSS) ($p = 0.006$). Nerve CSA in the initial scan in MRN and nerve ultrasound were inversely correlated with changes in the INCAT/ODSS over six years ($p < 0.05$).
Conclusion: This study confirms the relevance of imaging studies for treatment monitoring in CIDP showing that nerve ultrasound and magnetic resonance neurography can provide reliably CSA values of proximal nerve segments and that changes in nerve CSA for proximal nerve segments reflects the clinical course of CIDP patients.
Disclosure: Nothing to disclose.

EPO-512 | Drop attacks as a presenting form of superficial central nervous system siderosis

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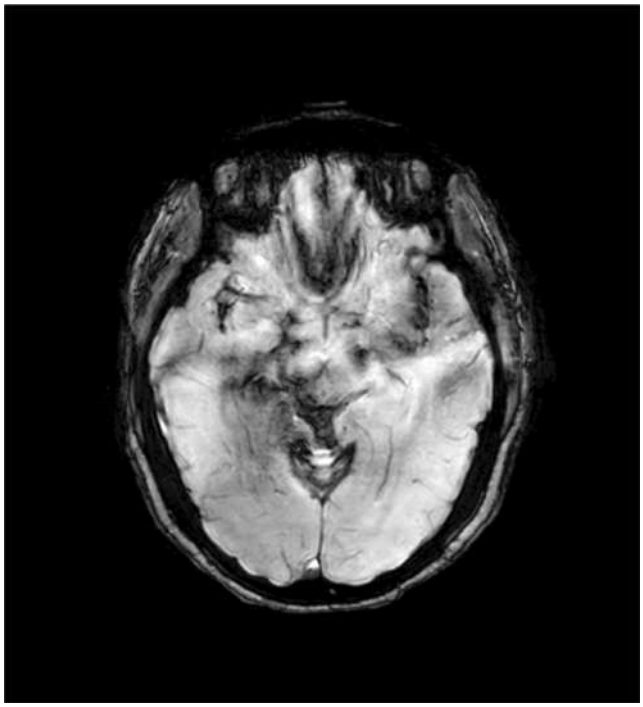
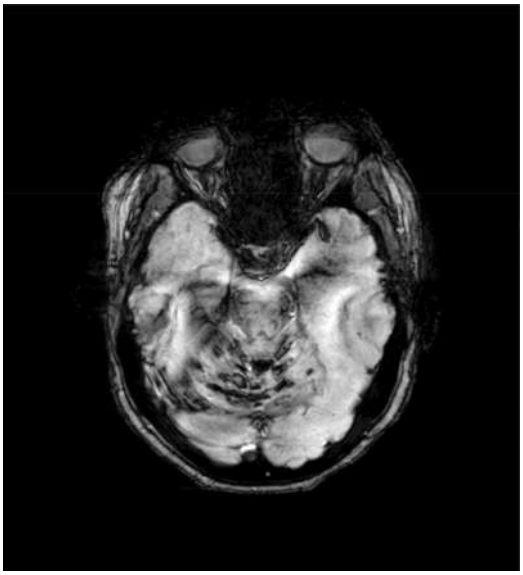
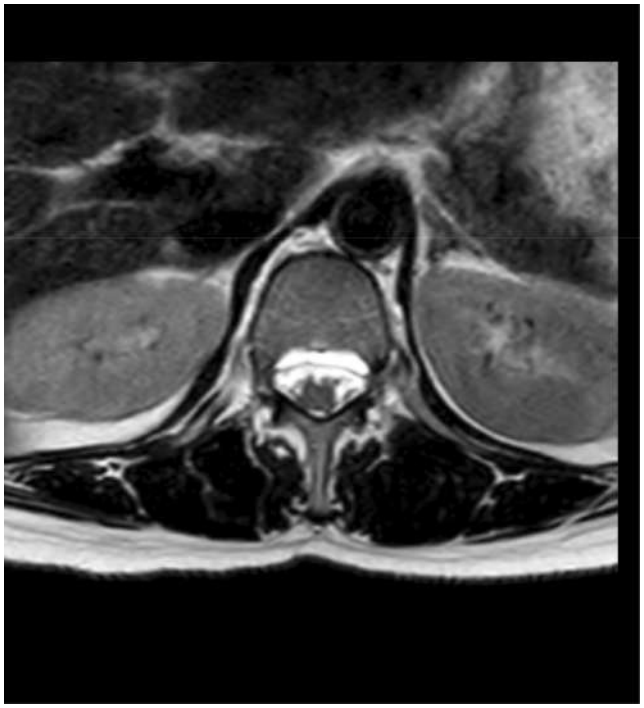
Background and Aims: Superficial siderosis of the CNS is a chronic condition with a broad differential diagnosis consisting of hemosiderin deposition in the subpial layers of the brain and spinal cord due to chronic bleeding into the subarachnoid space.
Methods: A 41-year-old female patient attended at neurology clinic for 4 months history of episodes consisting in sudden falls without warning. The patient's gaze remained fixed, with no speech, no sphincter relaxation or other abnormal movements with recovery in a few minutes but with a feeling of "slowness". The neurological examination is normal. In view of the suspicion of possible complex focal seizures, an EEG study was requested, as well as cranial and spinal MRI.
Results: EEG showed only isolated theta wave bursts of sharp morphology in the right temporal region. Axial T2-weighted brain MR images show hemosiderin deposition along the cerebellar folia, vermis and around the midbrain, pons and Sylvian fissures. Lumbar cord MRI T2-weighted image showed a fluid-filled epidural collection anterior to the spinal cord.



Axial T2_Sylvian fissures



Axial T2_cerebellar folia, midbrain, pons



Lumbar cord

Conclusion: Superficial central nervous system siderosis has a myriad of underlying aetiologies, which vary according to the age of presentation. The clinical picture is varied, depending on where the haemosiderin deposits are located, ranging from asymptomatic cases to frequent symptoms such as gait ataxia, hearing loss or myelopathy. Seizures may occur in less than 5% of patients.
Disclosure: Nothing to disclose.

EPO-513 | Neuroimaging of the brain in children with myotonic dystrophy type 1

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Background and Aims: Myotonic dystrophy type 1 (DM1) is characterized by multisystem symptoms, in particular damage of the central nervous system. The purpose of the study was to evaluate changes in brain in children with different forms of DM1.
Methods: 13 children underwent magnetic resonance imaging (MRI) on a Magnetom Avanto Siemens Healthineers (Germany) with a magnetic induction value of 1.5 Tesla using a head coil. The MRI protocol included T1, T2 and T2 FLAIR weighted sequences (WI).
Results: All children with congenital DM1 had changes in the brain based on MRI. Lesions in the white matter were identified in 66.7%, including periventricular localization (50%), frontal and temporal (33.3%), parietal and occipital (16.7%). A third of patients with congenital DM1 have ventriculomegaly. Only two patients (28.6%) with the childhood form had hyperintense foci in the periventricular region and frontal regions of the brain on MRI. The pattern of lesions in the white matter of the temporal regions characteristic of DM1 was not detected in any patient, either with congenital or childhood forms. Signs of atrophy of the gray matter of the brain when assessed on the GCA scale were detected in 66.7% of patients with the congenital form. Patients with the childhood form were not characterized by gray matter damage.
Conclusion: The congenital form of DM1 is characterized by more pronounced damage white and gray matter of the brain compared to the childhood form. Children are not characterized by a specific pattern of hyperintensity of the temporal poles, which apparently appears at a later age.
Disclosure: Nothing to disclose.

Epilepsy 3

EPO-514 | Abstract withdrawn

EPO-515 | Epileptic seizures and cardiac disturbances: Expanding the brain-heart connection

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Background and Aims: The objective of this work is to analyse cardiac rhythm disorders induced by epileptic seizures registered in a long-term video-electroencephalography (v-EEG) monitoring unit.
Methods: Single-centre retrospective study of cases of ictal bradycardia, atrioventricular block (AVB), asystole and atrial fibrillation (AF) in patients admitted to the long-term v-EEG monitoring unit of our hospital, between 2012 and 2023. We excluded cases with ictal tachycardia due to its high frequency and those with cardiac arrhythmia.
Results: Cardiac rhythm disorders produced by a concomitant ictal discharge were documented in 30 patients (3'3%) out of 908 monitoring conducted over the 12 years of the study. Ictal bradycardia was detected in 19 patients (2.1%), 7 of them occurring in the postictal phase; 9 patients (1%) presented ictal asystole, with the lengthiest episode lasting 31 seconds; 1 patient (0.1%) had ictal AVB, and 1 patient (0.1%) experienced ictal AF. Long-term v-EEG monitoring revealed a temporal onset in 21 patients and an extratemporal onset in 9 patients, which usually were frontal or fronto-central. Among the recorded cases of ictal asystole, 2 patients required pacemaker placement. No patient experienced Sudden Unexpected Death in Epilepsy (SUDEP).
Conclusion: Ictal cardiac rhythm disturbances are an uncommon, poorly known, and underdiagnosed entity that have prognostic implications due to their association with increased morbidity and mortality. In our series, they were mostly related to epilepsies with temporal onset or involvement. The role of combined long-term v-EEG and electrocardiographic (ECG) monitoring is essential for their diagnosis, particularly in patients who exhibit sudden generalized hypotonia during epileptic seizures.
Disclosure: No disclosure to declare.

EPO-516 | Status epilepticus and acute cauda equina syndrome following intrathecal lidocaine administration: A case series

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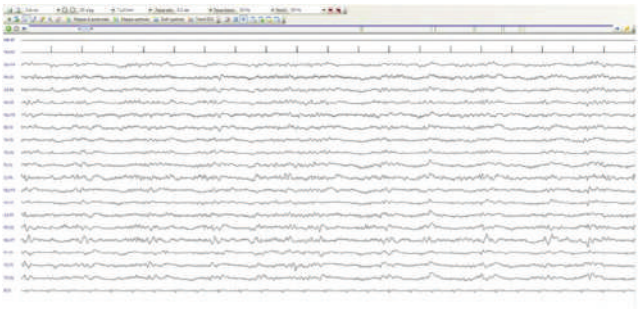
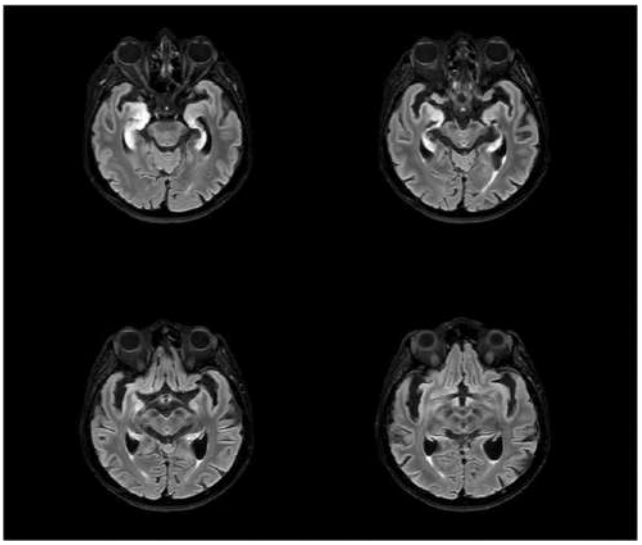
Background and Aims: Lidocaine (LA) is a widely used local anesthetic and analgesic, and a potential therapeutic option for status epilepticus; however, due to its neurotoxicity, it carries an associated risk of inducing life-threatening seizures and other neurological condition. The semiology and the treatment of these induced seizures remain poorly understood.
Methods: To describe the seizure-related behavior, clinical presentation, electroencephalographic patterns, and management strategies associated with incidental intrathecal LA administration.
Results: We present the three cases of two female of 80- and 42-year-old and a 39-year-old man who developed sudden cauda equina syndrome, bilateral mydriasis, altered state of consciousness, trismus, and clonic movements in the limbs after incidental paravertebral LA injection for chronic lumbar back pain. All patients were admitted to Intensive Care Unit. Blood and CFS tests were unremarkable. In two cases EEG showed generalized and lateralized periodic pattern. In one case, brain MRI showed bilateral hippocampal cytotoxic edema. Outcomes were various, one patient died and another developed mild cognitive impairment.



EEG_second_patient



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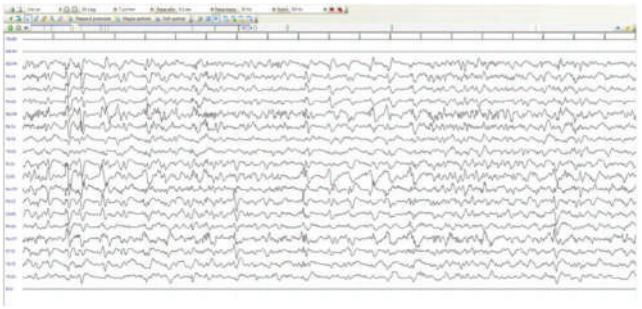

EEG_first_patient

Conclusion: To this day, toxicity of intrathecal lidocaine administration is not clearly defined. This work can help healthcare personnel to provide accurate management of this rare iatrogenic condition.
Disclosure: Nothing to disclose.

EPO-517 | Digital biomarkers and cognitive proxies for personalized care in epilepsy

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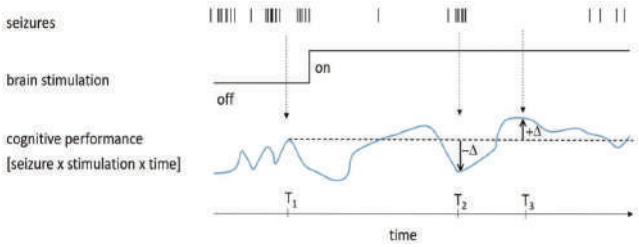
Background and Aims: Patients with epilepsy often suffer from cognitive impairments, including psychomotor speed, memory, attention, and executive function. The severity of these cognitive impairments may vary over time depending on seizure burden, interictal epileptic activity, medication and neuromodulation. In particular, intermittent deep brain stimulation may affect an individual's typical cognitive processing at short and intermediate time intervals. However, the severity and time course of these putative cognitive changes at the individual level cannot be adequately assessed by traditional neuropsychological tests.
Methods: Here we present pilot data from serial neuropsychological assessments in a cohort of pharmaco-resistant epilepsy patients in a controlled ANT-DBS ON/OFF/ON paradigm over several days ($n = 10$).
Results: We observed recognizable but partly inconsistent DBS effects on cognitive test performance, mainly in verbal and non-verbal memory domains, associated with active ANT-DBS. These results suggest that immediate (<24 h) and intermediate (>24h) patterns of DBS-induced cognitive effects may act independently. However, the time course of these dynamic changes is currently difficult to monitor using repeated point measures of neuropsychological test performance.
Conclusion: These partly inconsistent results favor a novel diagnostic approach: The widespread accessibility of smart devices offers new opportunities to use passively accessible biomarkers (heart rate, movement, written communication) as proxies for cognitive function in a continuous manner. We propose to use ecological "digital cognitive proxies" from smart devices that infer mental capacity from the speed, results and errors in cognitive tasks such as navigation, memory (codes, names, shortcuts), reading speed and writing errors to guide optimal personalized treatment while monitoring cognitive side effects.
Disclosure: None.



Cognitive performance in a particular domain (e.g. memory) fluctuates over time and is influenced by the interaction of seizure burden, pharmacotherapy, or neuromodulation. Point measurements over long periods of time (T1-T3) do not reveal the true fluctu.

EPO-518 | First seizure clinic: Experience at a tertiary hospital in Madrid

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Neurology, Fundación Jiménez Díaz Hospital, Madrid, Spain

Background and Aims: The diagnosis of epilepsy after a first seizure can be a challenge in clinical practice. The aim of this study was to analyze the diagnostic yield of a First Seizure Clinic (FSC) and describe the determining factors to establish a diagnosis of epilepsy.
Methods: Retrospective chart review for all patients referred to our FSC between June 2019 and December 2023. Our protocol includes a clinical evaluation within 1-6 days by an epilepsy specialist, a 1-hour sleep video-EEG and a brain-MRI.
Results: Ninety-five patients were included, 49/95 (51.6%) were diagnosed at the first visit: 28/95 (29.5%) were diagnosed of epilepsy and 21/95 (22.1%) with non-epileptic events. The diagnosis of epilepsy was based on the presence of previous unrecognized seizures in

11/28 patients (39.3%), on an abnormal EEG in 10/28 patients (35.7%), and on an abnormal MRI in 1/28 (3.6%). Eight patients lost follow-up after the first visit. During follow up, another 8 patients were diagnosed with epilepsy: 5/8 based on overnight video-EEG abnormalities and 1/8 on an abnormal MRI. Only in 2 patients the diagnosis remained unclear after follow-up. In the non-epileptic events group the diagnoses were convulsive syncope, anxiety, acute symptomatic seizures and TIAs.

Conclusion: In the setting of the FSC in our center, the diagnosis of epilepsy was mainly reached after a comprehensive clinical history and a 1 hour video-EEG. When the diagnosis of epilepsy remains unclear after a first seizure, an overnight video-EEG should be prioritized over brain MRI.

Disclosure: Nothing to disclosure.

EPO-519 | The impact of drug-resistant epilepsy in an outpatient clinic of a tertiary hospital

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Background and Aims: We aimed to describe the differences in medical management and complications between refractory and non-refractory epilepsy patients.

Methods: Longitudinal prospective study including adult patients with epilepsy (PWE) evaluated at least once in an outpatient clinic of a tertiary hospital during 2023. Demographic and clinical data were collected, and emergency department consultations (ED) and antiseizure medications (ASM) were documented at each visit. Patients were categorized into non-resistant or drug-resistant epilepsy (DRE) according to the ILAE criteria.

Results: 2835 PWE (4935 visits; 51.1% men) were included, of which 785 (27.7%) had DRE. Drug-resistance was more common in focal epilepsy (29.7% vs. 19.6% in generalized epilepsy; $p<0.001$), in younger patients (44.1±17.8 vs. 51.1±20.7 years; $p<0.001$), and in patients with an earlier onset (24.3±22.4 vs. 42.4±26 years; $p<0.001$). DRE rate was significantly higher ($p<0.001$) in mesial temporal sclerosis (69.9%), malformations of cortical development (54.4%), genetic (46.1%) and perinatal hypoxia (44.4%). Patients with DRE accounted for a higher rate of outpatient consultations [median per patient/year: 2 (1-3) vs. 1 (1-2), $p<0.001$], ED consultations (25.5% vs. 16.9%; $p<0.001$) and traumatic injury resulting from seizures (2.1% vs. 0.8%; $p=0.014$). ASM changes were also higher in DRE patients (43.7% vs. 20.2%, $p<0.001$), especially in patients with mesial temporal sclerosis (49.5% vs 28%; $p<0.001$).

Conclusion: In our cohort, DRE patients exhibit a younger age, an earlier onset, and a higher prevalence of focal-related etiologies. They generate more outpatient and ED consultations and more changes in ASM regimen. These results reflect the challenge of managing these cases in clinical practice.

Disclosure: Nothing to disclose.

EPO-520 | Towards therapeutic innovation in temporal lobe epilepsy: Focal adenosinergic modulation of hippocampal excitability

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Background and Aims: The adenosine A1 receptor (A1R) is a promising therapeutic target in epilepsy by mediating neuronal inhibition. In this study, we investigated whether A1R signaling is still functional in the intrahippocampal kainic acid (IHKA) mouse model for temporal lobe epilepsy (TLE). The feasibility of spatial selective inhibition was evaluated by illumination of specific hippocampal subregions for optical uncaging of CPA from coumarin-caged CPA (cCPA).

Methods: In the CA1 and DG of acute hippocampal slices, the effect of adding 40 nM of the A1R agonist N6cyclopentyladenosine (CPA) on population spike (PS) amplitude to field postsynaptic potential (fPSP) slope, an index of excitability, was evaluated in epileptic IHKA versus healthy mice. Subregion selective inhibition of fPSPs was evaluated through application of 405nm light pulses (10 pulses of 100ms at 0.1Hz) spatially restricted to CA1 or DG of healthy slices incubated with 3μM cCPA.

Results: Administration of CPA resulted in a similar decrease in PS amplitude to fPSP slope ratio in epileptic versus healthy mice for the CA1 and DG ($n=19$, Figure1). In a slice incubated with cCPA, the excitability decreased selectively in the illuminated hippocampal subregion ($n=1$, Figure 2).

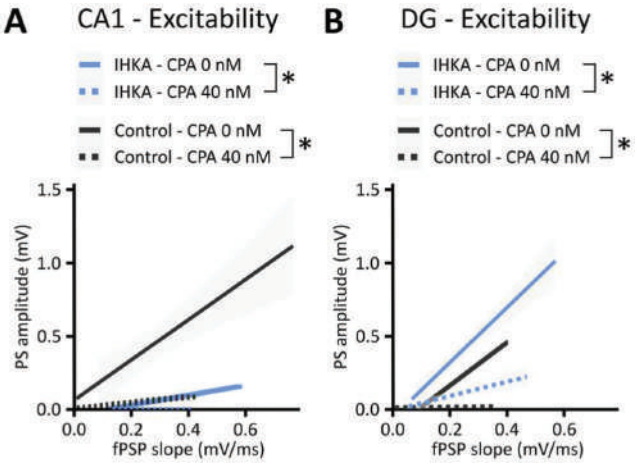

FIGURE 1 Similar decrease in CA1 and DG excitability (PS amplitude in function of fPSP slope) in epileptic IHKA versus healthy mice after administration of 40nM CPA. Data are shown as mean ± SEM. *$p<0.01$.

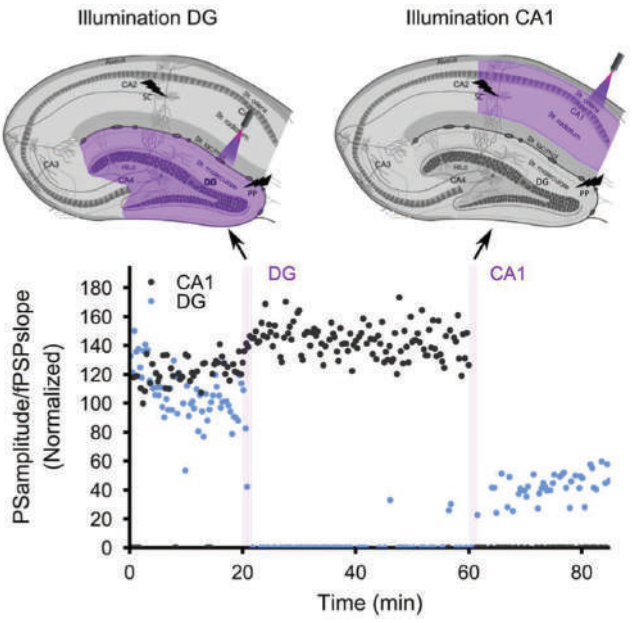

FIGURE 2 cCPA and focal illumination of DG or CA1 results in a decreased excitability (PS amplitude to fPSP slope) selectively in the illuminated region ($n = 1$).

Conclusion: The decrease in excitability is comparable in hippocampal slices of IHKA versus healthy mice upon exposure to CPA, indicating preserved A1R signaling in IHKA mice. The use of cCPA allows modulation of hippocampal subregions through localized illumination. These results indicate that photopharmacology has the potential to become a targeted therapy for TLE.

Disclosure: This research is funded by the Ghent University Special Research fund.

EPO-521 | Is the salivary concentration of lamotrigine and levetiracetam associated with clinical outcome and side effects?

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Background and Aims: The correlation between plasma and saliva concentration of anti-seizure medication (ASM) is well established. However, clinical acceptance of saliva therapeutic drug monitoring (TDM) is constrained by significant variability and limited sensitivity. We analysed the correlation between salivary levetiracetam and lamotrigine levels, and clinical efficacy and tolerance.

Methods: We collected blood and saliva samples over two years. Seizure freedom, defined as three times the longest pre-treatment inter-seizure interval or one year seizure-free without treatment changes, and adverse effects were assessed during programmed visits. Predictors of treatment response and adverse events were adjusted in a binary logistic regression model. Lamotrigine and levetiracetam median salivary and plasmatic concentrations were compared between groups categorised by treatment response and adverse effects.

Results: Among 296 adults with epilepsy, 84 (28%) achieving seizure freedom, were older, predominantly on monotherapy, and underwent fewer past ASM trials. 27 (9%), reporting adverse effects, had an older age at epilepsy onset. Seizure-free individuals on lamotrigine had a lower medication dosage (median 2.03 vs 3.26 mg/kg, $p = 0.07$) and salivary concentrations (median 1.39 vs 2.4 mg/L, $p = 0.11$). For levetiracetam, seizure-free individuals displayed lower plasma levels and medication dosage (median dosage 10.87 vs 19.23 mg/kg, $p < 0.000$), while those reporting side effects showed higher salivary concentrations (median 20 vs 14.40 mg/L, $p = 0.04$).

	TOTAL	ADV. EVENTS N= 27	NO ADV. EVENTS N= 269	P-VALUE	TEST USED	SEIZURE-FREE N= 84	ONGOING SEIZURES N= 190	P-VALUE	TEST USED
GENDER, FEMALE (PERCENTAGE)	159 (54%)	18 (67%)	141 (52%)	0.157	Pearson chi-square	39 (46%)	106 (56%)	0.152	Pearson chi-square
AGE, YEARS (MEDIAN, RANGE)	37 (17 - 82)	45 (20-81)	36 (17-82)	0.083	U Mann-Whitney	40 (19-74)	35 (17-82)	**0.045**	U Mann-Whitney
EPILEPSY DURATION, YEARS (MEDIAN, RANGE)	8.5 (0- 59)	9 (0-47)	8 (0-59)	0.265	U Mann-Whitney	9 (0-55)	8 (0-59)	0.355	U Mann-Whitney
AGE AT EPILEPSY ONSET, YEARS (MEDIAN, RANGE)	22 (15- 80)	31 (2-80)	21 (15-80)	**0.038**	U Mann-Whitney	22 (1-72)	22 (15-80)	0.307	U Mann-Whitney
GENERALIZED EPILEPSY	87 (29%)	5 (18%)	82 (30%)	0.182	Pearson chi-square	30 (36%)	45 (24%)	**0.045**	Pearson chi-square
STRUCTURAL EPILEPSY	147 (50%)	15 (55%)	132 (49%)	0.557	Pearson chi-square	44 (52%)	96 (50%)	0.841	Pearson chi-square
NUMBER OF PREVIOUS ASMS (MEDIAN, RANGE)	2 (1-10)	1 (0-6)	1 (0-10)	0.245	U Mann-Whitney	1 (1-7)	1 (1-10)	**0.021**	U Mann-Whitney
MONOTHERAPY	171 (58%)	15 (56%)	156 (58%)	0.807	Pearson chi-square	61 (73%)	94 (49%)	**0.000**	Pearson chi-square
PREVIOUS PSYCHIATRIC HISTORY	67 (23%)	7 (26%)	60 (22%)	0.699	Pearson chi-square	20 (24%)	38 (20%)	0.331	Pearson chi-square

TABLE General characteristics of participants.

Conclusion: This study provides insights about clinical relevance of saliva TDM, linking salivary levels to clinical response for lamotrigine, and adverse events for levetiracetam. Further validation on a larger scale and with other ASM is essential for strengthening these findings.

Disclosure: This study (NCT0273928clinical trials.gov) was independently monitored and funded by the Swiss National Scientific Foundation (grant 320030_163430 to JN). PV received personal funding for research from Ancrage Foundation and Novartis Stiftung für medizinisch-biologische Forschung unrelated to the current project. This external support played no role in the design, execution, or analysis of the present study.

EPO-522 | Abstract withdrawn

EPO-523 | Neuroimaging as a SUDEP predictor: what is known and what still needs to be uncovered? A systematic review

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Department of Neuroscience, Imaging and Clinical Science, "G. D'Annunzio" University of Chieti-Pescara, Chieti, Italy

Background and Aims: Sudden Unexpected Death in Epilepsy (SUDEP) is the most common cause of death in patients with poorly controlled epilepsy. To date, a higher risk of developing SUDEP is mainly identified by clinical factors, among which generalized tonic-clonic seizures and their frequency stand out. This review investigates the role of neuroimaging-based approaches as a tool to help predicting SUDEP.
Methods: We reviewed twelve articles investigating 62 SUDEP cases assessed with a variety of neuroimaging techniques. We set to compare these 62 cases with 469 epileptic patients and 132 non-epileptic controls (overall mean age 31.5 ±7.7). MRI, fMRI, PET and SPECT were carried out in all these groups.
Results: SUDEP and non-SUDEP cases differ anatomically and functionally. MRI data indicate differences in gray matter volumes in the hippocampal and cerebellar cortex. In addition, functional imaging revealed discrepancies in terms of network modulation within the brainstem, whose metabolism and perfusion deviate from physiological values assessed by PET and SPECT scans.
Conclusion: Correlations between the occurrence of SUDEP and neuroimaging alterations are emerging, but their predictive significance must be the object of further intensive investigation.
Disclosure: Nothing to disclose.

EPO-524 | Identification of risk factors for drug resistant epilepsy

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Background and Aims: Drug-resistant epilepsy (DRE) represents a significant challenge for epileptologists, affecting approximately 30% of their patients. Early identification of people at risk for DRE is crucial for optimizing both pharmacological and non-pharmacological management strategies. Our study aims to pinpoint the risk factors associated with DRE within the patient population at the Epilepsy Centre of the University of Cagliari.
Methods: Data were retrieved from the medical records of people treated at our Epilepsy Centre. To identify predictive risk factors for DRE, we employed a combination of univariate analysis and logistic regression to assess the collective impact of various factors. We investigated different conditions linked to DRE, including gender, age of onset, etiology (structural, genetic), history of status epilepticus, type of seizures (focal, generalized, combined), learning disabilities, comorbidities, illness duration, and family history of epilepsy.
Results: Out of a total of 804 subjects, 201 were identified as having DRE (26%). Univariate analysis revealed a significant association between DRE and age of onset, structural etiology, presence of status epilepticus, type of seizure, presence of psychiatric and neurological comorbidities, learning disability, and family history of epilepsy. Subsequent multiple regression analysis identified several factors significantly associated with DRE, including age of onset, structural etiology, psychiatric and neurological comorbidities, and learning disability.

Risk factor	OR	95%CI	p value
Age	1.00	0.99 -1.01	0.955
Gender	0.97	0.69-1.36	0.863
Status epilepticus	3.71	1.20-11.45	**0.022**
Combined epilepsy	14.40	3.09-67.11	**0.001**
Structural etiology	1.63	1.12-2.37	**0.011**
Genetic etiology	1.27	0.61-2.67	0.524
Infectious etiology	1.99	0.87-4.55	0.102
Neurological comorbidities	0.92	0.63-1.33	0.643
Psychiatric comorbidities	1.72	1.17-2.52	**0.006**
Learning disability	2.87	1.87-4.42	**0.001**
Family history of epilepsy	1.94	1.13-3.33	**0.016**

OR: odds ratio; **CI:** confidence interval

Statistical analysis of risk factors.

Conclusion: The presence of a structural etiology, psychiatric and neurological comorbidities, learning disability, and early age of onset were identified as significant risk factors for DRE. Early identification of these factors holds promise for improving the management of affected people and refining clinical strategies.
Disclosure: Nothing to disclose.

EPO-525 | Late seizure relapse after anterior temporal lobectomy: The prevalence and its prognostic factors

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Background and Aims: We investigated the proportion of late seizure relapse (LSR) and its prognostic factors after epilepsy surgery in patients with drug-resistant temporal lobe epilepsy (TLE).
Methods: This retrospective study recruited 178 adults who underwent anterior temporal lobectomy (ATL). We excluded if they had seizure recurrence in the first two years after surgery and if they had less than 3 years of follow-up. Finally, 99 patients were included. Seizure freedom was defined as ILAE outcome class 1 and 2. LSR

was defined as seizure relapse after initial 2-year seizure freedom. The Cox regression analysis was performed. Age, sex, and the potential variables exhibiting a p-value of <0.2 in the univariate analysis were entered in the initial model.

Results: The follow-up period after surgery ranged 36 to 191 months. Hippocampal sclerosis was the most common pathology (71.7%). The rate of LSR was 29.3% and its timing was mean 44.0±16.2 months after surgery. Univariate analyses showed that the presence of seizure risk factor, extratemporal interictal epileptiform discharges (IEDs) during video-EEG monitoring, ATL without hippocampectomy, weekly seizure recurrence before surgery, and vascular etiology had a p-value of <0.2 in association with LSR. The Cox regression showed that LSR was independently predicted by the presence of extratemporal IEDs (odds ratio 4.597, $p=0.002$) and ATL without hippocampectomy (odds ratio 2.679, $p=0.027$).

Conclusion: About one third of TLE patients with initial 2-year seizure freedom after ATL may have LSR. TLE patients with extratemporal IEDs or ATL without hippocampectomy may be at high risk for LSR.

Disclosure: Nothing.

EPO-526 | Cognitive symptoms in autoimmune limbic encephalitis: Long term follow up

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Background and Aims: Cognitive impairment is one of the cardinal symptoms of autoimmune limbic encephalitis. This study aims to describe long-term cognitive profile in a group of 9 patients diagnosed with autoimmune limbic encephalitis.

Methods: Clinical data and detailed neuropsychological assessment were collected from 9 patients one year after the acute phase of encephalitis. The average age of the patients was 62 years. Seven patients were males. Neuropsychological battery explored verbal and visuo-spatial memory, language, attentive and executive functions. Cerebrospinal fluid analysis (CSF), brain magnetic resonance imaging, brain 18-fluorodeoxyglucose positron emission tomographic imaging were performed. In 89% of CSF analysis autoantibodies were found (LG1 50%; CASPR2 38%; Glu3 peptide A e B 12%).

Results: All the patients showed severe cognitive deficits in the acute phase. In the long-term follow up only 2 patients showed a full neuropsychological recovery. 56% of the 9 subjects had verbal memory deficits, while visual memory impairment was observed in 33% of patients. Attention was affected in 44% of patients, while executive functions were impacted in 22% of cases, respectively. No language domain impairment was observed in any patients. Only 33% of patients have resumed their previous work activity

Conclusion: Verbal memory emerged as the most frequently impaired cognitive domain in long-term follow up of autoimmune limbic encephalitis. However, other cognitive domains were also affected. Despite being considered a form of encephalitis with a benign prognosis, in our case series, patients exhibited long-term cognitive deficits with an impact on social and occupational functioning.

Disclosure: Nothing to disclose.

EPO-527 | Effectiveness and tolerability of cenobamate as add-on therapy: A historical monocentric comparative study

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Background and Aims: Cenobamate is a novel antiseizure medication approved in Europe for adjunctive therapy in adults with drug-resistant focal seizures. However, there are limited data from clinical practice. In this study, our new data on cenobamate were compared with our historical data on lacosamide, perampanel, and brivaracetam.

Methods: Data were collected from our three studies conducted between 2016 and 2023. The retention rate, 50% response rate, and seizure freedom rate at 6 months, as well as the frequency of adverse events, were evaluated. Cenobamate was compared with the three antiseizure medications. Using Bonferroni correction, a result was considered statistically significant at a p-value <0.017.

Results: A total of 391 patients were included. In terms of retention rate, cenobamate was superior to other antiseizure medications ($p<0.001$). There was no significant difference in the 50% response rates and seizure freedom rates between patients treated with cenobamate, lacosamide, brivaracetam, and perampanel. The frequency of adverse events was higher with perampanel than with cenobamate ($p<0.001$).

Conclusion: The results of this study show that cenobamate was a superior option for adjunctive therapy in refractory epilepsies in terms of retention rate in our patients. Significantly more adverse events occurred with perampanel. The higher retention rate under cenobamate therapy compared to other antiseizure medications can most likely be explained by the high efficacy of cenobamate with a more favorable side effect profile. Due to a possible bias of the results, further prospective randomized controlled trials are needed to confirm these results.

Disclosure: Bernhard J Steinhoff has served as a paid consultant for Angelini Pharma, B. Braun Melsungen, Eisai, GW Pharmaceuticals, and UCB. Other authors have nothing to disclose.

EPO-528 | Attributional bias – Misinterpretation of social behaviour in people with epilepsy

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Background and Aims: Attributional bias is characterised by an impaired ability to predict behaviour of our environment based on social cues. As a consequence, we judge intentions of others as hostile and harmful rather than the result of chance or external factors. People with epilepsy (PWE) find it challenging to engage in social activities or maintain stable employment. Misinterpreting social situations can contribute to their social maladaptation and lower quality of life.

Methods: We examined 53 PWE, 26 with idiopathic generalised epilepsy (IGE), 27 with temporal lobe epilepsy (TLE) from Motol Epilepsy Centre in Prague, and 43 healthy controls (HC). We used the Ambiguous Intentions Hostility Questionnaire (AIHQ) to assess attributional bias (social misinterpretation). It yields 3 scores - aggression bias (AB), hostility bias (HB) and blame score (BS) in different types of situations in terms of intentionality - accidental, ambiguous and intentional. The higher the score in AIHQ, the more impaired the social judgement. We measured depression by Neurological Disorders Depression Inventory in Epilepsy (NDDI-E).

Results: PWE scored higher than HC in AB in ambiguous situations. Both IGE and TLE groups demonstrated HB in ambiguous situations, but TLE group also in accidental situations and IGE group in intentional situations. Duration of the disease or antiseizure medication did not correlate with scores in AIHQ. NDDI-E scores correlated with HB in TLE group.

Conclusion: Attributional bias is an unexplored area of social cognition in PWE. This study suggests an impairment of social judgement which may contribute to social dysfunction and affect quality of life in PWE.

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Headache 3

EPO-529 | Efficacy of mindfulness added to treatment as usual in patients with chronic migraine and medication overuse headache

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Background and Aims: To assess the efficacy of a six-session mindfulness-based treatment added to treatment as usual (TaU) on headache frequency and medication intake.

Methods: This is a phase-III single blind RCT single-center study. Patients were enrolled between November 2018 and December 2021, and followed-up for 12 months. 177 patients with Chronic Migraine and Medication Overuse Headache (CM and MOH) were randomized 1:1 to either TaU or mindfulness added to TaU (TaU+MIND). Exclusion criteria were: psychiatric comorbidities; pregnancy; secondary headaches; withdrawal from MOH at least twice in the previous two years; previous experience with mindfulness. TaU consisted of withdrawal from overused drugs, patients' education, and prescription of prophylaxis. Patients attending mindfulness sessions were taught on tackling the pain-pill automatism, and were encouraged to engage in a 7-10 minute/day self-practice. The primary endpoint was the achievement, at 12 months of ≥50% headache frequency reduction compared to baseline. Secondary endpoints included medication intake.

Results: Out or the 177 participants (median age 47.9 years [Q1-Q3: 40.1-54.2]; 19 [11.3%] males; median CM duration 14.6 years [Q1-Q3: 4.9-22.2]) 89 were randomized to TaU and 88 to TaU+MIND. Patients in the TaU+MIND group outperformed those in TaU for the primary endpoint, achievement of ≥50% headache frequency reduction (78.4% vs 48.3%; $p < 0.0001$). They also showed superiority in some secondary endpoints, namely headache frequency and medication intake.

Conclusion: : These findings show that a six-week mindfulness-based treatment as add on to TaU is superior to TaU for the treatment of patient with CM and MOH

Disclosure: Nothing to disclose.

EPO-530 | Cerebral compliance in pseudotumor cerebri and transversus sinus stenosis undergoing venoplasty or CSF puncture

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Background and Aims: Pseudotumor cerebri (PTC) has a high prevalence among women, and 30% to 93% of patients have transverse sinus stenosis (TSS). In addition, venoplasty improves symptoms in up to 87% of patients. Intracranial complacency (IC) can be a surrogate marker for intracranial hypertension. The FDA approved a non-invasive Brazilian method for monitoring intracranial pressure waves, Brain4care (B4C), in 2021. We aimed to compare the IC in patients with PTC and TSS only with lumbar punctures (LP) versus venoplasty.

Methods: This is an observational and single-centered study from 2020 to 2022. Inclusion criteria: ≥18 years with PTC; with presence of TSS. Data were reported as mean (± SD) or median (± IQR). Categorical variables were reported as percentage and compared using the X2 test or Fisher's test. *p*-Values were considered significant when <0.05, using SPSS.

Results: We enrolled 158 patients, among whom nine were excluded due to age: 12 without PTC, 13 without stenosis, 22 with CVT and 35 with missing data. We analyzed 67 patients: In the LP group (50), we found 100% female, mean age 37.6 (SD: 11.6), B4C mean TTP 0.24 (SD: 0.07) in lay-position and 0.23 (SD: 0.06) in sit-position. In the venoplasty group (17), we noticed 88.2% females, with a mean age of 45.6. (SD: 12.6), B4C mean TTP 0.24 (SD: 0.07), and 0.23 (SD: 0.06) in positions. There were no differences in IC between the two groups.

Variable	Lumbar puncture	Venoplasty	Total	P-Value[1]
Age, mean ±SD	37.6 ± 11.6	45.6 ± 12.6	39.6 ± 12.3	0.029
Gender - Male	0/50 (0.0%)	2/17 (11.8%)	2/67 (3.0%)	0.062
Time of symptoms, mean ±SD	8.8 ± 12.4	10.0 ± 17.0	9.1 ± 13.6	0.794
BMI, mean ±SD	33.6 ± 6.4	29.5 ± 5.3	32.6 ± 6.3	0.012
Obesity	38/50 (76.0%)	9/17 (52.9%)	47/67 (70.1%)	0.123
Hypertension	11/50 (22.0%)	9/17 (52.9%)	20/67 (29.9%)	0.029
Diabetes	3/50 (6.0%)	0/17 (0.0%)	3/67 (4.5%)	0.565
Dyslipidemia	4/50 (8.0%)	3/17 (17.6%)	7/67 (10.4%)	0.358
Hypothyroidism	7/50 (14.0%)	3/17 (17.6%)	10/67 (14.9%)	0.706
Migraine	12/50 (24.0%)	7/17 (41.2%)	19/67 (28.4%)	0.217
Smoking	3/50 (6.0%)	2/17 (11.8%)	5/67 (7.5%)	0.595
Others	10/50 (20.0%)	2/17 (11.8%)	12/67 (17.9%)	0.716
Abnormal campimetry	19/38 (50.0%)	9/13 (69.2%)	28/51 (54.9%)	0.336
Abnormal OCT	8/21 (38.1%)	5/10 (50.0%)	13/31 (41.9%)	0.701
Papilledema	31/50 (62.0%)	10/17 (58.8%)	41/67 (61.2%)	0.999
Image				
CT	4/50 (8.0%)	1/17 (5.9%)	5/67 (7.5%)	0.803
MRI	45/50 (90.0%)	16/17 (94.1%)	61/67 (91.0%)	
Angiography	1/50 (2.0%)	0/17 (0.0%)	1/67 (1.5%)	
Bilateral stenosis	19/50 (38.0%)	10/17 (58.8%)	29/67 (43.3%)	0.163
Hypoplasia	4/50 (8.0%)	7/17 (41.2%)	11/67 (16.4%)	0.004
Empty sella	18/50 (36.0%)	6/17 (35.3%)	24/67 (35.8%)	0.999
Posterior scleral flattening	7/50 (14.0%)	3/17 (17.6%)	10/67 (14.9%)	0.706
Optic nerve tortuosity	12/50 (24.0%)	4/17 (23.5%)	16/67 (23.9%)	0.999
Optic disc protrusion	10/50 (20.0%)	2/17 (11.8%)	12/67 (17.9%)	0.716
Microangiopathy	5/50 (10.0%)	2/17 (11.8%)	7/67 (10.4%)	0.999
Visual acuity				
Normal	23/41 (56.1%)	7/12 (58.3%)	30/53 (56.6%)	0.562
Unilateral decreased	6/41 (14.6%)	3/12 (25.0%)	9/53 (17.0%)	
Bilateral decreased	12/41 (29.3%)	2/12 (16.7%)	14/53 (26.4%)	
Dose of medicines				
Acetazolamide, median [quartiles]	500.0 [0.0; 750.0] (n = 50)	0.0 [0.0; 500.0] (n = 17)	500.0 [0.0; 750.0] (n = 67)	0.005
Topiramato, median [quartiles]	50.0 [25.0; 100.0] (n = 50)	0.0 [0.0; 50.0] (n = 17)	50.0 [0.0; 75.0] (n = 67)	0.052

(1) Age, duration of symptoms and BMI were compared using t-student tests, medication doses using the Mann-Whitney test and the rest of the comparisons using the Chi-square test

Baseline characteristics

Variable	Lumbar puncture	Venoplasty	P-Value[1]	Mean difference [IC95%][3]	P-Value[2]
B4C_lay_mean	1.27 ± 0.27	1.25 ± 0.26	0.843	-0.04 [-0.17 to 0.10]	0.61
B4C_lay_median	1.27 ± 0.27	1.26 ± 0.26	0.879	-0.03 [-0.18 to 0.11]	0.63
B4C_lay					
P1>P2	1/50 (2.0%)	0/17 (0.0%)	0.835		
P2~P1	21/50 (42.0%)	7/17 (41.2%)			
P2>P1	28/50 (56.0%)	10/17 (58.8%)		OR[3] = 0.50 [0.11 to 2.18]	0.35
TimeToPeak_lay_mean	0.24 ± 0.07	0.24 ± 0.07	0.883	0.00 [-0.04 to 0.04]	0.91
TimeToPeak_lay_median	0.24 ± 0.07	0.24 ± 0.06	0.983	0.01 [-0.04 to 0.05]	0.73
TimeToPeak_lay	0.24 ± 0.06	0.22 ± 0.07	0.346	-0.02 [-0.06 to 0.02]	0.27
B4C_sit_mean	1.20 ± 0.19	1.22 ± 0.26	0.832	0.00 [-0.12 to 0.13]	0.97
B4C_sit_median	1.20 ± 0.20	1.21 ± 0.26	0.880	0.00 [-0.13 to 0.13]	1.00
B4C_sit					
P1>P2	1/50 (2.0%)	2/17 (11.8%)	0.222		
P2~P1	23/50 (46.0%)	8/17 (47.1%)			
P2>P1	26/50 (52.0%)	7/17 (41.2%)		OR[3] = 0.43 [0.11 to 1.66]	0.22
TimeToPeak_sit_mean	0.23 ± 0.06	0.23 ± 0.06	0.746	0.00 [-0.04 to 0.04]	0.98
TimeToPeak_sit_mean	0.23 ± 0.06	0.24 ± 0.05	0.810	0.01 [-0.03 to 0.05]	0.58
TimeToPeak_sit_mean	0.23 ± 0.06	0.24 ± 0.06	0.493	0.02 [-0.02 to 0.05]	0.32

(1) T-student or Qui-square.
(2) Linear effect of the Lumbar Puncture Group vs Stent evaluated by linear model adjusted for age, sex and hypertension.
(3) Odds Ratio of the Lumbar Puncture vs Stent Group evaluated by logistic regression model adjusted for age, sex and hypertension.

Primary outcomes

Conclusion: We demonstrated no significant difference in IC between patients with PTC associated with TSS submitted only to LP vs venoplasty.

Disclosure: Nothing to disclose.

EPO-531 | Underdiagnosis and impact of menstrual migraine in real-world clinical practice

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Background and Aims: Patients with menstrual migraine (MM) experience more severe, disabling and prolonged attacks than non-MM patients. Research indicates that approximately 2/3 of female migraine sufferers may experience MM and diagnoses are often unreliable without a validated monitoring tool. This cross-sectional study aimed to assess how often MM is reported in clinical practice.

Methods: Data were drawn from the 2022/23 Adelphi Migraine Disease Specific Programme™, a real-world cross-sectional survey across France, Germany, Italy, Spain, the UK, and the USA. The cross-sectional study involved retrospective data collection from physicians and their female patients providing data on migraine diagnosis, including MM, and attack severity. Analyses were descriptive.

Results: There were 264 primary care practitioners (PCPs) and 340 neurologists who provided data on 3,049 female patients aged ≤55 years, with 32% ($n = 986$) diagnosed with MM. Physicians estimated that 38% of their patients had diagnosis of MM, with an additional 20% of patients without a physician-confirmed MM diagnosis who reported menstruation as a trigger for their migraines. Patients with MM experienced more severe migraine attacks than those without MM. Physicians tended to underestimate the severity, particularly for MM patients compared to those without MM. The reporting disparity in attack severity was more

pronounced in MM patients when managed by a PCP. (Table 1). Treatment prescribed to both patient groups were similar, but MM patients reported less satisfaction with their preventive treatment, than those without MM.

	Patients with Menstrual Migraine		Patients without Menstrual Migraine	
	Managed by Primary Care Practitioner	Managed by Neurologist	Managed by Primary Care Practitioner	Managed by Neurologist
Patient-reported overall migraine attack severity [n (%)]				
n	**179**	**138**	**285**	**261**
Very mild	10 (6)	5 (4)	29 (10)	22 (8)
Mild	61 (34)	49 (36)	105 (37)	82 (31)
Moderate	74 (41)	56 (41)	103 (36)	111 (43)
Severe	32 (18)	23 (17)	44 (15)	38 (15)
Very Severe	2 (1)	5 (4)	4 (1)	8 (3)
Physician-reported overall migraine attack severity [n (%)]				
n	**179**	**138**	**285**	**261**
Very mild	11 (6)	3 (2)	38 (13)	39 (15)
Mild	63 (35)	52 (38)	124 (44)	99 (38)
Moderate	96 (54)	67 (49)	103 (36)	98 (38)
Severe	9 (5)	15 (11)	20 (7)	23 (9)
Very Severe	0 (0)	1 (1)	0 (0)	2 (1)

TABLE 1 Patient and physician reported overall migraine attack severity. Note- data reported on patient/physician pairs, where patients had fully completed the patient-reported questionnaire and full physician-reported data were concurrently available.

Conclusion: Optimal treatment for MM requires heightened physician awareness, recognition, and understanding of its implications, aiming to alleviate additional burdens for affected females.

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EPO-532 | A machine-learning-based algorithm to predict response to anti-CGRP monoclonal antibodies in patients with migraine

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Background and Aims: The study aimed to determine whether machine-learning (ML)-based models can predict responses to monoclonal antibodies (mAbs) against the calcitonin gene-related peptide (CGRP) in patients with migraine using early predictors and to create a prediction tool.

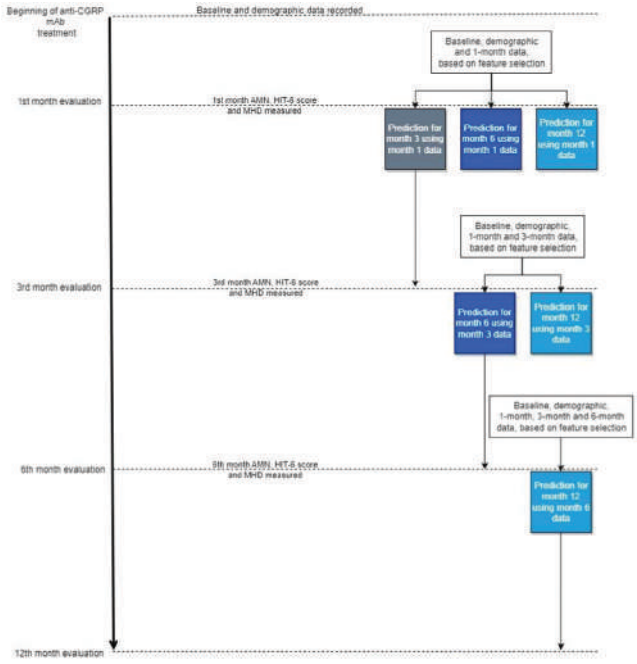
Methods: We collected data from patients receiving anti-CGRP mAbs for 12 months. Demographic and monthly clinical variables were collected, including monthly headache days (MHD), monthly days with acute medication use (AMD), number of analgesics, Headache Impact Test-6 (HIT-6). Response rates were categorized as <25%, 25-50%, 50-75%, and >75% reduction in MHD. ML models were trained using random forest algorithm. ML models were optimized to maximize the F1 score, and their performance was evaluated using standard evaluation metrics, including accuracy, precision, and area under the receiver operating characteristic curve (AUC-ROC). Sequential backward feature selection was employed to identify the most relevant predictors. Each model was given 11 baseline data inputs (type of mAb, age, gender, migraine diagnosis, disease duration, aura, MHD, AMD, HIT-6, number of analgesics) and month-based predictors for months 1, 3, 6.

Results: We included 336 patients treated with anti-CGRP mAbs. We developed 6 models to predict 3-,6-,and 12-month responses using early predictors. ML-based models yielded predictions with F1 score of 0.42-0.71 and AUC-ROC score of 0.44-0.72. Shapley Additive explanations summary plots were generated to interpret the contribution of each feature for each model. Based on these findings, a response prediction tool was developed.

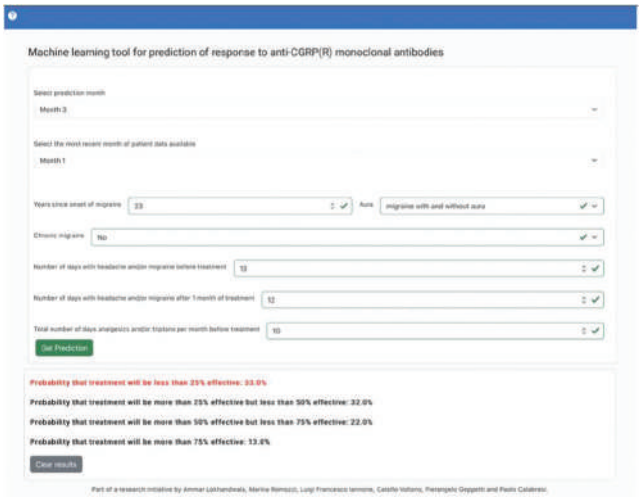
Table 1. Patients demographic and clinical features at baseline.	Overall population (n =336)
Demographics	
Age [years], mean ± SD	48.2±13.0
Sex female, n (%)	269 (80.1)
Migraine features	
Chronic migraine, n (%)	302 (89.9)
Medication overuse, n (%)	259 (77.1)
Aura, n (%)	28 (8.3)
Migraine duration [years], mean ± SD[a]	38.1±15.7
Chronicization duration [years], mean ± SD[b]	18.0±15.4
Monthly headache days, mean (SD)	22.9±6.9
Days with at least one analgesic use, mean ± SD	19.6±8.8
Analgesics number, mean (95%CI)	33.4 (30.1-36.8)
MIDAS score, mean ± SD	88.1±61.7
HIT-6 score, mean ± SD	67.8±6.4

Abbreviations: HIT-6, Headache Impact Test 6; MIDAS, Migraine Disability Assessment; SD, standard deviation. Percentages are expressed on column total. [a]Calculated on 317 patients. [b]Calculated on 293 patients.

Patients' demographic and clinical features at baseline.



Flow chart of the anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies calculator tool at 3, 6 and 12 months. AMNs, absolute number of analgesics; Headache Impact Test-6 (HIT-6); MHDs, monthly headache days.



Demo of the Machine-learning (ML)-based tool to predict anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies response at 3, 6 and 12 months.

Conclusion: The ML-based response prediction tool holds promise in predicting treatment outcomes for patients with migraine undergoing anti-CGRP mAbs treatment, potentially aiding in clinical decision-making and cost-optimization.

Disclosure: Nothing to disclose.

EPO-533 | Functional neurological symptoms in headache disorders: A case-series retrospective study

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Background and Aims: To evaluate functional neurological symptoms (FNS) within a population diagnosed with headache disorders and to investigate the influence of preventive headache treatments on FNS.

Methods: We conducted a retrospective study involving patients diagnosed with headache disorders according to the ICHD-3, presenting with FNS at an outpatient clinic from 2020 to 2022.

Results: We identified 23 patients (82.6% female, mean age 40 years) diagnosed with headache disorders, with episodic or chronic migraine being the most prevalent ($n = 17$, 73.9%), all without aura who presented with FNS. Most patients (60.9%) presented with multiple FNS (sensorimotor, visual, or related to speech); these were followed by sensory symptoms (30.4%), impaired gait, and non-epileptic seizures (4.3% each). FNS were mostly paroxysmal (65.2%) and occurred between and during headache crises, with a notable exacerbation of FNS during heightened headache episodes (65.2%). Neurological examinations revealed at least one positive sign of functionality in 69.6% of cases. Preventive treatment for headaches was started in 20 patients, predominantly antidepressant drugs (47.8%). Eight patients (34.8%) failed at least one preventive. During the follow-up period, 50% reported an improvement in headache frequency

(≥50%) and 75% patients had an improvement of their FNS. Patients with better control of headache frequency had higher rates of improvement of FNS (70% versus 30%).

Conclusion: In our study, the predominant presentation of FNS was characterized by its multiplicity, often displaying a paroxysmal nature and exacerbations during concurrent headache crises. The effectiveness of preventive treatment, aimed at reducing headaches, translated into improvement in FNS.

Disclosure: None.

EPO-534 | Efficacy of anti-CGRP mAbs in migraine: A comparative analysis between overweight and normal-weight populations

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Background and Aims: Migraine and excess weight share a relationship not yet fully understood. Moreover, the Body Mass Index (BMI) has been positively correlated with the frequency of migraine attacks. Anti-CGRP monoclonal antibodies (mABs) hold a pivotal role in targeting peripheral mediators in migraine treatments. Consequently, this study endeavors to assess the efficacy of mABs in a population characterized by excess weight compared to a normal weight control group

Methods: We enrolled 120 chronic migraine patients treated with anti-CGRP mAbs divided into two groups according to BMI (BMI > 25 and <25). Over a time period of 12 months, we recorded mean monthly headache, BMI, midas, headache intensity and acute medication intake every three months

Results: A monthly migraine frequency of 22+-7 days was found in the control group and 20+-7 days in the group of overweight patients before starting treatment. At month 12, an average of 9.5+-8.6 and 8.8+-7.0 days were found, respectively. Preliminary analysis of the data reveals a decrease in the monthly frequency of migraine in both the overweight patient group and the control group ($p < 0.001$). When comparing the difference in the decrease, it does not appear statistically significant ($p = 0.6$). Further analyses are still in progress

Conclusion: The current analysis reveals that antibody treatment retains efficacy in the overweight population in the same way as in the normal-weight group. There are limited data in literature on the use of CGRP inhibitor monoclonal antibodies in individuals who are overweight/obese and further studies are needed to better understand efficacy in this patient population

Disclosure: Nothing to disclose.

EPO-535 | The stigma of cluster headache and its comparison with migraine

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Background and Aims: Stigma refers to the situation in which an individual is disqualified from full social acceptance, manifesting itself in the form of stereotypes, prejudice and discrimination. There are validated measures to measure the stigma associated with neurological diseases, but cluster headache (CH) has not been investigated so far. Our aim is to study the stigma of CH and compare it with that of migraine.

Methods: This is a multicenter cross-sectional study conducted by junior members of the Spanish Headache Study Group. Migraine and CH patients were recruited. Stigma was assessed with the SSCI (Stigma Scale for Chronic Illness). Other psychosocial aspects (cognitive reserve, self-esteem, anxiety, depression, stress and catastrophizing) were evaluated by specific scores. Migraine cases were classified into refractory/refractory migraine (RRM) or non-refractory/refractory migraine (non-RRM) according to the EHF criteria. CR patients were classified into episodic (ECH) or chronic (CCH).

Results: Ninety-six patients were enrolled: 37 ECH, 19 CCH, 17 non-RRM and 23 RRM. SSCI score was higher in CCH and RRM, 56.0 (34.0-77.0) and 59.0 (39.0-71.0) respectively; in ECH it was scored 42.0 (30.5-64.0) and in non-RRM, 37.0 (30.0-52.5). The difference between non-RRM and CCH ($p = 0.038$), between non-RRM and RRM ($p = 0.006$) and between ECH and RRM ($p = 0.019$) was statistically significant. CCH and RRM also showed higher scores in the depression assessment with respect to non-RRM. No statistically significant differences were found in the rest of the assessments.

Conclusion: Chronic cluster headache patients, like resistant or refractory migraine patients, show a higher degree of stigma relative to non-resistant and non-refractory migraine.
Disclosure: Nothing to disclose.

EPO-536 | Impact of migraine preventive treatment on interictal burden

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Background and Aims: To analyze the impact of migraine preventive treatment on interictal burden (IB) and interictal predictors of response to preventive treatment.
Methods: Prospective cohort study in a headache unit. Patients with migraine who started treatment between January-February 2023 and followed up for 3 months were included. Epidemiological and clinical variables such as monthly migraine days (MMD), monthly consumption of NSAIDs and triptans, and IB (determined by the Migraine Interictal Burden Scale-4 and an ad-hoc questionnaire, including interictal symptoms) were collected at the beginning of treatment and at 3 months.
Results: 100 patients; 90 women (90%) (age mean 48.5 ± 10.9 years) 11% low-frequency episodic migraine; 20% high-frequency; 69% chronic. Of these last two groups, 54% started treatment with monoclonal anti-CGRP (Mab), 31% with botulinum toxin type A (OnabotA) and 8% with oral preventives. At similar reduction of MMD (61% vs. 58%), a greater decrease of IB (57% vs. 41%), consumption of NSAIDs (68% vs. 50%) and triptans (64% vs. 41%) with higher improvement index in response to symptomatic treatment (68.5% vs 46%) was observed in those patients treated with anti-CGRP compared to OnabotA.
Conclusion: In addition to reducing MMD, preventive treatment significantly reduces IB, being this reduction greater in patients treated with MaB. We also identified IA as a possible predictive factor of non-response to preventive treatment.
Disclosure: Nothing to disclose.

EPO-537 | Role of dexamethasone as a possible protective factor against long-COVID headache

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Background and Aims: Although respiratory symptoms prevail in COVID-19 infection, headache is one of the most common symptoms that may persist for months in the form of long-COVID headache. The aim of our study was to evaluate long-COVID headache characteristics and search for possible biomarkers.
Methods: We conducted retrospective analysis of 295 (126 women) hospitalized patients with COVID-19 infection in Slovakia after 12-15 months. Retrospectively we contacted patients via video call with self-administered questionnaire. In headache patients we searched for participants with persisting headache up to 15 months. Subsequently we evaluated persisting headache's phenotype and its possible biomarkers.
Results: 34.6% ($n = 102$) of patients had COVID-19 associated headache, with 41.2% ($n = 42$) reporting persisting headache. It was unilateral in 40%, pulsating in 38% and accompanied by nausea and phonophobia in 60% and 74% respectively. While no specific laboratory marker was associated with persisting headache, we found a significant association between persisting headache and treatment with dexamethasone. Patients treated with dexamethasone during hospitalization had lower chance of developing persisting headache (52% vs. 73% $p = 0.029$).
Conclusion: We confirmed persisting headache for 12-15 months in almost half of our patients with predominance of migraine-like characteristics. Patients with administered dexamethasone had a statistically lower probability of developing long-COVID headache. This has relevant implications into clinical practice, as long-COVID headache remains a therapeutic challenge worldwide with specific recommendations and a tailored approach needed.
Disclosure: Nothing to disclose.

EPO-538 | Anti-CGRP monoclonal antibodies effectiveness among men and women: Are there differences?

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Background and Aims: Migraine affects more women and there is evidence that supports the influence of female sex hormones on its pathophysiology. CGRP is the main neuropeptide that causes pain during migraine attacks and its blood levels can be modified by those hormones.
Methods: We reviewed 225 patients that started anti-CGRP monoclonal antibodies (mAbs) between 2019 and 2022, in order to ensure a long follow-up. 14 were excluded for lost to follow-up. Our objective is to assess if there are differences in the response to this treatment in males versus women.
Results: There were 189 women and 31 men with an average age of 45 years old. 77% of men and 79% of women had chronic migraine with an average of 5 preventive medications failed. The average reduction of monthly migraine days was 4 for women and 6 for men, while the average reduction of monthly headache days was 7 for women and 11 for men. 58% of men and 66 % of women achieved a reduction of 50% of monthly headache or migraine days.

Constipation was the main adverse effect for women (17%), but no men had it. There were not statistically significant differences between groups except from the response to an antibody switch that was higher in men (50% vs 22%)

Conclusion: In our series, response to anti-CGRP mAbs was similar in women and men, what suggests a significant role of CGRP in migraine pathophysiology in both sexes. Gastrointestinal adverse effects were not reported by men, so this should be assessed in future studies.

Disclosure: Nothing to disclose.

EPO-539 | Sleep quality assessment in resistant migraine

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Background and Aims: Resistant migraine is defined by having failed at least 3 classes of migraine preventatives and suffer from at least 8 debilitating headache days per month for at least 3 consecutive months without improvement. Sleep disorders are known contributors for resistant migraine. Pittsburgh Sleep Quality Index (PSQI) is a validated self-report questionnaire that assesses sleep quality. If higher than 5, it is considered pathological. We report a series of patients with resistant migraine in whom sleep quality was assessed.

Methods: We included patients suffering from migraine followed in Neurology appointments that fulfilled the European Headache Federation criteria for resistant migraine and were waiting to start anti-CGRP (calcitonin gene-related peptide) monoclonal antibody treatment and. PSQI was assessed.

Results: We included 34 patients, 91.2% female, mean age of 44.7 years. 61.8% had chronic migraine, 85.3% without aura. Only 29.4% were formally diagnosed with sleep pathology (26.5% insomnia, 2.9% obstructive sleep apnea) and 26.5% were medicated (17.6% trazodone, 11.8% benzodiazepine). Patients were medicated with a mean of 1.15 migraine preventatives, haven previously tried a mean of 3.32 preventatives. The mean number of monthly debilitating headache days was 12.03. 82.4% of patients had a pathological PSQI, with a mean score of 10.56. The most impaired component score was subjective sleep quality.

Conclusion: Our series' results suggest that sleep disorders could be underassessed in Neurology appointments and, therefore undertreated. Strengthening PSQI assessment in migraine patients could be of value in preventing resistant migraine, allowing therapeutic optimization.

Disclosure: Nothing to disclosure.

EPO-540 | Effectiveness and tolerability of lasmiditan as acute migraine treatment (DART): A real-world multicentric Italian study

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Background and Aims: Lasmiditan, a serotonin 5-HT1F receptor agonist, has been recently approved in Italy for the acute migraine treatment. We designed a prospective multicentric study to evaluate lasmiditan effectiveness and tolerability in the real-world setting (NCT05903040).

Methods: We enrolled 55 patients (87.3% females, 45.4 + 14.4 years, 21.8% – $n = 12$ with chronic migraine-CM, baseline monthly migraine days 9.1 + 7.2) from 13 Italian headache centers. Patients were instructed to treat up to four migraine attacks with lasmiditan 50 mg (20.4%) or 100 mg (79.6%). Using an ad hoc diary, we prospectively collected migraine-attack features every 30 minutes after lasmiditan administration, up to 2 hours (2 h).

Results: Preliminary analyses were conducted on 28 first-treated attacks (1/28 in a CM patient) and 49 total attacks. At lasmiditan intake, 42.9% patients rated migraine intensity as severe (0–3 rating scale). Pain freedom 2 h post-dose was reported in 35.7% (10/28) of first-treated attacks, and in 36.7% (18/49) of total attacks. The rate of pain freedom was not influenced by timing of lasmiditan intake ($p = 0.145$), baseline pain severity ($p = 0.262$) and presence of chronic vs episodic migraine ($p = 0.683$). Freedom from the most bothersome symptom 2 h post-dose was reported in 47.7% of attacks. Adverse events were reported in 26 of total attacks treated (53.1%),

predominantly as dizziness ($n=11$), fatigue ($n=8$) and paraesthesia ($n=6$). Tolerability was rated as good-to-excellent in 50% of cases.

Conclusion: Our real-world data support lasmiditan effectiveness in the acute treatment of migraine. Adverse events were reported in 53.1% of attacks.

Disclosure: CT has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Lundbeck, Novartis, Pfizer, and Teva; lectured at symposia and is a principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Lundbeck, Novartis, and Teva; received research grants from the European Commission, the Italian Ministry of Health, the Italian Multiple Sclerosis Foundation, and the Migraine Research Foundation; and serves as an associate editor for Cephalalgia and The Journal of Headache and Pain. R.D.I received speaker honoraria for scientific presentations from Eli-Lilly, and Teva, and has participated as advisory board for Pfizer. GV reports consultant fees from Lundbeck.

EPO-541 | The relationship of medication overuse to vertigo, sleep, anxiety, depression and comorbidities in migraine patients

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NIHR King's Clinical Research Facility, SLaM Biomedical Research Centre, and Wolfson Sensory, Pain and Regeneration Centre, King's College London, UK

Background and Aims: The global prevalence of medication overuse headache (MOH) is 1–2%. Migraine is the predominant risk factor, impacting 78% of individuals with MOH. Despite well-established evidence that MO can contribute to the deterioration and chronification of a pre-existing headache syndrome, little is known about its role in relation to existing comorbidities and other disabling symptoms of migraine. We sought to examine the relationship between medication overuse and the total number of comorbidities and the symptoms of vertigo, sleep disturbance, anxiety and depression.

Methods: Data were collected ($n=192$) through the use of patient self-completed health questionnaires utilising a variety of standardised tools including the Dizziness Handicap Inventory (DHI), Subjective Vertigo Questionnaire (SVQ), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Generalized Anxiety Disorder 7 (GAD-7), and Patient Health Questionnaire 8 (PHQ-8). Binomial logistic regression was applied to examine the predictive role of medication overuse in relation to symptoms of vertigo, poor sleep, anxiety, and depression and the total number of comorbidities.

Results: The model demonstrated that medication overuse was associated with an increased total number of comorbidities ($\chi^2(4)=6.978$, $p=0.008$). There was no statistically significant difference observed in scores related to the symptoms of vertigo, sleep disturbance, anxiety and depression.

Conclusion: This data shows medication overuse is associated with an increased total number of comorbidities in migraine patients. Moving forward, physicians must recognise the impact of other comorbidities, not only headache that may contribute to medication overuse.

Disclosure: Nothing to disclose.

EPO-542 | An interdisciplinary integrated one-stop-shop special outpatient clinic for idiopathic intracranial hypertension

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Background and Aims: Management of idiopathic intracranial hypertension (IIH) is complex requiring contributions from multiple specialized disciplines. In practice, this creates considerable organizational and communicational challenges for health care professionals and patients. To meet those challenges, we established an interdisciplinary integrated outpatient clinic for IIH (comprising neurology, neuroophthalmology, neuroradiology, neurosurgery and endocrinology) with a central coordination and a one-stop-shop concept. Here, we aimed to evaluate effects of this one-stop-shop concept on objective clinical outcome of patients with IIH.

Methods: Using the Vienna-IIH database, we compared the one-stop-shop era (1-JUL-2021 to 31-DEC-2022) to a reference group receiving standard care (1-JUL-2018 to 31-DEC-2019) regarding clinical outcome parameters (visual impairment/worsening, headache improvement/freedom) assessed 6 months after diagnosis. Multivariate binary logistic regression models were used to adjust for confounders (age, body mass index [BMI], CSF opening pressure, visual impairment and chronic headache at diagnosis).

Results: Baseline characteristics of the one-stop-shop group ($n=85$) and standard care group ($n=81$) were comparable (female: 90.6% vs. 90.1%; mean age: 33.6 vs. 32.8 years, median BMI: 31.8 vs. 33.0, median CSF opening pressure: 320 vs. 341 mmH_2O, visual impairment at diagnosis: 71.8% vs. 69.1%, chronic headache at diagnosis: 55.3% vs. 56.8%). Compared to standard care, the one-stop-shop concept was associated with a significantly higher likelihood of achieving both headache improvement (odds ratio [OR] 2.24, $p<0.001$) and headache freedom (OR 1.75, $p=0.031$), whereas the risk for visual impairment (OR 0.87, $p=0.231$) and visual worsening (OR 0.67, $p=0.354$) was not significantly reduced.

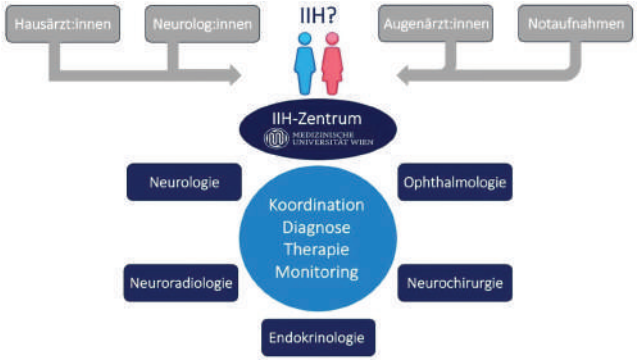

FIGURE 1 IIH one-stop-shop concept.

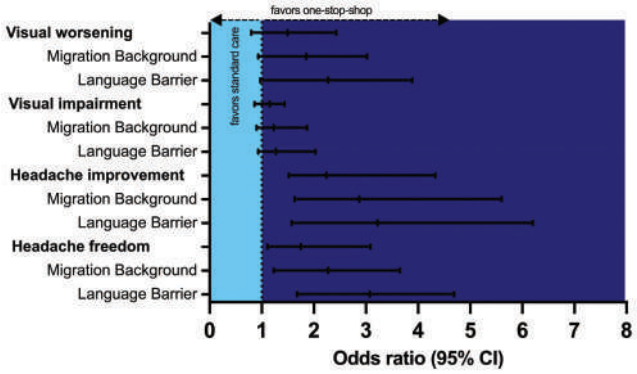

FIGURE 2 Outcome in the one-stop-shop concept compared to standard management.

Conclusion: Interdisciplinary integrated management of IIH significantly improves headache outcome and potentially also visual outcome.

Disclosure: GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Merck, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

Movement disorders 5

EPO-543 | The influence of thyroid disorders on the course of idiopathic adult-onset dystonia

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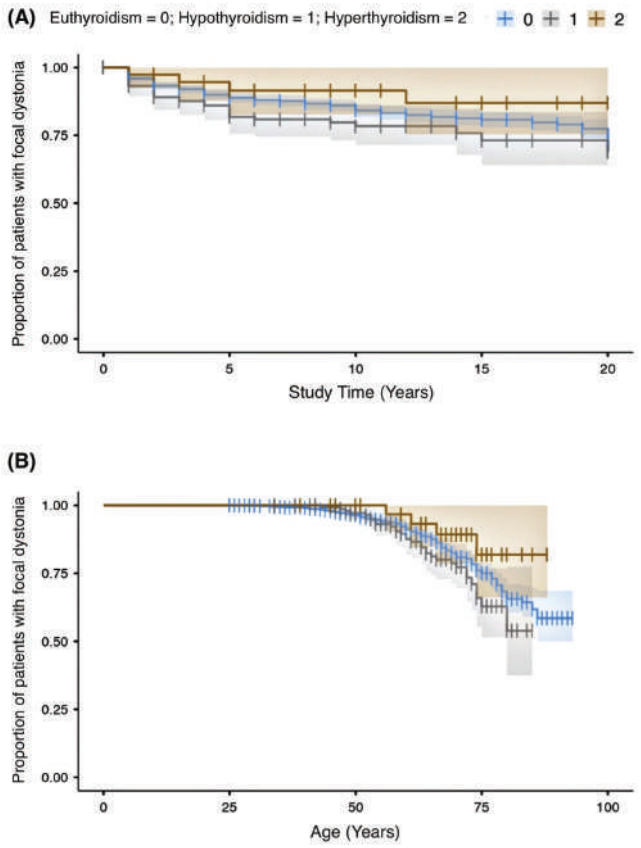
Background and Aims: A few earlier observations and recent controlled studies pointed to the possible contribution of thyroid diseases in idiopathic adult-onset dystonia (IAOD).

Methods: To investigate the association between thyroid status and clinical characteristics of IAOD, focusing on dystonia localization, spread, and associated features such as tremors and sensory tricks. Patients were identified from the Italian Dystonia Registry, a multicentre dataset of patients with adult-onset dystonia. The study population included 1518 IAOD patients. Patients with hypothyroidism and hyperthyroidism were compared with those without any thyroid disease.

Results: In the 1518 IAOD patients, 167 patients (11%; 95% CI, 9.5%–12.6%) were diagnosed with hypothyroidism and 42 (2.8 %;

95% CI, 1.99–3.74) with hyperthyroidism. The three groups were comparable in age at dystonia onset, but there were more women than men in groups with thyroid disease. We found more patients with blepharospasm in the hyperthyroidism group, but the difference lacked significance after the Bonferroni correction. The remaining dystonia-affected body sites were similarly distributed in the three groups, as did dystonia-associated features and spread.



Kaplan–Meier's survival analysis of the spread of dystonia in patients with focal onset. (A) Study time was represented by the time elapsed between dystonia onset and spread. (B) Study time was represented by age at spread.

Conclusion: Even if the frequency of patients with thyroid disease is higher than the general European population, we cannot discuss the results in terms of risk factors due to the different ascertainment methodology. However, our findings provided novel information indicating that the high rate of thyroid diseases is not specific for any distinct dystonia subpopulation and does not appear to influence the natural history of IAOD.

Disclosure: Nothing to disclose.

EPO-544 | Neuropathological characteristics of the patients with old-onset Parkinson's disease

K. Inoue[1]; H. Fujimura[1]; T. Saito[1]; K. Toyooka[1]; M. Yamadera[1]; C. Mori[1]; M. Sudo[1]; Y. Izumi[2]

[1]Department of Neurology, NHO Osaka Toneyama Medical Center, Toyonaka, Japan; [2]Department of Neurology, Tokushima University Faculty of Medicine

Background and Aims: The clinical features of the patients with old-onset Parkinson's disease (PD) are characterized by postural areflexia, frozen gait, hallucinations, cognitive impairment, and autonomic failure.

Methods: From a consecutive autopsy series of 187 patients, 25 patients, pathologically confirmed Parkinson's disease and aged 50 years or older at onset, were selected. Their median age at onset was 72 years, median age at death: 83 years and 18 males (72%). We compared the age of onset, sex, duration of disease, presence or absence of dementia, Lewy body (LB) score, and lesions of Alzheimer's disease (AD) in the group with onset under 75 (normal) and after 75 years of age (elderly).

Results: In PD cases that developed after the age of 75 years, the duration of the disease was significantly shorter, and many cases were clinically diagnosed with dementia. In the elderly group, LB scores tended to be smaller in the brainstem and larger in the limbic system and neocortex than in the normal group, but there was no significant difference. Many of the cases in both groups were accompanied by mild to moderate AD lesions, but only a small number were diagnosed with pathological AD.

Conclusion: In elderly PD, LB lesions to the limbic ~ neocortex may expand prematurely.

Disclosure: Nothing to disclose.

EPO-545 | MRI volumetric assessment of neuropsychiatric symptoms in multiple system atrophy

I. Ruiz Barrio; A. Horta Barba; A. Puig Davi; S. Martinez Horta; J. Kulisevsky; J. Pagonabarraga

Movement Disorders Unit, Neurology Department, Hospital de Sant Pau, Barcelona, Spain

Background and Aims: Multiple system atrophy (MSA) presents diverse motor and non-motor symptoms, with growing recognition of cognitive and neuropsychiatric manifestations. This study aims to address this gap by investigating neuropsychiatric symptoms and their neuroanatomical correlations in MSA.

Methods: Ten consecutive patients diagnosed with MSA based on current clinical criteria were included. Frontal Behavioral Inventory (FBI) and Neuropsychiatric Inventory (NPI) were administered to all patients. T1-weighted scans were obtained using a 3 Tesla Philips Achieva station, and structural image processing was conducted with FreeSurfer (v.7.4.1). Volumetric analysis, involving the correlation of

volumetric data with neuropsychiatric scales, was performed using R statistical software (v.4.3.0). Multiple comparisons were corrected using False Discovery Rate.

Results: High prevalence of neuropsychiatric symptoms was observed in MSA (44.4% with ≥3 points in FBI, mean NPI score 6.8 ± 3.9). Demographics are summarised in table 1. There were no significant differences among clinical subtypes in analyzed variables. Linear modeling revealed significant amygdala atrophy across higher scores of FBI and NPI ($p = 0.025$ and 0.014, respectively), independent of clinical subtype (Figures 1 and 2).

Conclusion: Neuropsychiatric symptoms, prevalent in both parkinsonian and cerebellar subtypes of MSA, may be associated with amygdala atrophy. Further studies exploring the pathophysiology of neuropsychiatric alterations in MSA are essential, considering the significant impact on daily activities.

Disclosure: Nothing to disclose.

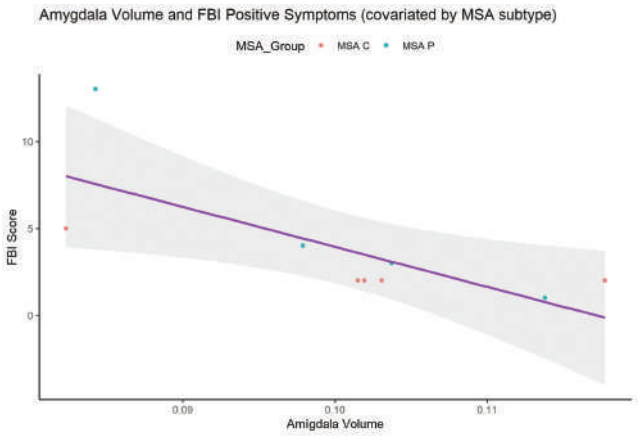


FIGURE 1 Correlation between amygdala volume and FBI positive symptoms.

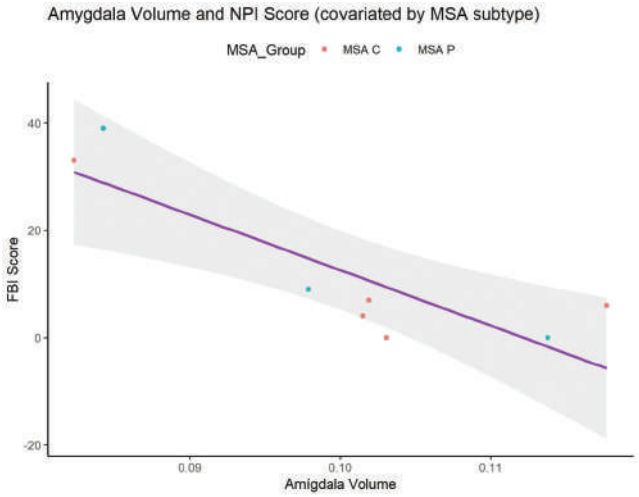


FIGURE 2 Correlation between amygdala volume and NPI score.

EPO-546 | MRI volumetric assessment of neuropsychiatric symptoms in multiple system atrophy

I. Ruiz Barrio; A. Horta Barba; A. Puig Davi; S. Martinez Horta; J. Kulisevsky; J. Pagonabarraga

Movement Disorders Unit, Neurology Department, Hospital de Sant Pau, Barcelona, Spain

Background and Aims: Multiple system atrophy (MSA) presents diverse motor and non-motor symptoms, with growing recognition of cognitive and neuropsychiatric manifestations. This study aims to address this gap by investigating neuropsychiatric symptoms and their neuroanatomical correlations in MSA.

Methods: Ten consecutive patients diagnosed with MSA based on current clinical criteria were included. Frontal Behavioral Inventory (FBI) and Neuropsychiatric Inventory (NPI) were administered to all patients. T1-weighted scans were obtained using a 3 Tesla Philips Achieva station, and structural image processing was conducted with FreeSurfer (v.7.4.1). Volumetric analysis, involving the correlation of volumetric data with neuropsychiatric scales, was performed using R statistical software (v.4.3.0). Multiple comparisons were corrected using False Discovery Rate.

Results: High prevalence of neuropsychiatric symptoms was observed in MSA (44.4% with ≥3 points in FBI, mean NPI score 6.8 ± 3.9). Demographics are summarised in table 1. There were no significant differences among clinical subtypes in analyzed variables (table 2). Linear modeling revealed significant amygdala atrophy across higher scores of FBI and NPI ($p = 0.025$ and 0.014, respectively), independent of clinical subtype (Figures 1 and 2).

Conclusion: Neuropsychiatric symptoms, prevalent in both parkinsonian and cerebellar subtypes of MSA, may be associated with amygdala atrophy. Further studies exploring the pathophysiology of neuropsychiatric alterations in MSA are essential, considering the significant impact on daily activities.

Disclosure: Nothing to disclose.

Table 1. Demographics and clinical variables

Age	63 (6.42)
Gender	60% male
MSA subtype	50% MSA-P
Disease duration	40 (13.8)
Education	12 (4.78)
UMSARS part 1	16.91 (2.91)
UMSARS part 2	17.55 (5.78)
UMSARS part 4	1.36 (0.5)
UPDRS 3	36.38 (15.43)
FBI disinhibition	3.78 (3.6)
NPI	12.25 (15.08)

Table 2. Differences between MSA subtypes

	MSA-P	MSA-C	P
Age	63	63	0.75
Disease duration (m)	31.5	42	0.46
Education	12	18	0.21
UMSARS part 1	15	16	0.8
UMSARS part 2	21	13	0.09
UMSARS part 4	2	1	0.17
UPDRS 3	32	44	0.13
FBI disinhibition	0.9	12.5	9
NPI	9	6	0.65

TABLE 1 and 2 Demographics and differences between MSA subtypes.

EPO-547 | **A randomized, double-blinded, placebo-controlled QTc study to evaluate BIA 286156 effect on cardiac repolarization**

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Background and Aims: Betaglucocerebrosidase (GCase) is encoded by the GBA1 gene. Its mutations are the most common genetic risk factor for Parkinson's disease (PD). BIA 286156 is an allosteric activator of GCase developed to treat the causative processes in GBA-PD. This study primarily aimed to evaluate the effect of BIA 286156 on QT interval corrected (QTc) for heart rate (HR) based on the Fridericia correction (QTcF) in healthy subjects.

Methods: Phase 1, randomized, double-blinded, placebo-controlled, 4-period crossover study. Subjects received 1 of 12 treatment sequences. A single dose of 60 mg or 150 mg BIA 28-6156, 400 mg moxifloxacin or placebo was administered in fed state (Table 1). Relationship between BIA 28-6156 plasma concentrations and change-from-baseline QTcF (ΔQTcF) was analyzed to exclude an effect of ΔΔQTcF >10 msec at clinically relevant plasma levels. HR, PR, and QRS intervals, and electrocardiogram (ECG) waveform morphology were evaluated. Incidence and severity of treatment emergent adverse events (TEAEs) were analyzed.

Results: A total of 37 subjects were enrolled, with 33 completing the study. Based on the concentration-QTc analysis, an effect on ΔΔQTcF exceeding 10 msec can be excluded within the full observed range of plasma concentrations of BIA 28-6156 up to ~7150 ng/mL. No clinically relevant effects on studied ECG parameters were found. No deaths or other serious AEs were reported. 2 subjects withdrew due to AEs.

Table 1: Overview of Study Treatment Periods and Treatment Sequences

Treatment Sequence (n)	Period 1	Period 2	Period 3	Period 4
1 (n=3)	B	C	A	D
2 (n=3)	C	D	B	A
3 (n=3)	A	B	D	C
4 (n=3)	D	A	C	B
5 (n=4*)	C	A	B	D
6 (n=3)	A	D	C	B
7 (n=3)	B	C	D	A
8 (n=3)	D	B	A	C
9 (n=3)	A	B	C	D
10 (n=3)	B	D	A	C
11 (n=3)	C	A	D	B
12 (n=3)	D	C	B	A

n = number of subjects

Notes: A, B, C and D = 1 of 4 possible study drug treatments:

- **Treatment A:** *Therapeutic dose:* 60 mg of BIA 28-6156 (1×60-mg BIA 28-6156 capsule+2 placebo capsules) in the fed state
- **Treatment B:** *Supratherapeutic dose:* 150 mg of BIA 28-6156 (2×60-mg BIA 28-6156 capsules+1×30-mg BIA 286156 capsule) in the fed state
- **Treatment C:** *Placebo control:* BIA 28-6156 matching placebo (3 placebo capsules) in the fed state
- **Treatment D:** *Positive control:* 400 mg of moxifloxacin (1×400-mg moxifloxacin capsule + 2 placebo capsules) in the fed state

* One subject was withdrawn from the study and only received the placebo treatment in Period 1. This subject was replaced and the replacement subject received all planned treatments according to the treatment sequence.

Conclusion: BIA-28-6156 doses were well tolerated, with a favorable safety profile. These results showed no clinically relevant effects on ECG parameters, constituting a negative thorough QT/QTc study.

Disclosure: Supported by Bial-Portela & C[a], S.A.

EPO-548 | Baseline variables associated with apomorphine sublingual film retention

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[1]*Department of Neurology, University Hospital Ulm, Ulm, Germany;* [2]*German Centre for Neurodegenerative Diseases, Ulm, Germany;* [3]*Department of Geriatrics, Kreisklinik Ebersberg, Ebersberg, Germany;* [4]*La Princesa University Hospital, Madrid, Spain;* [5]*Bial – Portela & Ca, S.A., Coronado, Portugal*

Background and Aims: The Phase 3 Study CTH-301 evaluated the long-term safety/tolerability and efficacy of apomorphine sublingual film (SL-APO) for treating OFF-episodes in Parkinson's disease patients with motor fluctuations. Data from this study were used to build a model to identify baseline variables that differ between patients who completed the study and those who discontinued during the dose optimisation or long-term maintenance phase due to either lack of efficacy or adverse events (AEs), therefore influencing retention.

Methods: Baseline variables were ranked based on their correlation (Chi-square) with the discrete target variable (completers vs non-completers due to lack of efficacy or AEs). A logistic regression classification algorithm with LASSO regularisation was used to select the final variables.

Results: Of 496 patients, 120 completed the study, 26 discontinued due to lack of efficacy, 167 due to AEs, and 183 due to other reasons. Median time on SL-APO was 204 days. Compared to completers, non-completers due to lack of efficacy demonstrated a higher levodopa total daily dose ($p<0.001$), lower rate of morning akinesia ($p=0.036$), higher rate of de novo enrolment (no previous SL-APO exposure; $p=0.048$) and higher number of levodopa intakes ($p=0.027$) (Figure 1). Compared to completers, non-completers due to AEs had a lower rate of concomitant dopamine agonists use ($p<0.001$) and higher rate of de novo enrolment ($p=0.019$) (Figure 2).

Figure 1. Key baseline variables identified for comparison between subgroups of patients who completed the study and those who discontinued due to lack of efficacy: (A) total daily levodopa dose at baseline; (B) presence of morning akinesia; (C) enrolment group (*de novo* vs roll-over*); (D) number of daily levodopa intakes. **De novo* patients were defined as those who started SL-APO treatment *de novo*, while roll-over patients were defined as those who had completed previous SL-APO studies (CTH-201, CTH-203, CTH-300, or CTH-302). SD, standard deviation; SL-APO, apomorphine sublingual film

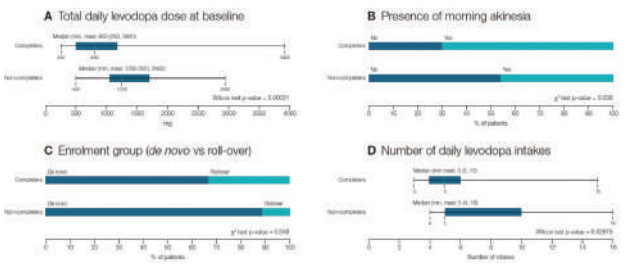
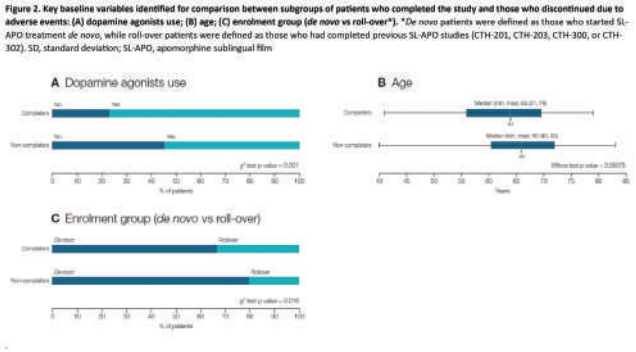


Figure 2. Key baseline variables identified for comparison between subgroups of patients who completed the study and those who discontinued due to adverse events: (A) dopamine agonists use; (B) age; (C) enrolment group (*de novo* vs roll-over*). **De novo* patients were defined as those who started SL-APO treatment *de novo*, while roll-over patients were defined as those who had completed previous SL-APO studies (CTH-201, CTH-203, CTH-300, or CTH-302). SD, standard deviation; SL-APO, apomorphine sublingual film



Conclusion: Levodopa dose and intakes, morning akinesia, previous SL-APO exposure and concomitant dopamine agonist use might influence retention. These results may help identify patients more likely to remain on SL-APO over the long term.

Disclosure: Supported by Bial.

EPO-549 | Efficacy and safety of levodopa in dystonia in Wilson disease (LIDWID): A randomized placebo-controlled trial

P. Kalita; D. Ahmed; D. Mahajan
Sanjay Gandhi Post Graduate Institute of Medical Sciences

Background and Aims: Dystonia is the commonest movement disorder in neurologic Wilson disease (NWD). Levodopa is used in primary dystonia, but has not been systematically evaluated in NWD. We report the efficacy and safety of levodopa compared to placebo in NWD patients with dystonia.

Methods: NWD patients having a Fahn-Marsden Dystonia Rating (FMDR) score of >20 were included in whom other possible causes were ruled out. Patients were randomized to levodopa-carbidopa (LCD) or placebo using 1:1 randomization. LCD (100 mg + 10 mg) was started in a dose of half tab thrice daily, and increased every week to 2 tablets thrice daily. Placebo group received saccharine tablet. Outcome was defined at 3 months. The primary outcome was improvement in FMDR score by >50%, and secondary outcomes were Neurological Severity score (NSS), Dysphagia Outcome and Severity Scale (DOSS) score and side effects.

Results: 13 patients each were randomized to LCD and placebo. Their baseline characteristics were comparable. Only one patient in each group achieved primary outcome. At 3 months, both LCD and placebo groups had significant improvement in FMRD score, NSS and DOSS score. The improvement in FMRD (55.00 ± 35.35 vs 45.92 ± 41.40; $p=0.55$), NSS (7.61 ± 4.61 vs 5.77 ± 3.37; $p=0.25$) and DOSS score (4.92 ± 1.70 vs 4.77 ± 2.16; $p=0.84$) however were not significantly different between LCD and placebo groups. Four patients had minor side effects (3 LCD and 1 placebo).

Conclusion: LCD is safe in NWD and well tolerated. Patients in both LCD and placebo group improved at 3 months, but LCD did not have advantage over placebo in reducing dystonia.

Disclosure: Nothing to disclose.

EPO-550 | Foslevodopa/foscarbidopa in advanced Parkinson's disease: Demonstration of savings from a societal perspective in the UK

K. Chaudhuri[1]; L. Bergmann[2]; J. Belsey[3]; T. Boodhna[4]; E. Leoncini[4]; J. Zamudio[5]
[1]*Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK;* [2]*AbbVie, Ludwigshafen, Germany;* [3]*JB Medical Ltd, London, UK;* [4]*AbbVie, Marlow, UK;* [5]*AbbVie, North Chicago IL, USA*

Background and Aims: In patients with advanced Parkinson's disease (aPD), adequate control of OFF time may not be achievable using oral/transdermal therapies. Clinical trials of Foslevodopa/foscarbidopa (LDp/CDP) have shown meaningful reductions in OFF-time and sleep disturbance – both strong predictors of healthcare resource use. Previous analyses have only considered direct medical costs: this analysis considers a broader societal perspective.
Methods: Clinical trial and real-world evidence were used to drive a cost-utility model comparing LDp/CDp with best medical treatment (BMT), which was accepted by the UK National Institute of Health and Care Excellence. Using outputs from this analysis, a societal impact model was developed. Quintiles of normalised OFF-time across a 16-hour waking day in each treatment group were applied to literature-based estimates for direct medical, non-medical and indirect costs. The resulting state-specific cost estimates were applied to the modelled aPD patient population.
Results: The mean overall cost of care per patient on BMT was estimated as £115,667 in year 1, rising to £123,943 in year 5 (2022 GBP). For LDp/CDp, the corresponding costs were £111,491 and £118,495 respectively. Savings were approximately evenly split across the three cost categories. If applied to all 17,500 aPD patients in the UK, this would amount to a net saving in LDp/CDp-treated patients of £73.1 million in year 1, rising to £95.4 million in year 5.
Conclusion: The use of LDp/CDp in aPD patients inadequately controlled on oral therapy, is associated with net annual savings of over £73 million compared to BMT, when considered from a societal perspective.
Disclosure: KRC: K. Ray Chaudhuri is a study investigator and has served as an advisory board member for AbbVie, UCB, GKC, Bial, Cynapsus, Lobsor, Stada, Medtronic, Zambon, Profile, Sunovion, Roche, Therevance, Scion, Britannia, Acadia, and 4D. He received honoraria for lectures from AbbVie, Britannia, UCB, Zambon, Novartis, Boehringer Ingelheim, Bial, Kyowa Kirin, and SK Pharma. He has received grants (investigator initiated) from Britannia Pharmaceuticals, AbbVie, UCB, GKC, and Bial, and academic grants from EU, IMI EU, Horizon 2020, Parkinson's UK, NIHR, PDNMG, EU (Horizon 2020), Kirby Laing Foundation, NPF, MRC, and Wellcome Trust. He receives royalties from Oxford University Press and holds intellectual property rights for the King's Parkinson's Pain Scale and Parkinson's Disease Sleep Scale. LB: Lars Bergmann is a full-time employee of AbbVie, and may hold AbbVie stock or stock options. JB: Jonathan Belsey has carried out commercial analytical consultancy work for a wide range of pharmaceutical and medical device companies. In the past 5 years, he has undertaken projects in the field of neuroscience for AbbVie, Bioprojet and Global Kinetics TB: Trishal Boodhna is a full-time employee of AbbVie, and may hold AbbVie stock or stock options. EL: Emanuele Leoncini is a full-time employee of AbbVie, and may hold AbbVie stock or stock options. JZ: Jorge Zamudio is a full-time employee of AbbVie, and may hold AbbVie stock or stock options.

EPO-551 | Fractures and emergency department contacts among patients with Parkinson's disease in denmark

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Background and Aims: Parkinson's Disease (PD) patients often experience symptoms like freezing of gait, axial rigidity, and postural instability, increasing their risk of falls. Osteoporosis in PD is common, which increases the risk of fractures if falling. Falls resulting in fractures could require surgical intervention, significantly contributing to morbidity and mortality. However, there is currently no data on fracture rates within the Danish PD population. This study aimed to analyze fracture rates and other fall-related injuries among Danish PD patients.
Methods: This study is a retrospective, nationwide analysis that used data from the National Patient Registry, Danish National Prescription Registry, and Statistic Denmark. We evaluated the standardized incidence ratio (SIR) of hip fractures, major osteoporotic fractures (MOF, including hip, vertebral, humerus, and forearm fractures), and traumatic emergency department (ED) visits in PD patients compared to the general population.
Results: The analysis incorporated 7,242 patients with PD and 2,851,000 matched controls. Hip fracture rates in patients with PD were four times higher compared to the general population, when standardised by sex and age. Additionally, the incidence rates of major osteoporotic fractures (MOF) and traumatic emergency department visits were three times and two times higher, respectively. When considering multiple fractures, the incidence rate of traumatic emergency department visits is 2.6 times higher in Parkinson's patients.
Conclusion: Our study shows a significantly increased risk of fractures for PD patients compared to the general population, indicating a need for optimal medical treatment, fall-prevention, and potential use of anti-resorptive medication in PD patient care.
Disclosure: Tove Henriksen (TH) has received honorary for talks from AbbVie, Britannia, Nordic Infucare, NeuroDerm, Convatec. TH has been a principal investigator for a study sponsored by AbbVie. TH has served as DMC board member at a study sponsored by Lundbeck. Ulla Sofie Lønberg is a former AbbVie employee Jenny Samuelsson is an AbbVie employee and shareholder of AbbVie stocks Peter Schwartz has nothing to disclose. This study was funded by AbbVie. AbbVie

participated in the study design, interpretation of data and in reviewing, and approving the final version of the abstract.

EPO-552 | Cognitive phenotyping of GBA-Parkinson's disease: A study on deep brain stimulation outcomes

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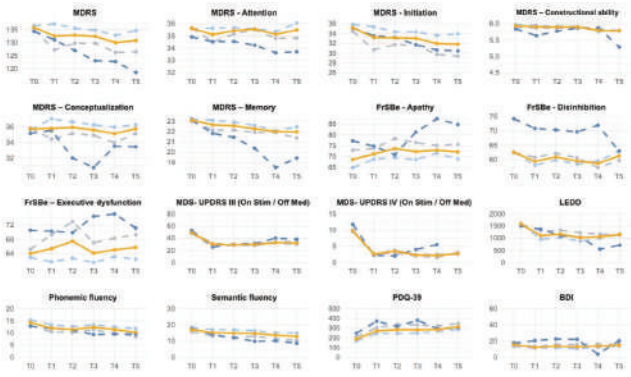
Movement Disorders Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau

Background and Aims: Glucocerebrosidase (GBA) gene in Parkinson's disease (PD) associates earlier onset and worse cognitive decline. Deep Brain Stimulation (DBS) in GBA-PD effectively treats motor symptoms but long-term cognitive effects are unclear. Our study investigated 5-year outcomes in GBA-PD-DBS.
Methods: Retrospective cohort at H.Sant Pau (Barcelona, Spain) of DBS-PD with pre/postDBS assessments: cognitive (MDRS), frontal behavior (FrSBe), verbal fluencies, motor (MDS-UPDRS), L-dopa (LEDD), life quality (PDQ-39), and depression (BDI). Non-GBA-PD cluster analysis was conducted based on first-year cognitive impairment (CI).
Results: Out of 96 PD patients, 13 (13.5%) were GBA-PD. Cluster analysis identified progressors//non-progressors. Progressors' trajectory showed similarities to GBA-PD in cognition, FrSBe and PDQ-39, whereas non-progressors remained stable. In 56 PD-patients with 5-year cognitive follow-up, 8 were gene-carriers. GBA-PD showed faster CI to dementia ($p=0.05$), especially in attention ($p=0.015$), conceptualization ($p=0.004$) memory ($p=0.05$), with no age or education baseline differences. Regarding FrSBe, GBA-PD exhibited worse baseline disinhibition ($p=0.03$) with progressive improvement, while apathy and executive dysfunction deteriorated like non-GBA-PD. Depression scales showed higher values during the first two years in GBA-PD ($p=0.04$). Motor outcomes, LEDD, and phonetic fluency showed no differences, while GBA-PD-semantic-fluency worsened over time ($p=0.02$). No long-term differences were found in GBA-PD-PDQ-39.



Evolution of studied variables. Groups: GBA-PD (dark blue), non-GBA-PD (orange), non-GBA-progressors (grey), non-GBA-non-progressors (light blue).

Conclusion: GBA-PD-CI was centered on attention, conceptualization, and memory; similar profile as progressors. Semantic fluency correlates with cognitive worsening in GBA-PD. From onset, GBA-PD-FrSBe was poorer and fluctuating but stable; also as progressors. Motor outcomes and quality of life were similar between GBA-PD, non-GBA-PD, and clusters, unaffected by CI. Previous surgery, FrSBe and fluencies, rather than MDRS/subscales, predict CI in non-GBA-PD-clusters.
Disclosure: Nothing to disclose.

EPO-553 | Neurophysiological architecture of visual categorization in Parkinson's disease with minor visual hallucinations

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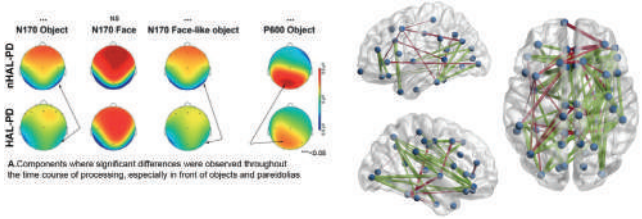
Movement Disorders Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background and Aims: Although minor hallucinations are common in Parkinson's disease (PD, its precise neural mechanisms remain partially understood. Here, we addressed behavioral and neurophysiological anomalies accompanying visual categorization in patients with minor hallucinations.
Methods: We performed task-related EEG on 23 patients with (HAL-PD) and 23 without (nHAL-PD) minor hallucinations during a visual-categorization task based on objects, faces and facial-pareidolias. We identified the main neurophysiological components along the time course of processing and we studied its spectral characteristics to build functional connectivity models based on the signal sources.
Results: No differences were found in any of the clinical/sociodemographic parameters. HAL-PD showed difficulties identifying the most ambiguous stimuli. The neurophysiological components along visual processing showed abnormalities in HAL-PD in: (1) early visual categorization processes (N170) for stimuli requiring less specialized analysis (objects [$t(23)=1.9$; $p<0.05$]; pareidolias [$t(23)=2.23$; $p<0.05$]) and (2), in the late processes of semantic attribution (P600) [$t=(23)=2.2$; $p<0.05$]. Time-frequency analysis showed a main slow-wave component (3 Hz–8 Hz) decreased in HAL-PD along the time interval of interest. The HAL-PD group showed an overall decreased connectivity between different areas of the brain (green), accompanied by an increased connectivity between left-sided inferior/anterior nodes of the semantic system and posterior nodes of the default-mode network.



Task-related components and connectivity analysis.

Conclusion: Minor hallucinations are associated with a combined impairment of early visual recognition (N170) and later semantic attribution (P600). This is accompanied by several differences in the neural architecture subserving these processes. Our results emphasize the use of inadequate semantic information to confer meaning to the deficiently processed stimulus as the central mechanism for minor hallucinations.
Disclosure: Nothing to disclose.

EPO-554 | Mixed brain pathology in neurodegenerative parkinsonism and dementia

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Background and Aims: The aim of the study was to assess the presence and proportion of mixed neurodegenerative pathology in a prospective cohort of patients treated for any phenotype of neurodegenerative parkinsonism and its impact on the accuracy of clinical diagnosis.
Methods: A total of 49 brains of patients who were diagnosed with neurodegenerative parkinsonism or dementia and who consented to join the donor programme were autopsied; neuropathological examinations were performed according to the standard protocol.
Results: There were 25 patients, in whom the pathological examination confirmed the presence of single pathology: 13 patients suffered from alfa-synucleinopathy (syn), 5 patients suffered from tauopathy (tau), 1 patient suffered from TDP-34-pathology (TDP-43) and 6 suffered from AD-related proteinopathy (AD). In 21 patient examinations revealed the presence of double pathology (4 syn/tau, 7 syn/AD, 6 tau/AD, 4 AD/TDP-43), and in 3 patients examination revealed the presence of triple pathology (syn/tau/AD). The correct clinical diagnosis was confirmed in 26 cases, the incorrect clinical diagnosis was done in 23 cases; 13 of them suffered from the mixed brain pathology.
Conclusion: The mixed brain pathology is relatively common finding at brain autopsy in patients who suffered from neurodegenerative parkinsonism, even when the recent and validated clinical diagnostic criteria were used during the diagnostic process. This fact should serve as a basis for the further discussion about their usefulness. These findings also point to the need of intensive research aimed at identifying biomarkers capable of predicting the corresponding types of pathological processes.
Disclosure: Supported by: MH CZ-DRO (FNOl, 00098892) and IGA LF 2023-015.

EPO-555 | Impact of ADORA2A gene polymorphism on Dyskinesia in Parkinson's disease

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Background and Aims: Parkinson's progression leads to motor complications and dyskinesias with levodopa use. This study investigates the link between ADORA2A gene polymorphisms (rs2298383, rs35060421, and rs5751876) and dyskinesia in Parkinson's patients, inspired by the positive effects of ADORA2A receptor antagonism on motor symptoms and dyskinesias.
Methods: A cohort of 200 Parkinson's disease (PD) patients, aged 25 and above, with a minimum of one year of levodopa treatment, participated in the study. Among them, 70 patients exhibiting dyskinesia were designated as cases, while 130 patients without dyskinesia comprised the control group. Genetic evaluations were conducted on both groups, utilizing DNA extracted from peripheral venous blood. The genetic analysis involved high-resolution melting analyses to assess and compare genetic profiles.
Results: While no significant association was observed between the investigated polymorphisms of rs5751876 and rs2298383 alleles and dyskinesia, the rs35060421 allele showed a notably higher frequency in the patient group (odds ratio: 1.39). In regression analysis, considering factors such as gender, age of disease onset, duration of levodopa treatment, and total drug dosage, the odds ratio for rs35060421 increased to 1.608. This suggests that the presence of this allele, in conjunction with other factors, elevates the risk of developing dyskinesia.
Conclusion: Patients with Parkinson's disease (PD) experiencing dyskinesia exhibited longer disease duration, more severe symptoms, and a higher dosage of levodopa. Although no statistically significant difference was identified between dyskinesia and the studied polymorphisms, there is a potential association suggesting that individuals with the rs35060421 polymorphism may face an increased risk of developing dyskinesia.
Disclosure: Nothing to disclose.

EPO-556 | Oropharyngeal adverse events in Parkinson's patients with motor fluctuations treated with apomorphine sublingual film

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Background and Aims: Study CTH-301 demonstrated that apomorphine sublingual film (SL-APO) was well-tolerated and efficacious for treating OFF-episodes in Parkinson's disease patients with motor fluctuations. This post-hoc analysis explored the occurrence of oropharyngeal treatment-emergent adverse events (TEAEs) in patients included in this study.

Methods: Study CTH-301 was a Phase 3, multicentre, open-label trial composed of a dose-optimisation (DO) and long-term safety (LTS) phase. Incidence, severity and time to onset of oropharyngeal TEAEs and discontinuations due to oropharyngeal TEAEs were evaluated. Baseline characteristics that differed between patients who developed oropharyngeal TEAEs and those who did not and between patients who discontinued due to oropharyngeal TEAEs and those who did not were also identified.

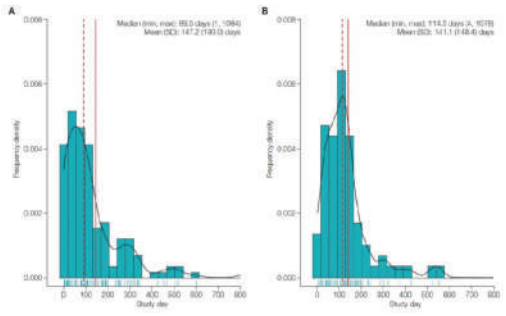
Results: Of 496 patients, 206 (41.5%) experienced oropharyngeal TEAEs and 81 (16.3%) discontinued due to oropharyngeal TEAEs (both DO + LTS) (Table 1). The majority of oropharyngeal TEAEs overall and those leading to discontinuation were mild or moderate (Table 1), with more severe TEAEs being associated with higher discontinuation rates. Median time to onset for oropharyngeal TEAEs and oropharyngeal TEAEs leading to discontinuation was 89.5 and 114.5 days from study initiation, respectively (Figure 1). Baseline characteristics significantly associated with the occurrence of oropharyngeal TEAEs were dopamine agonists use ($p < 0.001$), older age ($p < 0.01$) and other dopaminergic medications use ($p < 0.01$). Baseline characteristics significantly associated with occurrence of oropharyngeal TEAEs leading to discontinuation were older age ($p < 0.01$) and dopamine agonists use ($p = 0.042$).

Table 1. Summary of oropharyngeal TEAEs during the dose-optimisation phase and the long-term safety phase of Study CTH-301

	Dose-optimisation phase n=449	Long-term safety phase n=426	Dose-optimisation and long-term safety phase N=496
All TEAEs			
Any TEAEs, n (%); number of events	232 (51.7); 657	365 (85.7); 1966	446 (89.9); 2623
Oropharyngeal TEAEs			
Any oropharyngeal TEAEs n (%); number of events	53 (11.8); 78	178 (41.8); 475	206 (41.5); 553
Drug-related TEAEs, n (%); number of events	25 (5.6); 36	145 (34.0); 394	160 (32.3); 430
Mild*	20 (4.5); 30	67 (15.7); 141	79 (15.9); 168
Moderate*	5 (1.1); 5	72 (16.9); 148	75 (15.1); 152
Severe*	0	6 (1.4); 8	6 (1.2); 8
TEAEs leading to drug reduction, n (%); number of events	1 (0.2); 1	7 (1.6); 13	8 (1.6); 14
TEAEs leading to drug interruption, n (%); number of events	0	45 (10.6); 72	45 (9.1); 72
TEAEs leading to drug discontinuation, n (%); number of events	1 (0.2); 1	80.0 (18.8); 137	81 (16.3); 138
Mild*	1 (0.2);1	24 (5.6); 31	25 (5.0); 32
Moderate*	0	52 (12.2); 81	52 (10.5); 81
Severe*	0	4 (0.9); 5	4 (0.8); 5
TEAEs leading to death, n (%); number of events	0	0	0

*Based on the highest severity level for each subject, TEAE, treatment-emergent adverse events

Figure 1. Distribution of days to onset of oropharyngeal TEAEs during the dose-optimisation phase and the long-term safety phase of Study CTH-301: (A) any oropharyngeal TEAEs; (B) oropharyngeal TEAEs leading to discontinuation. Black lines indicate smoothed density estimate of the histograms; turquoise vertical lines on x-axes indicate days to onset of oropharyngeal TEAEs or discontinuation due to oropharyngeal TEAEs for each individual patient; dashed red lines indicate the median; continuous red lines indicate the mean. SD, standard deviation; TEAEs, treatment-emergent adverse events



Conclusion: Oropharyngeal TEAEs, including those leading to discontinuation, were mostly mild or moderate and predominantly occurred within the first few months of SL-APO initiation.

Disclosure: Supported by Bial.

EPO-557 | Remote monitoring of symptoms helps to maintain the quality of life in Parkinson's disease

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Background and Aims: Remote monitoring of patients provides objective information for the healthcare to adjust the treatment. Simultaneously the patient has a better insight into the disease giving opportunity for improvements in self-care and lifestyle. In AICCELERATE-project, we develop remote monitoring of persons with Parkinson's disease (pwp).

Methods: 26 pwps were randomized either to an intervention group ($N = 14$) provided with a wrist-worn wellness wearable (Polar Ignite 2), a videomonitoring solution (NeuroPath), and a mobile symptom diary (Health Village, HUS) or to a control group ($N = 12$). Patients were asked to use the devices monthly. All patients were clinically evaluated twice in 6 months by validated scores (MDS-UPDRS, NMSS and PDQ39). Adherence was evaluated by the number of measurements taken. Quality of life, Parkinson-symptoms and levodopa equivalent daily doses were compared between groups with statistical tests (Wilcoxon for pre-post comparisons and Mann-Whitney *U* for between group comparisons).

Results: During 6 months, patients had performed median of 4.8 video-monitoring sessions (12 motor tasks/session), reported symptoms 2.4 times with the diary, and used the wellness wearable for median of 103 days. Three patients wished to discontinue in the study during the follow-up. Quality of life (PDQ39) had improved after remote monitoring period compared to control group (the changes in PDQ-4.5 and 3.5, respectively, $p = 0.017$). There was no statistical difference between baseline demographics or the progression of symptoms between groups.

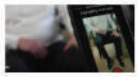
Device	Manufacturer	Data collected	Number of measurements, median (range)
	Polar, Kempele, Finland	Sleep duration and interruptions Steps/day	103 days (40-183)
	NeuroPath, Enghien, Belgium	Metrics and videos of 12 motor tasks	4,8 sessions, 58 videos (20-77 videos)
	Helsinki University Hospital, Helsinki, Finland	Questionnaire for motor and non-motor symptoms and disability	2 (0-7)

TABLE 1 Median number of remote measurements taken in 6 months at home by intervention group.

	Age (range)	Disease duration, years (IQR)	LEDD, (IQR)	PDQ39, baseline (IQR)	Change of PDQ39 (IRQ; p-value)	MDS-UPDRS, baseline (IQR)	NMSS, baseline (IQR)
Intervention group	68 (46-82)	4,6 (7,8)	475 (312)	23,5 (17)	-4,5 (7,8; 0,059)	33,5 (18)	18,5 (21)
Control group	69 (50-76)	4,0 (8,5)	425 (513)	29,5 (30)	13,5 (11,3; 0,107)	41,5 (37)	38,5 (32)

TABLE 2 Demographics at baseline and validated scores as median values in intervention and control groups. Interquartile range (IQR), range and *p*-values in parentheses. LEDD, levodopa equivalent daily dose.

Conclusion: Patients are motivated to use technology for months to acquire detailed information on their disease. The quality of life is not affected by monitoring, rather promotes better well-being.

Disclosure: The project has been funded by EU's Horizon2020.

Movement disorders 6

EPO-558 | Home-based non-invasive brain stimulation in combination with speech therapy in Parkinson's disease – Preliminary data

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Background and Aims: Hypokinetic dysarthria (HD) affects up to 90 % of Parkinson's disease (PD) patients, manifesting as reduced loudness, imprecise articulation, and impaired speech prosody. This ongoing study aims to investigate the effects of home-based transcranial direct-current stimulation (tDCS) as an add-on to the remote Lee-Silverman Voice Treatment (LSVT), compared to LSVT alone (coupled with sham stimulation), in PD patients.

Methods: Using a double-blinded, randomized design, PD patients are divided into two groups, receiving either real or sham anodal tDCS (2 mA, 20 min) of the right superior temporal gyrus (rSTG – auditory-feedback area) over 20 sessions in four weeks. Concurrently, both groups undergo remote LSVT. All participants undergo MRI scanning (fMRI-reading task and resting state) and evaluation by speech therapists, at baseline and after the treatment.

Results: Analysis of the first 12 subjects (6 sham, 6 real stimulation) revealed significant improvements for all participants in the Dysarthric profile scale Total score (median relative change = 5.87, $p = 0.005$) and Phonetics score (median relative change = 4.0, $p = 0.038$). Changes in Phonetics score correlated with changes in left supplementary motor area (lSMA) activations ($R = 0.678$, $p = 0.045$). Interestingly, changes in resting state connectivity between rSTG and lSMA were higher after real stimulation (median = 63.8) than after sham (median = −100.4), though not statistically significant ($p = 0.114$).

Conclusion: Preliminary data suggest that the remote LSVT is beneficial for PD patients and combination with home-based stimulation is feasible. We also observed neural correlates of induced speech improvements.

Disclosure: Nothing to disclose.

EPO-559 | Levodopa-induced dyskinesias impact on quality of life in Parkinson's disease: A 5-year follow-up study

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Background and Aims: Levodopa-induced dyskinesias (LID) are frequent in Parkinson´s disease (PD). Our aim was to analyze the change in the frequency of LID over time and identify LID related factors and know how LID impact on patients´ quality of life (QoL).

Methods: PD patients from the COPPADIS cohort were included. LID was defined as a non-zero score in the item "Time spent with dyskinesia" of the UPDRS-IV. It was applied at baseline (V0) and annually for 5 years. The 39-item Parkinson's disease Questionnaire Summary Index (PQ-39SI) was used to asses health-related QoL.

Results: The frequency of LID at V0 in 672 PD patients (62.4 ± 8.9 years old; 60.1% males) with a mean disease duration of 5.5 ± 4.3 years was 18.9% (127/672) and increased progressively to 42.6% (185/434) at 5-year follow-up (V5y) (Figure 1A). LID was associated with disease duration and time under levodopa therapy (Figure 1A-1D). Significant Independent factors associated with LID ($p < 0.005$) were a longer time under levodopa treatment and disease duration, a higher dose of levodopa, a lower dose of dopamine agonist and weight, and the presence of motor fluctuations and pain (Table 1). Patients with LID had a higher score on the PDQ-39SI in all visits ($p < 0.005$) and at V0 LID was independently associated with a greater score on the PDQ-39SI ($\beta = 0.073$; 95% CI, 0.274–4.534, $p = 0.027$; $R^2 = 0.62$) (Table 2).

Variables at baseline (V0)	Adjusted R-squared	OR	CI 95%	p
	0.52			
To have motor fluctuations		4.966	2.687 – 9.176	<0.0001
Levodopa daily dose		1.002	1.001 – 1.003	<0.0001
VAS-PAIN		1.156	1.060 – 1.261	0.001
Disease duration		1.013	1.004 – 1.022	0.005
DA equivalent daily dose		0.998	0.996 – 0.999	0.025
Weight		0.979	0.959 – 0.999	0.041
Time under levodopa therapy		1.105	1.003 – 1.219	0.044

Dependent variable: LID at baseline. Covariates were included in the multivariate analyzes using sequential logistic regression methods and only significant variables (p<0.005) were kept in the model. Hosmer and Lemeshow test = 0.576.

DA, dopamine agonist; VAS, Visual Analogue Scale.

TABLE 1 Factors associated with the presence of LID at baseline (V0) in the COPPADIS cohort ($N = 672$).

Variables at baseline (V0)	Adjusted R-squared	β	CI 95%	p
	0.62			
NMSS		0.441	0.129 – 0.178	<0.0001
FOGQ		0.222	0.407 – 0.826	<0.0001
VAFS		0.118	0.256 – 0.894	<0.0001
BDI-II		0.099	0.065 – 0.282	0.002
PDSS		-0.093	-0.088 – -0.015	0.005
Age		-0.075	-0.208 – -0.227	0.011
UPDRS-III		0.084	0.019 – 0.191	0.016
Levodopa-induced dyskinesia		0.073	0.274 – 4.534	0.027

Dependent variable: PDQ-39SI at baseline. Covariates were included in the multivariate analyzes using sequential logistic regression methods and only significant variables (p<0.005) were kept in the model. Durbin-Watson test = 1.81.

BDI-II, Beck Depression Inventory-II; FOGQ, Freezing of Gait Questionnaire; NMSS, Non-Motor Symptoms Scale; PDSS, Parkinson's Disease Sleep Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAFS, Visual Analog Fatigue Scale.

TABLE 2 Effect of LID (levodopa-induced dyskinesia) on quality of life after adjustment to other covariates at baseline (V0) in the COPPADIS cohort ($N = 672$).

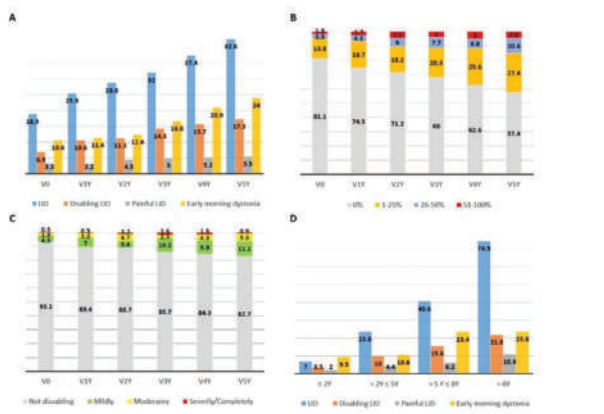

Figure 1. A. Frequency of LID, disabling LID, painful LID and early morning dystonia at baseline (V0; N=672) and annually for 5 years. V1y (12 months ± 1 month; N=604); V2y (24 months ± 1 month; N=517); V3y (36 months ± 2 months; N=482); V4y (48 months ± 3 months; N=465); V5y (60 months ± 3 months; N=434). B. Frequency of awake time with LID according to the UPDRS-IV-item 32 at V0, V1y, V2y, V3y, V4y and V5y. C. Degree of severity of LID according to the UPDRS-IV-item 33 at V0, V1y, V2y, V3y, V4y and V5y. D. Frequency of LID, disabling LID, painful LID and early morning dystonia at V0 regarding the time under levodopa therapy in the group of patients receiving levodopa at V0 (N=490). P value < 0.0001 for all analysis except for early morning dystonia (p=0.032). LID, levodopa-induced dyskinesias; UPDRS, Unified Parkinson's Disease Rating Scale.

Conclusion: LID are frequent in PD patients. A higher dose of levodopa and lower weight were factors associated to LID. LID impact on QoL.

Disclosure: The authors report no conflict of interest.

EPO-560 | Effects of sensory modulation on balance control, a preliminary study with healthy individuals and chronic stroke

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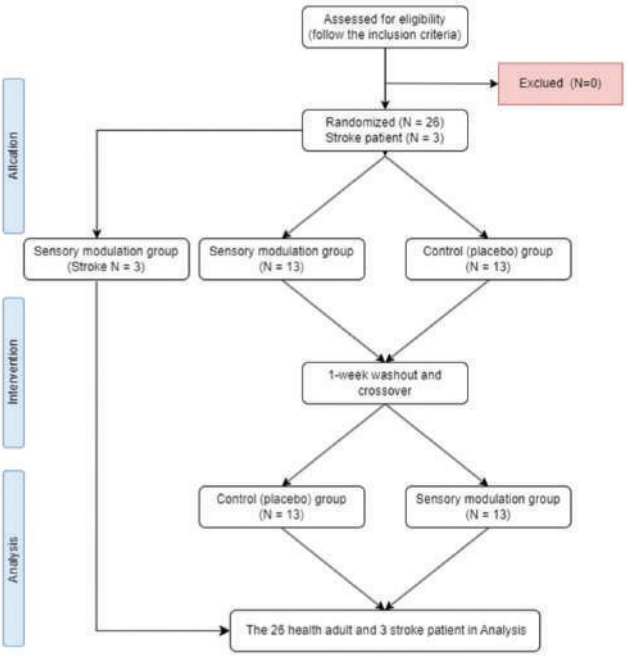
Background and Aims: Individuals with sensory deficits rely on feedforward control for better motor performance. Additional sensory afferent input can induce feedforward control. EEG event-related synchronization/desynchronization (ERD/ERS) and theta-gamma

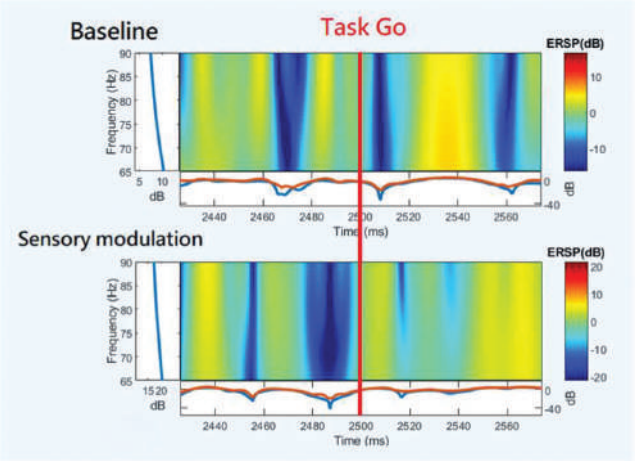
coupling are thought to be related to feedforward control. This study aims to determine if sensory afferent input induced by local vibration (sensory modulation) induces feedforward control.

Methods: Participants underwent a sensory modulation experiment and placebo experiment in random order. Participants first received 30 s of high-frequency vibration stimulation on the dominant foot's tibialis anterior muscle, then received balance assessment and training (five rounds total). The placebo condition used sham vibration. The Balance Index (Biodex balance system) and EEG (TMSi-64 channel system) were collected before and after sensory modulation. The EEG data were processed with time-frequency analysis and the frequency-profile of theta and gamma bands and ERD/ERS peak values were calculated. Pearson's correlations determined theta-gamma coupling and two-way repeated measures ANOVA was used to compare the ERD/ERS between the two conditions. The statistical significant level was set to <0.05.

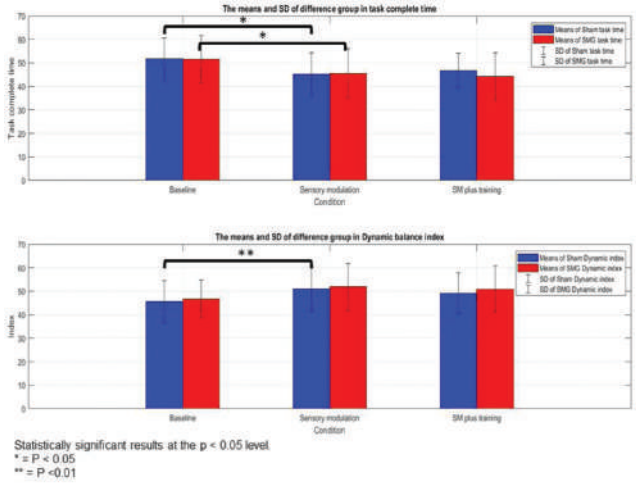
Results: Our study with 26 healthy adults found that sensory modulation significantly improved the dynamic balance index ($p=0.004$) and induced greater theta gamma phase-amplitude coupling in the motor cortex ($r=0.9$; $p<0.001$). Our results also found that the gamma ERD in the sensory modulation condition was significantly lower, but earlier than the placebo condition ($p=0.013$).



The study flowchart.



With the intervention of sensory modulation, the sensory modulation group showed greater and earlier event-relative desynchronization peaks in the time-frequency analysis of EEG measurements.



The sensory modulation group and the Sham group showed a significant reduction in task completion time at baseline and after sensory modulation. The sensory modulation group showed a significant increase in balance dynamic index at baseline and after sensitivity.

Conclusion: Our study found that sensory modulation with local vibration can induce feedforward control, and a similar trend was also observed in stroke patients.

Disclosure: Nothing to disclose.

EPO-561 | The use of opicapone for motor fluctuations in Parkinson: Real-life experience of two Italian Movement Disorders Centers

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Background and Aims: Opicapone (OPC) is used as add-on to L-Dopa (LD) therapy for management of motor fluctuations (MFs) in Parkinson's disease (PD). Its benefit on PD population has been established by different clinical trials, and a recent post-hoc analysis has demonstrated its better tolerability when used early in iPD. Data are missing about the use of OPC on Italian population of PD patients, so the aim of this paper is to report the real-life experience of the two Centers of Trieste and Trento.

Methods: Retrospective data have been gathered of Italian PD patients followed for at least two years after OPC introduction for MFs.

Results: 152 patients have been enrolled, 35% reported adverse events (AEs) on the two-year follow-up. 27% discontinued OPC because of a severe AE, which in 76% of cases was a dopamine-related AE. Univariate analysis recognized as clinical predictors of treatment discontinuation because of any AE were age, disease duration, MFs duration, Hoehn-Yahr stage, past history of hallucinations or addictive behaviour, mild cognitive complaint, falls, and for treatment discontinuation due to dopamine-related AE were age, MFs duration, Hoehn-Yahr, previous addictive behaviour, MCI, and falls. Predictors of OPC withdrawn accordingly to multivariate were MFs duration and Hoehn-Yahr.

Conclusion: Real-life data on Italian PD population confirm good tolerability and safety of OPC for the treatment of MFs, moreover when introduced early according to disease course and LD treatment pathway. MFs duration and Hoehn-Yahr stage have been shown to be important predictors of OPC therapy maintenance over a follow-up of at least 2 years.

Disclosure: Nothing to disclose.

EPO-562 | Clinical correlates of iron deposition within subcortical nuclei in early drug-naïve Parkinson's disease patients

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Background and Aims: Iron deposition using Quantitative Susceptibility Mapping (QSM) has been reported in patients with Parkinson's disease (PD)1. We explored the association between 3TMRI-derived iron deposition content within 12 bilateral subcortical nuclei and several motor, nonmotor and neuropsychological features in a cohort of 58 early drug-naïve PD patients.

Methods: Disease severity was assessed by UPDRS-III, nonmotor symptoms by Nonmotor symptoms scale (NMSS), autonomic dysfunction by Scale for Outcomes in Parkinson's disease for Autonomic symptoms (SCOPA-AUT), behavioral symptoms by Beck Depression Inventory (BDI-II), Parkinson Anxiety Scale (PAS) and Apathy Evaluation scale (AES). An extensive neuropsychological assessment was acquired and a *z*-score for each cognitive domain was calculated. QSM values were extracted from 12 bilateral subcortical nuclei by applying the HybraPD atlas2. A partial correlation analysis was run between MRI and clinical data.

Results: We found significant correlations between the iron content within bilateral dentate nuclei and UPDRS-III scores; left externus globus pallidus/right red nucleus and AES scores; left subthalamic nucleus/externus globus pallidus and *z*-score executive; bilateral putamina/right externus globus pallidus and *z*-score attention; left substantia nigra (pars reticulate) and PAS scores; right substantia nigra (pars compacta) and BDI-II scores; right red nucleus and several thalamic subregions and SCOPA-AUT scores.

Conclusion: The presence of specific clinical features is associated with increased iron deposition within different subcortical nuclei in PD patients in the early stages. These findings may be associated with a more severe clinical picture at baseline and may potentially lead to more rapid worsening over time.

Disclosure: The Authors have no disclosures.

EPO-563 | Subacute cerebellar ataxia: Always look for malignancy: A case report

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Background and Aims: Intracellular anti-SOX1 antibodies are associated with several neurological síndromes. Lambert-Eaton syndrome and subacute cerebellar degeneration (CD) are the most frequent. Almost all cases are paraneoplastic, and small cell lung carcinoma (SCLC) is the most frequently detected malignancy.

Methods: Case description.

Results: We present the case of a 62-year-old male patient, exsmoker, with mild active alcohol intake, who seeked neurology consultation for a 9-month progressive gait and speech disorder. On neurological examination, he had moderate dysarthria, hypermetric saccades on horizontal plane, mild bilateral dysmetria, and severe gait ataxia, requiring constant bilateral support. There was no cognitive impairment. On further questioning, he had lost 10 kg during that period. He was diagnosed with subacute cerebellar

degeneration. Brain magnetic resonance showed mild cerebellar atrophy, possibly related to chronic alcohol intake. Focusing on treatable causes, lumbar puncture revealed normal CSF cell count, glucose and proteins, but positive anti-SOX1 antibodies were found in serum and CSF (confirmed with indirect immunofluorescence and Western Blot). Electromiography showed no evidence of Lambert-Eaton. Seeking for occult malignancy, a carinal adenopathy was found on PET-CT scan and a biopsy revealed a SCLC stage III. Three months after chemotherapy and 2 cycles of immunoglobulins, his neurological condition has mildly improved, now being able to walk with one support.

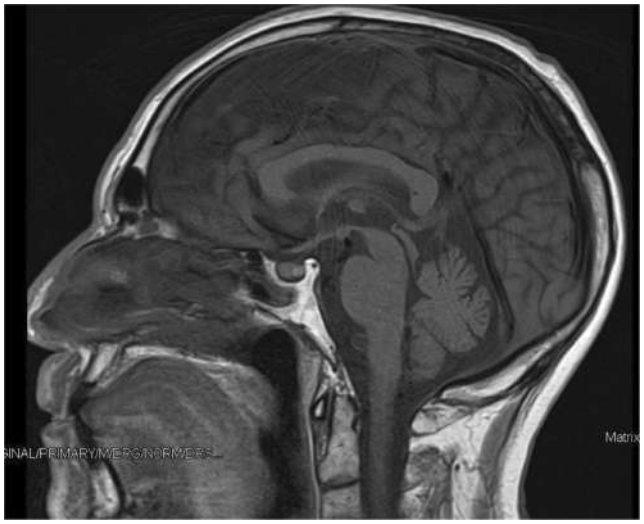

IMAGE 1 Mild cerebellar atrophy in MRI.

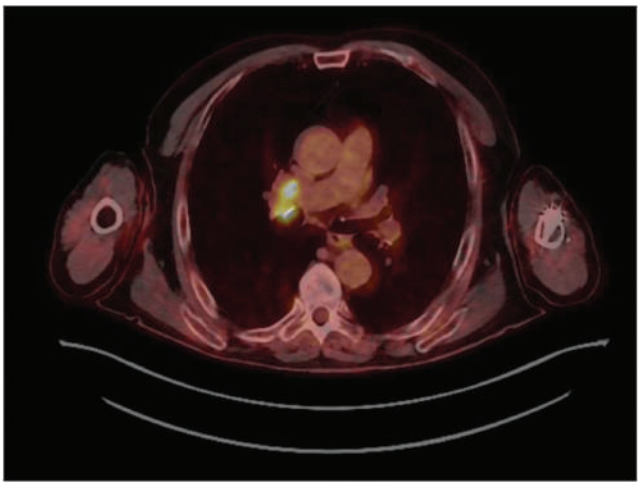

IMAGE 2 A pathological carinal adenopathy is found in PET-CT scan.

Conclusion: Subacute cerebellar degeneration has some treatable causes. When anti-SOX1 antibodies are found, search for malignancy is a must. Knowledge of paraneoplastic neurological syndromes can improve cancer detection and treatment.

Disclosure: None.

EPO-564 | Effectiveness of a multidisciplinary approach to prevent falls and gait impairment in patients with Parkinson's disease

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Background and Aims: Managing Parkinson's disease (PD) requires a multidisciplinary approach to address the diverse needs of patients. We aimed to study the short and long-term effectiveness of a multidisciplinary telemedicine program in addition to in-office usual care in non-demented patients with PD at risk for falling.

Methods: Longitudinal, randomized, case-control study. All participants in the office were evaluated at baseline, four, and eight months (V0, V1, and V2). Patients included in the telemedicine program received additional multidisciplinary care with nurse, neurologist, and occupational therapist interventions from V0 to V1. The severity of motor, non-motor symptoms, and quality of life were compared at each visit.

Results: Fifty patients were included, 25 patients [telemedicine program, 48% males, mean age of 71.1 ± 9.0 years, median number of falls (last month) of 1.0 (IQR: 0.0; 1.5)] and 25 patients [control group, 52% males, mean age of 69.2 ± 9.4 years, median number of falls (last month) of 1.0 (IQR: 0.0; 2.0)]. When both groups were compared, in the telemedicine group, apathy, and depression symptomatology, freezing of gait and balance were improved at V1 compared to V0 (all p values < 0.0001), and freezing of gait and balance at V2. In post-hoc analyses, quality of life improvement was correlated with improvement in depression in the telemedicine group.

Conclusion: By leveraging multidisciplinary telemedicine interventions in addition to in-office visits, healthcare providers can deliver patient-centric care, improving non-motor symptoms and gait impairment in PD. These hybrid interventions could solve current barriers to health systems with limited capacity.

Disclosure: This work was supported by the project PI19/00670 of the Ministerio de Ciencia, Innovación y Universidades, Instituto de Salud Carlos III, Spain.

EPO-565 | Reduced glucocerebrosidase activity in patients with sporadic Parkinson's disease

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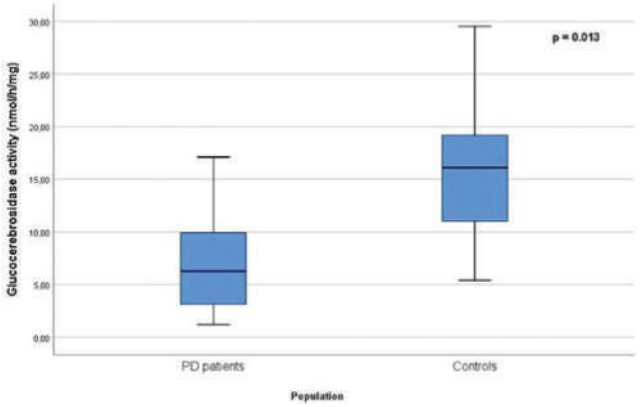
Background and Aims: The pathogenesis of sporadic Parkinson's disease (PD) is thought to be resulting from a complex interplay between genetic and environmental factors. While GBA1 mutation is a

confirmed risk factor of PD, little is known about glucocerebrosidase (Gcase) activity in sporadic PD. Our work aims to measure the Gcase activity in sporadic PD patients and matched healthy controls and identify any clinical or biological correlation with disease severity.

Methods: Flow cytometry was used to measure lysosomal Gcase activity in lymphocytes from 50 sporadic PD patients and 50 age/gender-matched healthy controls. All participants underwent a neurological examination, including a motor severity assessment by MDS-UPDRS score and modified Hoehn and Yahr scale (H&Y), along with a measure of blood glucose and lipids.

Results: Gcase activity was significantly reduced in PD group (6.84 nmol/h/mg ± 4.16 vs 16.06 ± 5.9; $p = 0.013$; OR = 2.13). Within PD group, lower Gcase activity was correlated with age >65 ($p = 0.049$; OR = 1.27) and PD onset before 50 ($p = 0.046$; OR = 1.49). Enzymatic activity was not correlated to the other studied variables: Sex, BMI, PD duration, MDS-UPDRS score, H&Y stage, glucose and lipids levels ($p > 0.05$).



Glucocerebrosidase activity in PD patients and controls.

Conclusion: Our study revealed a reduced glucocerebrosidase activity in patients with sporadic PD but did not find a correlation with its severity. Larger sample studies are needed to corroborate these findings. If confirmed, it could be a step towards the first biomarker for PD.

Disclosure: Nothing to disclose.

EPO-566 | Effect of fecal microbiota transplantation on clinical symptoms of Parkinson disease – A pilot study

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Background and Aims: The gastroenteric tract is involved in the pathogenesis of Parkinson's disease (PD) from its early, premotor stage. Gut bacteria may play a role in the pathogenesis and progression of PD. The aim of the study is to assess the impact of Fecal Microbiota Transplantation (FMT) on clinical symptoms of PD.

Methods: 25 patients with a diagnosis of PD were included in the analysis. Patients were randomly assigned to two groups: FMT from healthy donor or identically looking placebo produced from the patients' stool. Patients and clinicians were blinded to group allocation. FMT/placebo were administered into the distal part of the small intestine via colonoscopy. Patients underwent clinical assessments before and 1, 3, 6 and 12 months after the procedure (v0, v1, v3, v6 and v12 respectively). UPDRS I-IV, EQ5D, Constipation Assessment Scale (CAS), PDQ-39, NMSS, Gastrointestinal Dysfunction Scale for PD (GIDS-PD) were performed. Levodopa equivalent daily dose (LEDD) was calculated for each visit. Statistical analysis was performed with R version 4.1.2.

Results: Significant differences in LEDD between visits v1-3 after the procedure ($p = 0.003$) and difference in EQ5D between v1-3, v1-12 and v0-12 ($p < 0.05$) were observed. CAS and GIDS-constipation subscale varied significantly between v0-12 ($p < 0.05$). Significant differences were observed between V1 and 3 in several subscales of NMSS, particularly assessing psychiatric symptoms. No significant change in UPDRS III in the "off" state was observed.

Conclusion: FMT may influence clinical picture of PD, especially regarding its non-motor symptoms. Results suggest that the impact of the procedure diminishes with time, so repeated interventions could be considered.

Disclosure: Nothing to disclose.

EPO-567 | Long-term monitoring of copper metabolism parameters during treatment in patients with Wilson's disease

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Background and Aims: In Wilson's disease (WD), therapy aims to achieve homeostasis of copper metabolism and prevent excessive copper accumulation and deficiency. WD patients require lifelong treatment and regular monitoring of copper metabolism parameters.

Methods: This retrospective study is based on medical records collected from patients diagnosed with WD from the 1970s to 2022. The study groups included compliant patients, 237 treated with D-penicillamine (DPA) (89 hepatic, 120 neurological, 28 asymptomatic) and 228 with zinc sulfate (ZS) (94 hepatic, 70 neurological and 64 asymptomatic). The daily urinary copper excretion (UCE), serum copper and ceruloplasmin concentrations were analysed before and during long-term treatment.

Results: A significant decrease in serum copper and ceruloplasmin is observed during the first year of therapy, regardless of medication type. These parameters stabilise in the following years, but a slight increase occurs after ten years. A greater decline is obtained in the neurological form than in the hepatic and asymptomatic. The

pattern of UCE differs in the DPA group, with a significant increase within half a year of starting treatment. In the ZS group, the trend is similar to the other copper metabolism parameters.

Conclusion: The copper metabolism parameters reach optimal values in the first year of treatment and then stabilise. The decrease in serum copper leads to decreased ceruloplasmin, which can increase during long-term therapy improving liver functions. Patients with a neurological form are more prone to excessive decopperization. The obtained ranges of copper metabolism results may contribute to developing optimal long-term monitoring of WD patients.

Disclosure: Nothing to disclose.

EPO-568 | Correlations between CSF biomarkers of AD, neuropsychological tests and UPDRS-III in a cohort of PD patients

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Background and Aims: Cerebrospinal fluid (CSF) biomarkers for biological diagnosis of Parkinson's Disease (PD) are lacking a wide clinical application. CSF biomarkers of amyloidopathy, tauopathy and neurodegeneration have been used in the last decades to measure Alzheimer's disease (AD) pathology in vivo and as a predictor of cognitive impairment in AD and have been proven to predict cognitive decline in PD as well. The objective is to assess the correlations between CSF biomarkers of AD pathology and cognitive/motor impairment in a cohort of PD patients.

Methods: We recruited 89 subjects with a diagnosis of PD. A lumbar puncture was performed and AD CSF biomarkers were quantified. When lumbar puncture was done, neuropsychological battery and UPDRS-III were performed. Correlations between CSF biomarkers, neuropsychological tests and UPDRS-III at the time of lumbar puncture and at last follow-up were carried out.

Results: Our results revealed a statistically significant correlation between biomarkers of amyloidopathy (Aβ42 and Aβ42/40) and poorer performances in MMSE, RAVLT delayed recall, Spatial Span, Raven matrices, MFTC, semantic verbal fluency, ROCF delayed recall. Interestingly, *t*-tau and *p*-tau levels were found to predict the % change between the UPDRS-III score at the baseline and follow-up, also when corrected with follow-up duration, LEDD and baseline UPDRS score.

Conclusion: This study highlighted how biomarkers of amyloidopathy can predict worse performances in some common neuropsychological tests. Furthermore, tau species showed potential in identifying PD patients at risk of accelerated motor decline, suggesting a possible synergistic role of tau with alpha-synuclein in the clinical progression of Parkinson's disease.

Disclosure: Nothing to disclose.

EPO-569 | Contribution to efficacy by active metabolites of suvecaltamide in a preclinical rat model of essential tremor

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Background and Aims: Suvecaltamide (JZP385), a potent, selective T-type calcium channel modulator, reduced the functional impact of essential tremor (ET) in a phase 2 trial (NCT03101241). We present the pharmacokinetic/pharmacodynamic (PK/PD) relationship and contribution to anti-tremor efficacy in a harmaline-induced rat ET model for suvecaltamide and its active metabolites (JZZ05000034 = M01, JZZ05000035 = M02).

Methods: Tremor was quantified using piezoelectric signals in rats receiving harmaline (15 mg/kg, intraperitoneal) 1 hour before single oral doses of suvecaltamide or its metabolites (analytes). Plasma and brain analyte concentrations were measured in satellite experiments following harmaline and analyte administration.

Results: Suvecaltamide dose-dependently suppressed existing tremor when administered post-harmaline, with significant effects at ≥1 mg/kg. Tremor reduction was rapid and sustained during 4-hour recordings. All analytes were measurable in plasma and brain. While suvecaltamide concentrations peaked early and then decreased, active metabolite concentrations were more sustained over the experimental period. When dosed directly, both metabolites reduced tremor at plasma concentrations consistent with those achieved after suvecaltamide administration. Plasma suvecaltamide, M01, and M02 concentrations at 1 mg/kg were consistent with those achieved at steady state in humans at projected therapeutic doses. We characterized the PK/PD relationship of the suvecaltamide total active moiety in rats and utilized CaV3 potency and unbound plasma concentrations to translate to humans.

Conclusion: These results illustrate contributions to efficacy by active suvecaltamide metabolites in rats, which must be considered clinically given they are predicted to translate to human efficacy. These data support continued clinical development of suvecaltamide for adults with moderate-to-severe ET (NCT05122650) or residual Parkinson's disease tremor (NCT05642442).

Disclosure: Supported by Jazz Pharmaceuticals. All authors are full-time employees of Jazz Pharmaceuticals who, during this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc.

EPO-570 | Cerebellar ataxia in mitochondrial pathology: Review based on a case series

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Background and Aims: Cerebellar involvement in mitochondrial pathology is under-recognized, especially when it manifests as the initial symptom without a family history of such conditions. This study aimed to characterize the casuistry and clinical features of patients presenting with cerebellar ataxia due to mitochondrial pathology.

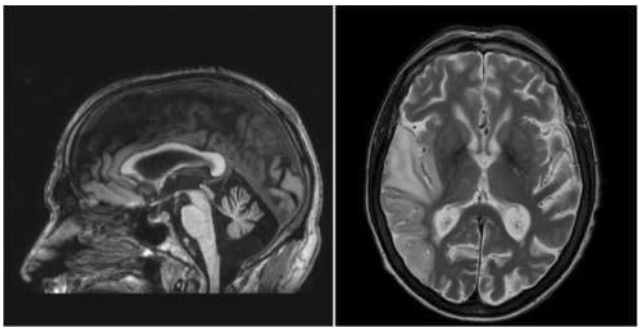
Methods: A descriptive, retrospective, single-center study was conducted on patients assessed in the ataxia unit of a tertiary hospital over five years. Patients diagnosed with mitochondrial cerebellar ataxia (CAM) were included, and demographic, clinical, and neuroimaging data were examined.

Results: Out of 221 patients, six were diagnosed with CAM (prevalence 2.7%). The average onset age was 48.3 years, with a diagnostic delay of 11.7 years. None had a family history of mitochondrial pathology, although two had history of deafness and diabetes. All patients presented with ataxia, scanning dysarthria and oculomotor impairment: ophthalmoparesis (cases 1, 2, 3, 5), gaze-evoked nystagmus (4). Other common clinical features included reduced visual acuity due to optic atrophy (4, 5, 6), sensory-motor polyneuropathy (2, 3, 4, 5, 6), myopathy (1, 2, 3) and spasticity (4), alongside other neurological manifestations such as stroke-like episodes (1), generalized epilepsy (1, 3, 5), chorea (3) and pes cavus (5, 6). Systemic symptoms included diabetes, early-onset hearing loss, and dilated cardiomyopathy. MRI findings reflected predominantly cerebellar atrophy or vermian volume loss. Genetic mutations were identified in genes including MT-TL1 (cases 1, 2), POLG (3) OPA1 (4), and TSFM (5, 6).

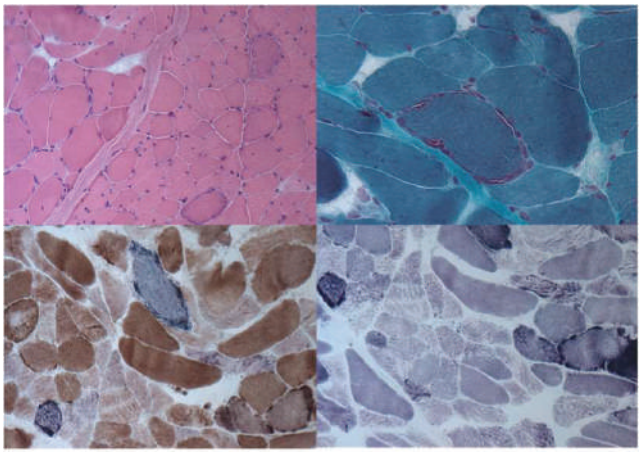
Symptoms		Mutation
Neurological		
Ataxia	6/6 (100%)	MELAS, POLG, OPA1, TSFM
Dysarthria	6/6 (100%)	MELAS, POLG OPA1, TSFM
Chorea	1/6 (16,6%)	POLG
Epilepsy	4/6 (66,6%)	MELAS, POLG, TSFM (5)
Stroke-like episodes	1/6 (16,6%)	MELAS (1)
Polyneuropathy	5/6 (83,3%)	MELAS (2), POLG, OPA-1
Spasticity	1/6 (16,6%)	OPA-1
Myopathy	3/6 (75%)	MELAS (1,2) ,POLG
Cognitive impairment	3/6 (50%)	MELAS (1) , POLG, TSFM (1)
Pes cavus	2/6 (33,3%)	TSFM
Ocular		
Ophtalmoparesis	4/6 (66,6%)	MELAS (1,2), POLG, OPA1
Ptosis	1/6 (16,6%)	MELAS (2)
Optic atrophy	3/5 (50%)	OPA1, TSFM
Gaze evoked nystagmus	1/6 (33,3%)	OPA1
Others		
DM	2/6 (33,3%)	MELAS (1,3)
Cardiomyopathy	3/6 (50%)	MELAS (2), TSFM (5,6)
Hearing loss	3/6 (50%)	MELAS (1,2), TSFM (5)

Supplementary tests		
MRI	Cerebellar atrophy Ischemic cortico-subcortical lesions	5/6 1/6
Muscle biopsy	Compatible with mitochondriopathy Negative Not performed	1/6 2/6 3/6
Laboratory	Elevated GDF 15	2/6
EMG	Sensorimotor polyneuropathy	5/6
Genetic test	Mutation MT-TL1 gene POLG-1 gene OPA-1 gene TSFM gene	 2/6 1/6 1/6 2/6

Clinical characteristics and supplementary studies results.



MRI- (A) T1-sagittal (B) T2- axial.



Muscle biopsy- (A) Hematoxylin-eosin (B) Gomori trichrome stain (C) COX (D) SDH.

Conclusion: Mitochondrial etiology should be considered in the differential diagnosis of late-onset cerebellar ataxias, even in the absence of family history. Recognizing associated symptoms could aid the diagnosis, with implications for prognosis, therapy, and genetic counseling.

Disclosure: Nothing to disclose.

EPO-571 | Wearable sensor detects early morning bradykinesia (EMB): From Parkinson's watch to bedside

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Background and Aims: Early Morning Bradykinesia (EMB) is clinically noted as early morning off (EMO) period which presents with motor and a range of non-motor symptoms (Rizos et al 2014) often undetected in clinical practice with a negative effect on quality of life in Parkinson's disease (PD). Continuous objective monitoring using the PD validated Personal KinetiGraph (PKG) can detect EMB in clinically unrecognized cases.

Methods: We report interrater reliability of detecting EMB using PKG criteria from two blinded who visually identify EMB from PKG reports and commented on severity (moderate or severe).
Results: A total of 100 PKG reports of PwP were analyzed (63% female and 37% male, median Hoehn and Yahr (HY) score 2–3), mean disease duration 9.4 years (±7.1), mean levodopa equivalent daily dose 633.98 mg (±558.24). EMB was observed in 73% PD and was reported as moderate in 64.3%, severe in 35.6%. Cohen's Kappa Interrater reliability score was 0.71 (substantial) for EMB diagnosis and 0.51 (moderate) for severity. No statistical significant correlations were found between EMB and motor scales.
Conclusion: PKG is an objective measurement device with a good interrater reliability for the identification of EMB and its severity. Our findings provide important evidence of the use of PKG for nocturnal monitoring in PD.
Disclosure: All authors report no conflict of interest.

EPO-572 | Elevation of alpha-fetoprotein in patients with dystonia

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Background and Aims: Alpha-fetoprotein (AFP) is a glycoprotein produced by the liver, and it is a tumor marker. Elevated levels are nevertheless associated with ataxia telangiectasia (AT), caused by a mutation in the ATM gene. The variant form of AT usually manifests in adolescence or adulthood, dystonia may be the only symptom. Telangiectasia and other symptoms of classic AT may be absent. Therefore, AFP seems to be an important biomarker in patients with dystonia. A screening study was conducted to determine the incidence of alpha-fetoprotein elevation in patients with dystonia.
Methods: Patients with dystonia occurred before the age of 50 years, were included. Alpha-fetoprotein levels were examined on an Atellica IM analyzer, with normal levels in the range of 0–8 ng/ml. Whole exome sequencing (WES) was performed in patients with elevated AFP levels.
Results: A total of 167 patients (48 men) were included, mean age of 56.5 years (±10 years). Elevated AFP levels (8.1–96.7 ng/ml) were detected in 14 (8.3%) patients (2 men), mean age 61.8 years (±12 years). In patients with elevated AFP levels, neither ATM nor any other mutation was detected in WES. The incidence of elevated AFP levels for the Atellica IM analyzer is 1.6% in the healthy population.
Conclusion: Elevated AFP levels with negative results in WES were present in a higher number of patients than it corresponds to the healthy population. This is a result that should be confirmed/refuted by further studies. AFP should be considered as a new biomarker in dystonia patients.
Disclosure: Nothing to disclose.

MS and related disorders 5

EPO-573 | Benefits of early highly effective vs escalation treatment in relapsing MS estimated using a treatment-sequence model

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Background and Aims: Uncertainty about disproportionate impact on healthcare budgets limits implementation of early highly effective treatment (EHT) in multiple sclerosis (MS). Therefore, it is necessary to estimate cost-effectiveness of escalation vs. EHT disease-modifying treatment (DMT) sequences.
Methods: Using a health-economic approach, we analyzed health benefits (relapse rate reduction, disability prevention), direct/indirect DMT and societal costs of escalation vs. EHT DMT sequences. In scenario analyses, we allowed (1) earlier use of alemtuzumab and (2) a single retreatment with cladribine.
Results: In our model, we showed that the ratio between costs and quality-adjusted life years for the most cost-effective EHT and escalation sequence results into a similar net health benefit with higher costs but also higher QALYs associated with an EHT vs escalation strategy. Earlier use of alemtuzumab is more cost-effective than in later lines, even when aggravating the impact of its side effects tenfold. Retreatment with cladribine was more cost-effective in both escalation and EHT sequences.
Conclusion: Certain EHT sequences are equally cost-effective to escalation sequences and are likely to result in more health at uncertain additional costs. The favourable cost-benefit ratio of cladribine and alemtuzumab suggests that a wider application of affordable highly-effective therapies could promote the cost-effectiveness both EHT and escalation approaches.
Disclosure: I.S. has received honoraria from Merck, Biogen Idec and Sanofi. B.H.A.W. declares no conflict of interest. S.A.H. and M.M.V. are shareholders of Huygens & Versteegh which conducts research for government organizations and pharmaceutical companies, including research in MS. J.S. received lecture and/or consultancy fee from Biogen, Merck, Novartis, and Sanofi Genzyme.

EPO-574 | Choroid plexus volume as proxy of higher cerebrospinal fluid inflammatory activity in multiple sclerosis

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Background and Aims: In our study, we investigate the hypothesis that Choroid Plexus volume (CPv) enlargement serves as a surrogate marker for heightened inflammatory cerebrospinal fluid (CSF) activity. This last, in turn, contribute to damage gradients observed in the normal-appearing white matter (NAWM) near the ventricles of patients with relapsing Multiple Sclerosis (MS) at disease onset.
Methods: Our cross-sectional evaluation involved 108 subjects. Using the nephelometric method and the Reiber formula, we quantified IgM intrathecal synthesis (ITMS) as an inflammatory activity biomarker in CSF. We performed advanced post-processing MRI analysis, encompassing brain, lesion and choroid plexus (CP) volume assessment. Additionally, we used T1/T2 mapping to evaluate the NAWM damage gradient.
Results: Comparing MRI features between the groups and exploring the link between NAWM damage gradient and CPv, we employed multiple linear regression models. Among the 108 patients subjected to MRI analysis, 32 tested positive for ITMS (ITMS+), while 76 were ITMS-negative (ITMS-). Importantly, ITMS+ and ITMS- patients exhibited comparable baseline clinical and demographic characteristics. While no significant differences were found in brain and lesion volumes between the two groups, CPv was notably enlarged in the ITMS+ group (beta 0.57, 95% c.i. 0.35–0.79, $p < 0.001$). Additionally, a significant relationship emerged between the T1/T2 ratio gradient and CPv (beta = 0.46, <0.001).
Conclusion: Our findings suggested a potential role for the CP in influencing NAWM changes. Further research is essential to validate this hypothesis and identify specific CSF biomarkers associated with CPv and NAWM damage.
Disclosure: E.P. received funding from Biogen, Merck, Sanofi, Novartis. M.P.A received funding from Biogen Idec, Merck Serono, Bayer Schering and Sanofi. E.D.M., I.A., C.B., V.P., A.C., C.F., E.F., report no disclosures.

EPO-575 | Demographic, clinical and serum parameters for the prediction of apheresis outcome in the steroid-refractory MS relapse

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Background and Aims: The optimal treatment strategy for steroid-refractory MS relapses remains unclear. We investigated the predictive power of multiple serum parameters, demographic and clinical data on apheresis outcome.
Methods: We examined sera of 38 participants of the IAPEMS-trial (randomized-controlled trial to evaluate the safety and efficacy of immunoadsorption versus therapeutic plasma exchange in steroid refractory MS relapses, NCT02671682) and conducted statistical analysis using serum parameters, demographic and clinical trial data. We classified apheresis outcome assessing the improvement of the affected functional system score four weeks after the procedure.
Results: In binary logistic regression analysis younger age (OR 0.948, 95% CI 0.903–0.995, $p = 0.03$) and lower sGFAP concentrations (RR 0.948, 95% CI 0.903 –0.995, $p = 0.03$) were associated with a favorable relapse outcome. In addition, we observed a strong trend towards a positive apheresis outcome with higher sNfL (RR 1.413, 95% CI 0.965–2.069, $p = 0.08$). Further analysis of our data showed no predictive power for further serum parameters (immunoglobulins, immunoglobulin free light chains, CXCL13, CXCL12, BCMA, BAFF), Symbol Digit Modalities Test (SDMT) and optical coherence tomography (OCT) measures in our study.
Conclusion: In line with published data, our study confirmed that patients with younger age and lower serum GFAP levels are more likely to benefit from apheresis. The potential predictive value of sNfL needs to be investigated in further prospective studies.
Disclosure: None of the authors have any disclosure related to this study.

EPO-576 | Real-life efficacy and safety of ofatumumab for highly active multiple sclerosis: The San Raffaele Hospital experience

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Background and Aims: Ofatumumab is a highly effective treatment for multiple sclerosis (MS), approved in Europe in April 2021. Post-marketing information is still limited. We report our real-life experience (San Raffaele Hospital MS cohort, Milan, Italy).
Methods: Data from MS patients receiving ofatumumab for at least 1 year were obtained: clinical information, neuroradiological examinations and lymphocyte subsets values were collected.
Results: Among 100 MS patients receiving ofatumumab, 37 were treated for at least 1 year (33 relapsing-remitting-RRMS; 4 relapsing-RMS; mean age 38.42 ± 10.6 years; 27 females, 10 males; mean disease duration 8.77 years – range 0.5–31.9; median EDSS 2.0 – range 0–8.0; 15/37 treatment-naïve; mean follow up 1.16 years – range

1.00–1.78). During the year before treatment start 35/37 patients showed MRI activity (2/37 shifted from Natalizumab for safety reasons), while 27/37 also experienced relapses. While treated with ofatumumab, no patients showed further relapses, while only 3/37 had persistent MRI activity (3/3 at rebaseline examination 6 months after treatment start, none with Gd-enhancing lesions). CD19+ lymphocyte count was available at 3 months in 24/37 participants: all patients showed B cells depletion (i.e. <0.5% – mean 0.09% – range 0.0–0.33%), with persistence at 1 year. Treatment was well tolerated, with no serious adverse event: 31/37 patients reported fever after first injection, while only 3/37 after titration; 5/37 patients presented mild-to-moderate upper respiratory tract infections. No pregnancy occurred.

Conclusion: Our short-term data suggest ofatumumab is effective, safe and well tolerated in MS. Long-term follow-up and larger cohorts are needed to confirm our observations.

Disclosure: LM received compensations for speaking activities and/or for participating to advisory board from Merck, Celgene, Biogen, Sanofi, Novartis, Roche, Alexion. FM received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva. FE received compensation from Merck and Biogen. AG received consulting fee from Novartis. CZ received compensation for speaking activities and/or consulting activities from Biogen, Bristol Myers Squibb, Janssen, Roche, Astrazeneca, Sanofi, Merck, Alexion, Novartis. LF received compensation for speaking activities and/or travel from Novartis, Merck, Jannsen. IG, SG, SMM, TZ, have nothing to disclose.

EPO-577 | Patient-reported fatigue in patients with relapsing multiple sclerosis receiving ocrelizumab: MoOzaRt interim analysis

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Background and Aims: Fatigue is considered the most common and one of the most debilitating symptoms in multiple sclerosis (MS). MoOzaRt aims to assess the impact of ocrelizumab on patient-reported long term (trait) and transient (state) fatigue in patients with relapsing forms of MS (RMS) under therapy with ocrelizumab.

Methods: The ongoing non-interventional study MoOzaRt (ISRCTN55332718) aims to recruit ~740 RMS patients initiating therapy with ocrelizumab from Germany and Switzerland. The primary endpoint is the change in the Fatigue Scale for Motor and Cognitive Functions (FSMC) total score from baseline to month 24, evaluating trait fatigue. Secondary endpoints include changes in state fatigue (Visual Analogue Scale, VAS), in Expanded Disability Status Scale (EDSS) and in safety.

Results: The first interim analysis (data cut off Dec 14, 2023) included 80 patients (72.5% female, mean age 37.5 (SD 9.9) years) with a mean EDSS score of 2.31 (SD 1.39) (table 1). Overall, FSMC total scores remained stable over 12 months ($N = 71$), while the proportion of patients with severe fatigue decreased markedly from in this period (table 2). VAS scores and detailed patient reported outcomes will be presented at the EAN.

Baseline characteristics	Total (N=80)
Sex, female, N (%)	58 (72.5)
Age at baseline [years], mean (SD)	37.5 (9.9)
Any medication history, N (%)	55 (68.8)
Number of relapses within 0-12 months prior to study enrolment, N (%)	
0	25 (32.9)
1	39 (51.3)
EDSS score, mean (SD)	2.31 (1.39)
Time since first MS symptoms [years], mean (SD)	8.71 (8.41)
Time since first MS diagnosis [years], mean (SD)	6.77 (6.92)
Previous treatments and therapies, N (%)	59 (73.8)

TABLE 1 Baseline characteristics.

FSMC	Baseline (N=80)	Month 6 (N=71)	Month 12 (N=71)	Month 18 (N=29)
FSMC total score, mean (SD), [95%KI]	51.8 (23.0), [46.7; 56.9]	50.5 (22.8), [45.1; 55.8]	51.1 (22.4), [45.8; 56.5]	48.9 (25.1), [39.3; 58.4]
FSMC total score category, N (%)				
Normal	30 (37.5)	28 (39.4)	27 (38.0)	13 (44.8)
Mild	12 (15.0)	8 (11.3)	9 (12.7)	3 (10.3)
Moderate	7 (8.8)	12 (16.9)	15 (21.1)	3 (10.3)
Severe	31 (38.8)	23 (32.4)	20 (28.2)	10 (34.5)

TABLE 2 FSMC scores at baseline and month 6, 12 and 18.

Conclusion: The first interim analysis of the MoOzaRt study revealed stable FSMC total scores with a trend towards a decline in the proportion of patients with severe trait fatigue already during the early treatment phase. Further results will deepen our insights into the specific impact of ocrelizumab on trait and state fatigue and factors that may influence fatigue in RMS patients.

Disclosure: IKP: Almirall, Biogen, BMS, Celgene, Genzyme, Janssen, Merck, Novartis, Roche, Teva // speakers bureau or advisory board, consulting fees; The German MS Society, Celgene, Novartis, Roche, Teva // research grants. JL: Roche // employee TM: Roche // employee EW: Roche // employee HS: Almirall, Biogen, BMS, Genzyme, Janssen, Merck, Novartis, Roche, Teva // speakers bureau or advisory board, consulting fees, travel reimbursement; Biogen, Novartis, Teva // research grants; Biogen, Novartis, Roche // data monitoring or steering committees.

EPO-578 | Updated real world immunogenicity data on Tysabri S.C. and Tysabri I.V.

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Background and Aims: Natalizumab (Biogen), approved for relapsing forms of multiple sclerosis, is available in both subcutaneous (SC) and intravenous (IV) formulations, with administration intervals of every four weeks (Q4W) or every six weeks (Q6W) in off-label use. This study offers a real-world observational analysis of the immunogenicity, tolerability, and effectiveness of Tysabri administered through both SC and IV methods over a 24-month period at a single academic center.

Methods: Anti-natalizumab antibody in serum (NTZ-Ab, Unilabs, Copenhagen, Denmark) are tested at baseline and at every 3rd administration. All subjects are followed with EDSS, relapse rate, JCV index and yearly brain MRI.

Results: There are 242 patients with mean length of follow up: 20.4 months (0.7–26.7) divided into 4 cohorts based on their treatment pattern: (1) Switch from IV-Q6W to SC-Q6W (SC-Q6W), $n=156$; (2) Ongoing IV-Q6W (IV-Q6W), $n=38$; (3) Treatment-naïve to IV-Q4W (IV-N), $n=13$; and (4) Treatment-naïve to SC-Q4W (SC-N), $n=35$. We observed three cases of NTZ-Ab positivity (1.2%). One patient on long term treatment Q6W had NTZ-Ab+ at the time of switch from IV to SC and thereafter (listed in SC-Q6W cohort); the treatment was discontinued. Two patients in the SC-N cohort showed persistent NTZ-Ab from 3 months on treatment. One of them remains on treatment with no clinical or radiological disease activity despite of persistent NTZ-Ab+ and one was switched to a different treatment due to radiological activity. There was no new occurrence of NTZ-Ab later during treatment.

Conclusion: The immunogenic potential of Tysabri is low and NTZ-Ab occur early.

Disclosure: This study is supported by Biogen. EKH received honoraria/research support from Biogen, Merck Serono, Novartis, Roche, and Teva; has been a member of advisory boards for Actelion, Biogen, Celgene, Merck Serono, Novartis, and Sanofi Genzyme. JLP has received research funding from Biogen and honoraria from Merck Serono, Novartis and Roche. OV has nothing to disclose. KW, ZB, AG, and AD are employees of and may hold stock and/or stock options in Biogen.

EPO-579 | Evaluating association of chronic active lesions with disability in multiple sclerosis: A systematic literature review

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Background and Aims: Chronic active lesions (CAL) are important component of multiple sclerosis (MS) disease pathology and indicate the presence of a smoldering neuroinflammatory processes. Yet, only recent advances in magnetic resonance imaging (MRI) and positron emission tomography have made it possible to identify CAL in vivo in people with MS (pwMS). Several studies assessed the association between CAL and disability accumulation in pwMS.

Methods: A systematic literature search was conducted following PRISMA guidelines 2020 using PubMed, Embase, and Cochrane Library on April 21, 2023. The review included studies assessing associations between CAL and clinical/radiological outcome of disability accumulation in people with any MS phenotype.

Results: A total of 149 unique studies were identified and 31 met the inclusion criteria. Of these, 21 evaluated paramagnetic rim lesions (PRL) using susceptibility-based MRI, 9 evaluated slow expanding lesions (SEL) on T1-weighted (T1-w)/T2-w MRI, and 1 studied both. The presence of PRL was associated with disability accumulation in 19 studies, with 9 of those studies reporting an association between the number or volume of PRL and disability accumulation. SEL were associated with disability accumulation in 10 studies, with 5 of those studies reporting association between the number or volume of SEL and disability accumulation.

Conclusion: This literature review found significant associations between CAL and disability accumulation that may lead to transitioning to progressive disease in pwMS. This illustrates role of CAL and smoldering disease in MS in driving disability accumulation. CAL remains an important unmet therapeutic target and development of treatments promoting their resolution is crucial.

Disclosure: Nothing to disclose.

EPO-580 | EMbrace the diversity in MS with a Value Based Healthcare (VBHC) implementation model in Portugal

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Background and Aims: Managing multiple sclerosis (MS) is challenging, due to its chronic degenerative nature, young patient population, and unpredictability and diversity of its symptoms. In such a setting, adoption of a Value-based Healthcare (VBHC) approach can increase efficiency and improve care by incorporating patient values and quality of life considerations. This paper outlines the implementation of a VBHC framework in three Portuguese multiple sclerosis centers, with different multidisciplinary teams, as part of the European consensus "S.O.S. MS Project".

Methods: The Portuguese project (EMbrace), started in March 2021, includes a basic education on VBHC concepts, an analysis and refinement of the patient journey in each center and a prospective longitudinal collection of a standard dataset comprising patient-reported outcomes. Periodic meetings allow the sharing of experiences and practices. Central to this initiative is the application of a process reengineering methodology to healthcare environments, focusing on five pillars: patient-centered value, work rhythm, waste-minimization, definition of value streams, and continuous improvement.

Results: EMBrace resulted in an alignment of clinical pathways, validation of Key Performance Indicators, and benchmarking against international models. Its implementation faced challenges in timing and data collection, highlighting the need for more streamlined processes and the integration of technology. Nevertheless, it demonstrated the feasibility of a VBHC approach in MS care and its potential for more efficient, patient-centric healthcare models.

Conclusion: The EMbrace Project, still in development, has the potential to significantly influence MS care by providing evidence to guide implementation of VHBC projects.

Disclosure: This project has been supported by ROCHE that facilitated the contact between all the centers, coordinated the meetings and provided know-how and technical assistance. The authors have no other disclosures relevant to this work.

EPO-581 | 8-Point change in symbol digit modalities test scores: Findings from the phase 3 SUNBEAM and DAYBREAK ozanimod trials

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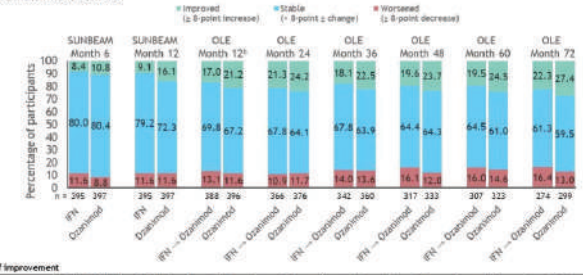
Background and Aims: In a post hoc analysis of the phase 3 SUNBEAM trial, more ozanimod-treated participants had clinically meaningful (≥4-point) improvement on the Symbol Digit Modalities Test (SDMT) than those treated with interferon beta-1a (IFN). In this analysis, the long-term effects of ozanimod on cognitive processing speed (CPS) in participants with relapsing multiple sclerosis (RMS) were evaluated using 8-point SDMT change, which may better represent individual-level CPS changes than a 4-point threshold.

Methods: In SUNBEAM (NCT02294058), adults with RMS were randomly assigned oral ozanimod 0.46 or 0.92 mg/d or intramuscular IFN 30 μg/wk for ≥12 months (mean treatment duration 13.5 months); completers were eligible for an ozanimod 0.92 mg open-label extension (OLE) trial (DAYBREAK, NCT02576717; database lock: 7 April 2023). The percentage of participants with 8-point SDMT change relative to SUNBEAM baseline is reported.

Results: SUNBEAM participants entering the OLE were included (ozanimod 0.92 mg, $n = 397$; IFN, $n = 395$). Mean (SE) baseline SDMT scores were 48.0 (0.69) and 47.4 (0.68), respectively. Compared with participants receiving IFN, those in the ozanimod group were more likely to achieve 8-point SDMT improvement at SUNBEAM month 12 (nominal $p = 0.0048$; Figure). After IFN-randomised participants switched to ozanimod, statistical group differences were no longer apparent (Figure). After 6–8 years of ozanimod (end of OLE), the proportion of participants with 8-point improvement was numerically, but not nominally significantly, higher in the continuously ozanimod-treated group compared with those initially randomised to IFN (Figure).

Figure. Categorical analysis of participant-level changes in SDMT relative to SUNBEAM baseline[a]



Odds of Improvement

	SUNBEAM Month 6	SUNBEAM Month 12	OLE Month 12[b]	OLE Month 24	OLE Month 36	OLE Month 48	OLE Month 60	OLE Month 72
OR (95% CI)	1.3 (0.8–2.2)	1.9 (1.2–2.9)	1.3 (0.9–1.8)	1.1 (0.8–1.6)	1.2 (0.8–1.8)	1.1 (0.8–1.7)	1.2 (0.8–1.8)	1.2 (0.8–1.8)
Nominal *P* value	0.2366	0.0048	0.2204	0.5456	0.2933	0.5139	0.3205	0.3378

Intent-to-treat population. Percentages may not add to 100 due to rounding. *P* values are nominal because treatment comparisons in this post hoc, exploratory analysis were not subject to multiplicity adjustment. *P* values were calculated for odds ratio for clinically meaningful SDMT improvement (>=8-point increase) relative to SUNBEAM baseline in continuous ozanimod vs IFN groups using a generalised estimating equation model adjusted by baseline SDMT score; stratification factors (region [Eastern Europe vs rest of the world] and baseline Expanded Disability Status Scale score category [<=3.5 vs > 3.5]), age at baseline, brain volume at baseline, treatment and the interaction between the treatment and time point as fixed effects, assuming unstructured within-subject covariate structure; for the DAYBREAK OLE visits, treatment duration during SUNBEAM was added as a fixed effect in addition to those stated above.
[a]Participants randomised to IFN in SUNBEAM switched to ozanimod 0.92 mg in the DAYBREAK OLE 12–24 months after SUNBEAM baseline.
[b]OLE month 12 visit included data collected after OLE first dose date up to OLE month 12.
IFN, interferon beta-1a; OLE, open-label extension; OR, odds ratio; SDMT, Symbol Digit Modalities Test.

Conclusion: Long-term ozanimod treatment protects from cognitive deterioration. These data support the early use of ozanimod in patients with RMS.

Disclosure: JD: personal compensation for consulting from Biogen Idec, Bristol Myers Squibb, Janssen Pharmaceuticals, and Novartis; speaker for Consortium of MS Centers; and grant funding from Biogen Idec, Canadian MS Society, Consortium of MS Centers, EMD Serono, and National MS Society. All authors' disclosures will be included in the presentation. This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Noud van Helmond, MD, PhD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

EPO-582 | Real-world data on effectiveness and tolerability of Ofatumumab at short-term follow-up

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Background and Aims: Ofatumumab is a highly effective disease-modifying therapy (DMT) for relapsing multiple sclerosis (MS). Real-world outcome data are needed for clinical practice. Our aim was to describe effectiveness and tolerability at 6 and 12-month follow-up.

Methods: Patients diagnosed with MS starting Ofatumumab between December 2022-December 2023 were included. Baseline demographics, disease characteristics and clinical/radiologic features were collected. Effectiveness/tolerability outcomes were assessed after 6 and 12 months.

Results: We included 43 relapsing MS patients; 29 (67.4%) were women. Mean age was 37.2 ± 10.2 years and disease duration was 10.1 ± 7.9 years. Median baseline EDSS was 3 (range: 0–6). The median number of relapses in the two previous years was 1 (range: 0–4). Last MRI before Ofatumumab showed 5–10 lesions in 11 (25.6%) patients, 10–30 in 20 (46.5%) and >30 in 11 (25.6%); 32 (74.4%) had spinal-cord lesions. Prior DMT exposure was reported in 31 (72.1%) vs 12 (27.9%) naive patients. Switch to Ofatumumab was mostly due to ineffectiveness (27/31 [87.1%]) vs lack of tolerability/safety (4/31 [12.9%]). There were no discontinuations during a mean follow-up of 8.6 ± 2.9 months. Only 3 (7%) patients had a relapse, which happened in the first 6 months. At 6-month and 12-month follow-up median EDSS was 2.8 (range: 0–6) and 1.5 (range: 0–6), respectively. Overall, 3/21 (14.3%) had EDSS worsening in the first year and 2/21 (9.5%) had new lesions on rebaseline 6-month MRI. Adverse events occurred in 30/41 (73.2%) patients, mainly at the first injection (21/30 [70%]); the most common was flu-like syndrome in 25/30 (83.3%).

Conclusion: Ofatumumab was effective and well-tolerated in our population. Most patients were stable; few had disease activity early after starting Ofatumumab and were therefore not considered treatment failures. Minor self-limited tolerability issues were reported.

Disclosure: Nothing to disclose.

EPO-583 | Epstein-Barr virus DNA in the cerebrospinal fluid of multiple sclerosis patients and controls

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Background and Aims: Epstein-Barr virus (EBV) infection is a major risk factor for multiple sclerosis (MS). We examined the presence of EBV DNA in the cerebrospinal fluid (CSF) and blood of MS patients and controls and estimated the proportions of EBV-positive B cells in CSF and blood.

Methods: CSF was collected at diagnostic lumbar punctures from 45 MS patients and 45 HLA-DR15 matched controls; all subjects were EBV seropositive. Cellular DNA was amplified and representative samples were obtained in 28 cases and 28 controls. In a subset of participants, non-amplified DNA from CSF cells and blood B cells were analysed. Multiple droplet digital PCR (ddPCR) runs were performed to assess the cumulative EBV positivity rate.

Results: One of the 45 MS patients and none of the 45 controls was positive for EBV DNA in CSF supernatants. CSF cellular DNA was analysed in eight independent ddPCRs: EBV DNA was detected at least once in 18 (64%) of the 28 MS patients and in 15 (54%) of the 28 controls ($p = 0.59$, Fisher's test). The cumulative EBV positivity increased up to 59%, suggesting that all subjects would have tested EBV positive, had more DNA been analysed. The estimated proportion of EBV positive B cells was >1/10,000 in both CSF and blood.

Conclusion: EBV-DNA is equally detectable in the CSF cells of both MS patients and controls with ddPCR, and the probabilistic approach indicates that the true positivity rate approaches 100% in

EBV-positive individuals. The proportion of EBV positive B cells appears higher than previously estimated.

Disclosure: JL: Congress expenses; Merck. SML: Lecture fees Merck, Biogen, Novartis, Janssen, Teva; congress expenses Roche, Merck, Novartis; advisory fees Roche, Novartis, UCB Pharma, Argenx. PJT: Lecture and consulting fees Roche, Merck, Biogen, Novartis, Janssen, Sanofi, Alexion; congress expenses Biogen, Merck. KKE: Lecture fees: Novartis, Celltrion, Sobi. JKN: Congress expenses; Biogen, Novartis, Merck.

EPO-584 | Final analysis of long-term hepatic safety of ozanimod in an open-label extension trial of relapsing multiple sclerosis

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Background and Aims: We report long-term hepatic safety during an open-label extension study (DAYBREAK) of ozanimod.

Methods: Patients with relapsing multiple sclerosis who completed a phase 1–3 ozanimod trial were eligible for DAYBREAK (NCT02576717), where they received ozanimod 0.92 mg/d. Liver enzymes were measured every 3 months for 3 years, then every 6 months. Database lock: 7 April 2023.

Results: The 2494 patients had a mean (SD) 60.9 (17.9) (range 0.03–81.5) months of ozanimod exposure during DAYBREAK. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels ≥3× upper limit of normal (ULN) or bilirubin >2× ULN were infrequent (<4% each; Table 1); there were no cases of severe drug-induced liver injury (DILI). Mean (SD) time to onset was 27.3 (17.7) and 30.2 (18.9) months for ALT and AST ≥3× ULN, respectively, and 16.4 (15.8) months for bilirubin >2× ULN. First ALT >1×ULN during DAYBREAK primarily occurred during year 1. Consecutive ALT elevations ≥3× ULN were uncommon (Table 1). Hepatobiliary treatment-emergent adverse events (TEAEs) occurred in 104 (4.2%) participants (Table 2) and led to treatment discontinuation in 2 (0.08%); 10 (0.4%) discontinued due to hepatic enzyme elevation–related TEAEs. Fifteen (0.6%) patients had serious hepatobiliary TEAEs (Table 3).

Table 1. Hepatic Laboratory Abnormalities at Any Visit During DAYBREAK Based on Laboratory Testing

	DAYBREAK Participants (N=2494[a])
Maximum ALT, n (%)	
>1xULN	1017 (40.9)
>=3xULN	91 (3.7)
>=5xULN	20 (0.8)
Consecutive ALT abnormalities[b]	
>=3xULN	22 (0.9)
>=5xULN	6 (0.2)
Maximum AST, n (%)	
>1xULN	548 (22.0)
>=3xULN	42 (1.7)
>=5xULN	18 (0.7)
Maximum bilirubin, n (%)	
>1xULN	577 (23.2)
>2xULN	73 (2.9)
>3xULN	9 (0.4)

[a]Of the 2494 participants, 2489 had nonmissing postbaseline assessments on which these analyses are based
[b]Refers to elevations confirmed on >=2 consecutive elevations.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; SD, standard deviation; ULN, upper limit of normal.

Table 2. Hepatobiliary TEAEs During DAYBREAK

	DAYBREAK Participants (N=2494)	
	n (%)	IR/1000 PY[a] (95% CI)
Any hepatobiliary TEAE	104 (4.2)	8.4 (7.0–10.2)
Hepatobiliary TEAEs that occurred in ≥2 participants in the overall DAYBREAK population[b]		
Hyperbilirubinemia	27 (1.1)	2.2 (1.5–3.1)
Cholelithiasis	16 (0.6)	1.3 (0.8–2.1)
Cholecystitis chronic	12 (0.5)	1.0 (0.5–1.7)
Hepatic cyst	8 (0.2)	0.5 (0.2, 1.1)
Hepatic steatosis	5 (0.2)	0.4 (0.2–0.9)
Biliary dyskinesia	4 (0.2)	0.3 (0.1–0.8)
Chronic hepatitis	4 (0.2)	0.3 (0.1–0.8)
Hepatitis	4 (0.2)	0.3 (0.1–0.8)
Cholestasis	3 (0.1)	0.2 (0.1–0.7)
Gallbladder polyp	3 (0.1)	0.2 (0.1–0.7)
Hypertransaminasemia	3 (0.1)	0.2 (0.1–0.7)
Sphincter of Oddi dysfunction	3 (0.1)	0.2 (0.1–0.7)
Steatohepatitis	3 (0.1)	0.2 (0.1–0.7)
Cholecystitis	2 (0.08)	0.2 (0.0–0.6)
Cholecystitis acute	2 (0.08)	0.2 (0.0–0.6)
Hepatic cytolysis	2 (0.08)	0.2 (0.0–0.6)
Hepatic lesion	2 (0.08)	0.2 (0.0–0.6)
Hepatitis toxic	2 (0.08)	0.2 (0.0–0.6)
Hepatomegaly	2 (0.08)	0.2 (0.0–0.6)
Nonalcoholic steatohepatitis	2 (0.08)	0.2 (0.0–0.6)

[a]IR per 1000 person-years is calculated as number of persons/person-years x 1000 for specific system organ class category or preferred term subcategory. Person-years for each category/subcategory: for a person in a particular category/subcategory, the time on study is calculated based on the date the person first has a TEAE within the category/subcategory (date of first TEAE - first dose date of study drug + 1)/365.25; for persons who do not have a TEAE in the category/subcategory, the time on study is the study duration (last dose date of study drug - first dose date of study drug +1)/365.25.
[b]Additional hepatobiliary TEAEs that occurred in a single participant each (0.04%) in the total DAYBREAK population included biliary colic, biliary polyp, biliary tract disorder, cholangitis, drug-induced liver injury, gallbladder disorder, hepatic function abnormal, hepatitis acute, hepatitis chronic active, hepatotoxicity, liver disorder, and liver tenderness.
CI, confidence interval; IR, incidence rate; PY, person-years; TEAE, treatment-emergent adverse event.

Table 3. Serious Hepatobiliary TEAEs

	DAYBREAK Participants (N=2494), n (%)
Any serious hepatobiliary disorder	15 (0.6)
Cholelithiasis	6 (0.2)
Cholecystitis chronic	3 (0.1)
Cholecystitis acute	2 (0.08)
Biliary polyp	1 (0.04)
Cholecystitis	1 (0.04)
Cholestasis	1 (0.04)
Chronic hepatitis	1 (0.04)

TEAEs, treatment-emergent adverse events.

Conclusion: After up to nearly 7 years of ozanimod in DAYBREAK (mean 60.9 months), ALT and AST elevations ≥3× ULN remained infrequent. Severe DILI did not occur in this dataset. Consecutive ALT elevations ≥3× ULN were uncommon. Rates of serious hepatic TEAEs and hepatic TEAEs leading to discontinuation were low. Postmarketing hepatic safety findings are gathered and reported separately.

Disclosure: KWS: Consulting for Biogen, Celgene, Genzyme, Merck, Novartis, Ono Pharma, Roche, Synthon, and Teva. All authors' disclosures will be included in the presentation. This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Noud van Helmond, MD, PhD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

EPO-585 | Reliability of a digital cohort in multiple sclerosis: The MSCopilot® French patients

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Background and Aims: We describe the feasibility of collecting sociodemographic and functional parameters using MSCopilot®, a clinically validated software as a medical device, and the representativeness of this French digital cohort of patients with multiple sclerosis (PwMS).

Methods: Real world data from the MSCopilot® database were collected between October-2017 to September-2023. Adult PwMS who had provided informed consent were included. MSCopilot® was used at home without supervision to collect sociodemographic and treatment self-reported data and perform the digital active tests that evaluate four functional parameters (walking capacity, low contrast visual acuity, cognitive processing and dexterity).

Results: A total of 1755 PwMS were included with a 2:1 female/male ratio (1204/551), consistent with the French MS population albeit slightly younger (41.1 ± 12 years). The majority of patients self-reported an EDSS score < 4 (71.4%, average score = 2.3 ± 2). Among the four digital assessments, three revealed significant group differences between patients with EDSS <4 and ≥4, the latter group showing a decreased performance in walking capacity, cognitive function and hand dexterity ($p < 0.01$).

Conclusion: MSCopilot® enables the characterization of key functional parameters in a real-life digital cohort mirroring the French MS population sociodemographic parameters. This demonstrates the significance of digital cohorts in providing additional insights for a better understanding of the disease through real world evidence.

Disclosure: L. Carment, P. Drouin, L. Ahamada, A. Plaud, LE. Pillet, A. Vives, S. Zinai are employees of Ad Scientiam, A. Tourbah is a member of its scientific committee and received honoraria for lectures, travel grants and research support from Biocara, Hikma, Novartis, Roche.

EPO-586 | Central vein sign analysis in confluent multiple sclerosis lesions separated with an automated algorithm

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Background and Aims: The Central Vein Sign (CVS) is an MRI marker that, among demyelinating syndromes, is pathognomonic of multiple sclerosis (MS). However according to the NAIMS guidelines, confluent white matter lesions (WMLs) must be excluded as in these cases veins cannot be unequivocally assigned to each lesion component. This criterion, limiting number of evaluable WMLs, sometimes prevents reliable evaluation of the CVS. In this study performance of an automated algorithm for confluent WMLs segmentation into each component was explored.

Methods: RRMS patients ($n = 11$; disease duration 17 years; EDSS 4) who had performed standardized 3T MRI scans, including FLAIR* sequences were recruited. Confluent WMLs, usually not eligible for CVS evaluation according to NAIMS criteria, were not excluded and their individual components were identified by LesDiv algorithm developed by Pixyl Medical.

Results: The patients showed 748 lesions. Among the 589 non-confluent lesions, 272 fulfilled the NAIMS criteria for CVS analysis and out of them 206 were perivenular (PVL) (76%). Among the 159 confluent lesions the LesDiv algorithm identified 427 sub-components. Out of them 81 (19%) were eligible for the CVS analysis and of these 78 were PVL, increasing to 353 (30%) the number of WMLs eligible for the CVS analysis and to 80% (284/353) the total PVL proportion observed in these patients. The mean proportion of PVL/ patient increased from 67% to 70%.

n=11	median	(range)
Age, years	38	(27-50)
Disease duration, years	17	(<1-31)
EDSS	4.0	(0-6.0)
Number of DMTs received prior to MRI	3	(1-6)
	n	(%)
Gender, female	9	(81%)
MS phenotype: RR-MS	6	(54%)
Patients treated with AHSCT	6	(54%)
Patients receiving treatments at MRI	5	(46%)

Table 1: Clinical-demographic characteristics of the patient population at the time of the MRI scan.

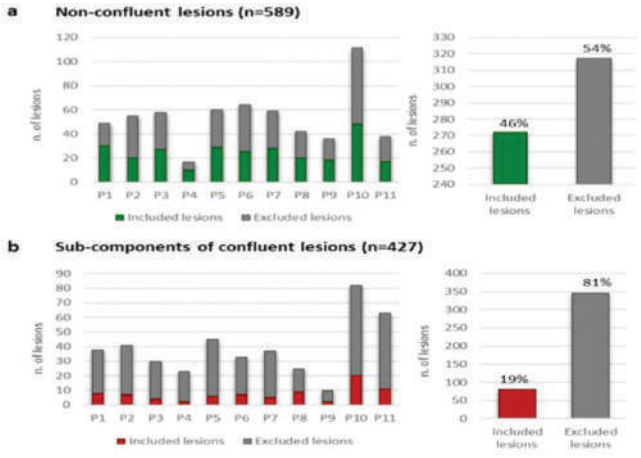

Fig 1: Number of non confluent lesions (a) and sub-components of confluent lesions (b) included and excluded according to NAIMS criteria.

Fig. 2: Comparison between the %PVL obtained from the analysis of non-confluent lesions (green line) and the %PVL after the inclusion of sub-components of confluent lesions (blue line).

Conclusion: Segmentation of confluent WMLs in their individual components increases WMLs number fulfilling the NAIMS criteria for inclusion in CVS analysis and eventually also PVL proportion.

Disclosure: Nothing to disclose.

EPO-587 | **Long-term outcomes with ozanimod in the DAYBREAK extension trial by number of MS relapses during the phase 3 trials**

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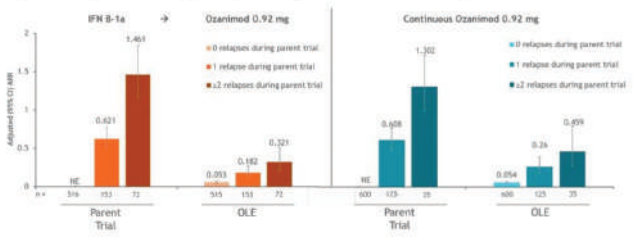
Background and Aims: Early intervention with ozanimod results in control of multiple sclerosis (MS) disease activity that is maintained with long-term use. Whether long-term efficacy differs among patients with varying degrees of disease activity is unknown. Here we examine long-term outcomes (6–7 years) among patients who had 0, 1, or ≥2 relapses during the first 1–2 years of continuous ozanimod 0.92 mg/d or intramuscular interferon (IFN) beta-1a 30 μg/wk followed by ozanimod 0.92 mg/d.

Methods: In phase 3 "parent" trials, adults with relapsing MS were randomised to oral ozanimod 0.46 or 0.92 mg/d or intramuscular IFN 30 μg/wk for ≥12 (SUNBEAM–NCT02294058) or 24 months (RADIANCE–NCT02047734), after which they were eligible for open-label ozanimod 0.92 mg/d in an open-label extension trial (DAYBREAK–NCT02576717). Clinical and radiologic outcomes from parent-trial baseline through DAYBREAK month 60 (database lock: 7 April 2023) were compared among patients who experienced 0, 1, or ≥2 relapses during SUNBEAM/RADIANCE.

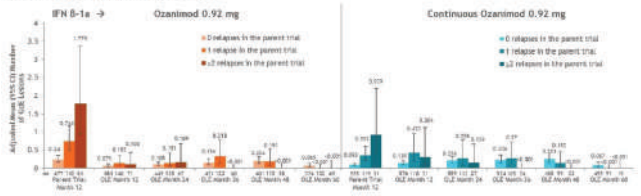
Results: Patients with 1 or ≥2 relapses during SUNBEAM/RADIANCE had numerical decreases in mean annualised relapse rate during DAYBREAK (Figure 1). Patients in all relapse groups who switched from IFN to ozanimod in DAYBREAK had numerical decreases in mean gadolinium-enhancing and new/enlarging T2 lesion counts that were maintained through month 60 (Figures 2–3). Lesion counts in patients treated with continuous ozanimod remained low through OLE month 60 in all relapse groups.

Figure 1. Adjusted ARR by Relapse Group and Treatment during Parent Trial



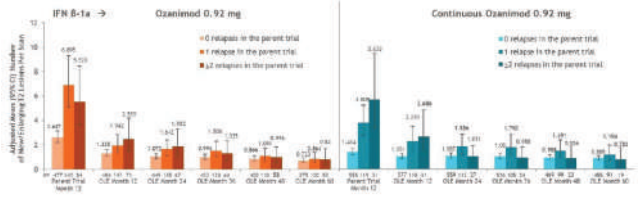
The phase 3 parent trial treatment period includes parent study day 1 through the end of treatment during the parent study; the OLE treatment period is from OLE study day 1 through the last dose date or data-cutoff date, whichever occurred first. Analyses were based on the negative binomial regression model with parent treatment group, adjusted for region (Eastern Europe vs rest of the world), age at parent baseline, and the parent baseline number of gadolinium-enhancing lesions. The natural log transformation of time on treatment is used as an offset term to adjust for patients having different exposure times. ARR, annualised relapse rate; IFN, interferon; NE, not estimated; OLE, open-label extension.

Figure 2. Adjusted Mean Number of GdE Lesions by Relapse Group and Treatment during Parent Trial



The adjusted mean (95% confidence interval) number of GdE lesions was derived using a negative binomial model, adjusted for study, region (Eastern Europe vs rest of the world), age at baseline, and baseline number of GdE lesions. GdE, gadolinium-enhancing; IFN, interferon; OLE, open-label extension.

Figure 3. Adjusted Mean Number of New/Enlarging T2 Lesions per Scan by Relapse Group and Treatment during Parent Trial



The adjusted mean (95% confidence interval) number of new/enlarging T2 lesions per scan relative to baseline (parent baseline for the parent trials; DAYBREAK baseline for DAYBREAK) was derived using a negative binomial model, adjusted for study, region (Eastern Europe vs rest of the world), age at baseline, and baseline number of GdE lesions; the log of the number of postbaseline scans was an offset term in the model. GdE, gadolinium-enhancing; IFN, interferon; OLE, open-label extension.

Conclusion: Regardless of prior relapse trends in phase 3 trials, long-term treatment with ozanimod for up to 60 months in DAYBREAK was associated with clinical and radiologic improvement.

Disclosure: LF: Has received fees for consultancy and/or advisory board participation from Bristol Myers Squibb, EMD Serono, Genentech, Horizon Therapeutics, Novartis, Sanofi, and TG Therapeutics; has received speaker fees from EMD Serono, the MS Association of America, and Sanofi; has received honorarium for participation in educational programs from Medscape, Inc and the MS Association of America; has received program sponsorship from EMD Serono; and grant support from EMD Serono, Genentech, NIH/NINDS, and PCORI through her institution. All authors' disclosures will be included in the presentation. This study was sponsored by Bristol Myers Squibb. Writing and editorial assistance was provided by Noud van Helmond, MD, PhD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb.

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EPO-588 | Real-world safety and effectiveness of ocrelizumab in different treatment lines in RMS – CONFIDENCE interim analysis

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Background and Aims: CONFIDENCE (ML39632, EUPAS22951) is a German non-interventional, post-authorization safety study including multiple sclerosis (MS) patients newly treated with ocrelizumab (OCR) and other disease-modifying therapies. This analysis included real-world patients with RMS treated with OCR up to 5.5 years.

Methods: Data cut-off was 11/10/2023. Safety and effectiveness were described for OCR in treatment-naïve patients (TN-patients) and patients with ≥1 prior MS-specific therapies (pwPMST). Safety analysis included OCR patients with ≥1 dose; effectiveness analyses for patients with ≥1 follow-up visit(s) evaluated annual relapse rate (ARR), Kaplan-Meier estimate for 24-week confirmed disability progression (CDP) and 24-week confirmed disability improvement (CDI), as well as Treatment Satisfaction Questionnaire for Medications© (TSQM).

Results: Mean (SD) observation time for safety was 3.21 (1.32) years with 2267 patients equaling 7743.41 patient years (of which 404 TN-patients, 780 pwPMST ≥3). Adverse events (AEs) occurred in 56.7/100 patient years (PY) in TN-patients (88.7/100PY in pwPMST ≥3); 22.9/100PY were classified as System Organ Class (SOC) "Infections and infestations" (32.3/100PY in pwPMST ≥3). Mean (SD) observation time for effectiveness was 3.21 (1.31) years with 2261 patients; overall ARR was 0.11 (SD 0.31). Over 48 months, 78.7% and 75.8% of TN-patients ($n = 326$) and pwPMST ≥3 ($n = 667$), respectively, did not experience CDP; 18.7% of TN-patients vs. 13.7% of pwPMST ≥3 reached CDI; overall population TSQM global satisfaction was 70.57 (20.15) at baseline and 79.39 (19.34) after 48 months.

Conclusion: Here we present real-world safety and effectiveness of OCR in different treatment lines in RMS. No new safety signals with increasing exposure time to OCR were observed.

Disclosure: MB: honoraria for lecturing, consulting and/or travel expenses for attending meetings from Biogen, Bristol-Myers Squibb, Das Fortbildungskolleg, Florian Schmitz Kommunikation, Janssen, Merck, Novartis, RG Ärztefortbildung, Roche, Sandoz, Sanofi, Teva, Viatris MW: research support from the DFG (WE 3547/5-1, WE3547/7-1; in association with SFB TRR 274), from Novartis,

TEVA, Biogen-Idec, Roche, Merck and the ProFutura Program of the Universitätsmedizin Göttingen; travel funding and/or speaker honoraria from Biogen-Idec, Merck Serono, Novartis, Roche, TEVA, Bayer and Genzyme; editor for PLoS One SGM: honoraria for lecturing, travel expenses from Almirall, Amicus Therapeutics Germany, Bayer Health Care, Biogen, Celgene, Diamed, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis, Novo Nordisk, ONO Pharma, Roche, Sanofi-Aventis, Chugai Pharma, QuintilesIMS and Teva; his research is funded by BMBF, BfR, DFG, Else Kröner Fresenius Foundation, G-BA, DAAD, Hertie Foundation, IZKF Muenster, DGN, Alexion, Almirall, Amicus Therapeutics Germany, Biogen, Diamed, Fresenius Medical Care, Genzyme, HERZ Burgdorf, Merck Serono, Novartis, ONO Pharma, Roche, Teva PD: employee of F. Hoffmann-La Roche AG SB, JL, SHS: employees of Roche Pharma AG PD, SB, JL: shareholders of F. Hoffmann-La Roche AG TZ: grants and personal fees from Biogen, Roche, Merck, TEVA, Almirall; grants, personal fees and non-financial support from Genzyme, Novartis; personal fees from Bayer, BAT, Celgene, Gilead.

EPO-589 | Alemtuzumab in relapsing-remitting multiple sclerosis: Navigating efficacy and autoimmune challenges

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Background and Aims: Alemtuzumab effectively addresses highly active relapsing-remitting multiple sclerosis (RRMS). However, it poses potential autoimmune complications, notably thyroid eye disease (16% of cases).

Methods: We describe a case with alemtuzumab-Induced thyroid eye disease.

Results: A 58-year-old non-smoking woman, with no family history, was diagnosed with RRMS in 1996 following symptom onset in 1994. Her clinical course involved recurrent relapses, leading to hospitalizations. Treatment initially comprised interferon beta-1b and intravenous immunoglobulin. Due to inadequate disease control, she transitioned to natalizumab and later fingolimod due to the risk of progressive multifocal leukoencephalopathy. In 2017, with an EDSS of 4 and ongoing activity, alemtuzumab was considered. Meeting prerequisites, she underwent the first alemtuzumab cycle. Six months later, elevated anti-thyroid-stimulating hormone receptor antibodies, painful exophthalmos, decreased visual acuity, along with horizontal ophthalmoparesis emerged, leading to a diagnosis of Graves' disease-related orbitopathy. It was promptly managed with bilateral orbital decompression. Despite treatment (antithyroid medication, mycophenolate mofetil, tocilizumab, and methylprednisolone), progressive visual acuity decline ensued, culminating in thyroidectomy. In the latest evaluation, thyroid function normalized, with a persisting temporal scotoma and limitations in left eye abduction and elevation. Post-thyroidectomy, she underwent a second alemtuzumab cycle without complications. Imaging studies revealed no new lesions, with no reported relapses in the past year, ARR 0.

Conclusion: Despite lacking specific risk factors for alemtuzumab-associated thyroid eye disease, except gender, the patient proved unresponsive to immunosuppression, necessitating thyroidectomy. This case highlights alemtuzumab's efficacy in RRMS while underscoring the need for monitoring due to potential autoimmune complications, with a favorable clinical outcome despite challenges.

Disclosure: Nothing to disclose.

EPO-590 | OzEAN interim analysis: Treatment satisfaction, QoL, and fatigue in RRMS patients after 1-year ozanimod use in Germany

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Background and Aims: Ozanimod (OZA) was approved in 2020 for the treatment of adults with relapsing-remitting MS (RRMS) in the EU. Patient-reported outcomes from routine clinical care represent an important data gap.

Methods: OzEAN (NCT05335031) is a prospective, noninterventional study currently enrolling adult RRMS patients across 80 sites in Germany. This interim analysis reports first real-world data on quality of life (QoL), fatigue (FSMC) and treatment satisfaction after 1 year of OZA.

Results: This analysis included 317 patients treated with OZA for an average of 17.7 months. At 6 months, most patients showed either improved or stable physical QoL (PCS) (40.1% each, $n = 39/96$), whereas 18.8% ($n = 18$) showed worsened PCS. At 12 months, most patients showed either stable or improved (39.3% each, $n = 22/56$) PCS, 21.4% ($n = 12$) showed worsened PCS. At 6 months, 46.7% ($n = 49/105$) of patients showed improved, 32.4% stable ($n = 34$) and 21.0% ($n = 22$) worsened mental QoL (MCS). At 12 months, 50.0% ($n = 29/58$), 29.3% ($n = 17$) and 20.7% ($n = 12$) of patients showed improved, stable, and worsened MCS, respectively. 60.9% ($n = 112/184$) of patients suffered from fatigue at baseline. At 12 months, the percentage of patients without fatigue increased from 39.1% to 44.3%; mean baseline and 12-month FSMC was 51.6 (± 20.7; $n = 184$) and 49.4 (± 20.5; $n = 79$), respectively. Treatment satisfaction was high, especially regarding side effects (91.8 ± 18.9; $n = 82$) and convenience (92.6 ± 11.9; $n = 82$), with 67 of 82 patients reporting no side effects after 12 months OZA.

Conclusion: This interim analysis indicates a positive effect of ozanimod on patient QoL and fatigue, along with high treatment satisfaction.

Disclosure: Funding: This study was supported by Bristol Myers Squibb. MB: honoraria for lecturing, consulting, and/or travel expenses for attending meetings from Bayer, Biogen, Boehringer, Bristol

Myers Squibb, Coloplast, Daiichi-Sankyo, Das Fortbildungskolleg, Merck, Novartis, Roche, Sanofi, and Teva TG: advisory board honoraria from Bristol-Myers Squibb VB: advisory board honoraria, speaker's honoraria, and scientific honoraria from Merck, Novartis, Roche, Sanofi-Genzyme, and Teva MK: advisory boards and speaker fees / travel grants from Merck, Sanofi-Genzyme, Novartis, Biogen, Janssen, Alexion, Celgene / Bristol-Myers Squibb and Roche; research grants from Merck, Roche, Novartis, Sanofi-Genzyme and Celgene / Bristol-Myers Squibb JF: research support and/or travel expenses for attending meetings from Roche, Novartis, BMS, Hexal, Almirall, Merck, Bayer, Teva, and Zambon WKB: advisory board honoraria and scientific honoraria from Bristol Myers Squibb, Novartis, Merck, Hexal, Roche and Vertanical SB, MM, and MD: employees and/shareholder of Bristol-Myers Squibb GmbH & Co TZ: advisory board fees from Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, Sanofi, and Teva; speaker fees from Almirall, Alexion, Biogen, Bristol Myers Squibb, Hexal, Novartis, Roche, Sanofi, Teva, and Viatris; and research support from Biogen, Bristol Myers Squibb, Novartis, Roche, Sanofi, and Teva.

EPO-591 | Cardiovascular disease in patients with multiple sclerosis and their association with course, disability and progression

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Background and Aims: Comorbidities are thought to be a negative prognostic factor in people with multiple sclerosis (pwMS) although the association between cardiovascular diseases (CVDs) and MS disability severity is conflicting. The aim of this study is to explore the association between CVDs and the risk of disability worsening and secondary MS progression (SPMS).

Methods: frequency and incidence of CVDs were calculated. The independent risk of reaching EDSS 4, EDSS 6 and SPMS conversion was computed for CVDs by using multivariable Cox-regression models.

Results: A total of 622 pwMS were included (72.8% female; age: 51.4 years [42–60]; follow-up: 12.3 years (7–21). CVDs reached a frequency of 40.7% with an incidence of 3 cases every 100 pwMS per year of follow-up and the commonest were hypertension (23.5%) followed by hyperlipidemia (11.7%) and type 2 diabetes mellitus (6.3%). CVDs were common in progressive MS course and the number of incident cases increased with increasing patient's age ($rs = 0.37$; $p < 0.0001$) and MS duration ($rs = 0.32$; $p < 0.0001$). T2DM at diagnosis or at any point before the index condition singled out as independent risk factor of reaching EDSS 4 (HR = 1.99 [95% CI 1.02–3.90], $p = 0.04$), EDSS 6 (HR = 1.61 [95% CI 0.9–2.8], $p = 0.09$) and SPMS conversion (HR = 1.74 [95% CI 0.99–3.1], $p = 0.055$).

Conclusion: CVDs are common in pwMS wherein are mainly associated with disease duration, progressive course and older age. T2DM was the only CVDs associated with higher risk of disability worsening and MS progression despite hypertension classically was also associated with bad MS prognosis.

Disclosure: Nothing to disclose.

EPO-592 | Post SARS-CoV-2 vaccination immune response in patients with MS treated with varying doses of parenteral cladribine

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Background and Aims: A vaccination against SARS-CoV-2 is recommended in the multiple sclerosis (MS) group of patients. However, the effects of DMTs on the humoral and cell-mediated response after SARS-CoV-2 vaccination in MS patients remain unclear. The aim of this analysis is to compare the immune response to SARS-CoV-2 vaccination in MS patients treated with cladribine and those receiving DMTs.

Methods: The study group consisted of 18 patients diagnosed with progressive multiple sclerosis (PMS) who received different doses of cladribine in parenteral formulation. The antibody titers specific to *N* protein and S1 spike protein were measured in all patients, on average 12 months after the last dose of the vaccine. Then 11 patients were treated with cladribine only, 3 patients treated cladribine with at least one disease modifying drug in the past, 4 patients with at least one disease modifying drug). Patients who qualified for the study had received at least one dose of the vaccine against SARS-CoV-2.

Results: Conducted analysis shows that 91% of patients treated with cladribine showed the presence of vaccination antibodies against the SARS COV-2 virus. One patient, with lymphopenia 0.65×10^9 and an incomplete dose of cladribine, did not obtain a positive antibody titer indicating the acquisition of immunity. No adverse effects on the post-vaccine immune response have been shown in patients treated with at least 2 disease modifying drugs.

Conclusion: Parenteral cladribine treatment with different dosing schemes had no negative significant effect on the generation of the immune response to the SARS-CoV-2 virus post vaccination.

Disclosure: Nothing to disclose.

EPO-593 | Performance of the NMOSDCopilotTM digital tool for unsupervised self-assessment of NMOSD: The OPTIS study design

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Background and Aims: Neuromyelitis Optica Spectrum Disorder (NMOSD) is characterised by unpredictable relapses leading to the accrual of neurological disability. Regular patient assessments help understand disease burden before, during, and after relapses, which supports clinical decision making. NMOSDCopilotTM, a Software as a Medical Device, supports self-assessment by NMOSD patients. It features a smartphone application collecting active digital biomarkers of walking, dexterity, cognitive and vision functions, and e-questionnaires (pain, fatigue, bladder and bowel control and quality of life). A web portal allows clinicians to access patients' data.

Methods: OPTIS is a prospective, open-label, multicenter, single group study enrolling adults with AQP4-IgG+ NMOSD in the United States, France, and Germany. It is designed to validate the clinical performance and the safety of NMOSDCopilotTM and demonstrate its usability. Patients will use NMOSDCopilotTM to complete tests and questionnaires during clinical visits at baseline, 6- and 12-months, as well as standard clinical evaluations (Timed 25-Foot Walk, 9-Hole Peg Test, Symbol Digit Modalities Test, Sloan Low-Contrast Letter Acuity Test). Remote self-assessments will be completed every month for 12 months.

Results: OPTIS will evaluate the correlation between NMOSDCopilotTM digital active tests and standard in-clinic testing in 103 patients with AQP4+ NMOSD. Other objectives include evaluating reliability and reproducibility of tests in NMOSDCopilotTM, as well as the safety, usability, adherence, and satisfaction with the tool.

Conclusion: The OPTIS study will generate evidence on the clinical performance of NMOSDCopilotTM. NMOSDCopilotTM has the potential to enable frequent patient self-assessments of neurological function, characterise burden of disease, and facilitate clinician disease management decisions.

Disclosure: This work was funded by Ad Scientiam (Paris, France) and was supported by a collaborative research agreement from Alexion Pharmaceuticals Inc. (Boston, USA). Michael Levy is an employee of the Massachusetts General Hospital (Boston), one of the OPTIS study sites. Elias Sotirchos is an employee of the Johns Hopkins University School of Medicine (Baltimore), one of the OPTIS study sites. Jerôme De Sèze is an employee of the Hôpital Civil (Strasbourg), one of the OPTIS study sites. Sami Fam, Dan Case, Adrian Kielhorn, Emrah Aras are employees of Alexion Pharmaceuticals Inc. Loïc Carment, Emma Touré Cuq, and Alizé Vives are employees of Ad Scientiam.

EPO-594 | Aquaporin-4 positive NMOSD: An atypical pathology with nerve root enlargements and peripheral nervous system damage

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Background and Aims: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory disease of the central nervous system (CNS). Recent studies have reported damage to the peripheral nervous system (PNS) in NMOSD. However, most studies have focused on NMOSD lesions localized in the transitional zone between the CNS and PNS at the root level. The aim of this report is to describe a patient with autoantibodies against aquaporin-4 (AQP4) positive NMOSD, presenting with demonstrated nerve root enlargements and PNS damage in demyelination.

Methods: Conducted a descriptive analysis encompassing clinical, imaging, blood and cerebrospinal fluid (CSF) examination, and electrophysiological assessments.

Results: A 72-year-old woman was admitted to our hospital in March 2023 due to limb weakness. Neurological examination revealed a positive relative afferent pupillary defect, muscle weakness in her limbs, hyporeflexia of the lower extremities and sensory disturbance below Th1 level. An MRI demonstrated a left internal capsule lesion, longitudinal extensive transverse myelitis at the level of C4-Th10, nerve root enlargements, and high-intensity signals in the bilateral cervical/lumbar cord. Positive anti-AQP4 antibodies in both serum and CSF led to the diagnosis of NMOSD. Testing for anti-myelin oligodendrocyte glycoprotein, -neurofascin-155, -Contactin-1, and -ganglioside antibodies returned negative results. Her symptoms significantly improved following six sessions of plasma exchange.

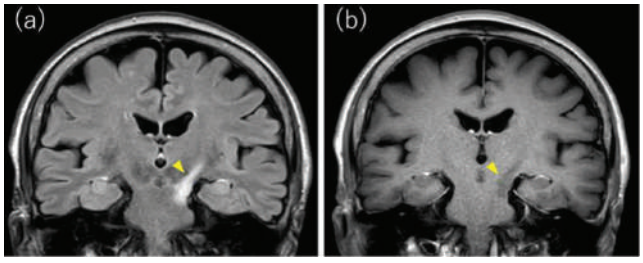

FIGURE 1 Brain MRI: FLAIR image reveals a high signal in the left internal capsule (a), while T1W1 image exhibits a low signal intensity in the same area (b). MRI, magnetic resonance imaging; FLAIR, fluid-attenuated inversion recovery.

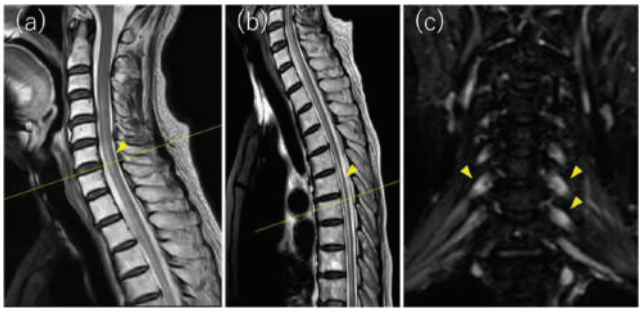

FIGURE 2 Spine MRI: Spinal MRI illustrates longitudinal extensive transverse myelitis at the level of C4-Th10 (a), (b) and associated nerve root enlargements (c).

Conclusion: This report represents one of the few cases of anti-AQP4 antibody-positive NMOSD with demonstrated nerve root enlargements, contributing to an expanded understanding of NMOSD pathology. We discussed the pathomechanisms of the nerve root enlargements in this case.
Disclosure: Nothing to disclose.

EPO-595 | Assessing the clinical value of the central vein sign by MRI for the differential diagnosis of multiple sclerosis

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Background and Aims: Patients with diffuse symptoms often present a few non-specific hyperintense lesions on cranial MRI, raising diagnostic doubts. The central vein sign (CVS), indicative of a vein within a white matter lesion visible on MRI, is considered suggestive of multiple sclerosis. Objective: To study the utility of the central vein sign in differentiating diagnoses in patients with T2 hyperintense lesions, employing the SWI sequence in brain MRI.
Methods: Prospective study. Standard and SWI sequence brain MRIs were performed on Multiple Sclerosis patients and those with uncertain diagnosis who presented hyperintense lesions in T2. Clinical, CSF and OCT data were collected in cases with uncertain diagnoses.
Results: Ten patients were analyzed: 5 with uncertain diagnosis and 5 with MRI-confirmed MS. MS patients showed between 80–100% of T2 hyperintense lesions with CVS on SWI sequence. All five patients with uncertain diagnosis tested negative for CSF IgG OCBs. Among them, two had no CVS lesions: one was later diagnosed with migraine and small vessel disease, and the other tested positive for MOG antibodies. Two others showed up to 20% of lesions with CVS: one has recently diagnosed with double negative NMOSD and the other with MOGAD. One patient, presenting with headache, had 80% of lesions with CVS; however, two performed lumbar punctures were negative for IgG OCBs, and the MRI findings did not meet the MAGNIMS criteria.
Conclusion: The central vein sign could be useful to rule out the diagnosis of MS in patients with uncertain diagnosis.
Disclosure: Nothing to disclose in relation with the abstract.

EPO-596 | BDNF and NTRK2 gene polymorphisms associations with fatigue in a cohort of multiple sclerosis patients

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Background and Aims: Numerous studies have focused on the role of brain-derived neurotrophic factor (BDNF) and tropomyosin-related kinase B (TrkB) signalling in psychiatric and neurological disorders, including multiple sclerosis. There are conflicting data regarding the effects of BDNF and neurotrophic receptor tyrosine kinase 2 (NTRK2) genetic polymorphisms on brain atrophy, cortical thickness, neuroinflammation, neuroplasticity, as well as cognitive decline in patients with multiple sclerosis (pwMS). This study aimed to explore a possible correlation of BDNF and NTRK2 polymorphisms with cognitive impairment and fatigue in pwMS.
Methods: We enrolled 40 pwMS, who underwent venous sampling to analyse BDNF polymorphism rs6265 and NTRK2 polymorphisms rs1387923, rs1565445, and rs2769605. Subsequently, patients were administered various clinical tests or questionnaires, including Fatigue Severity Scale (FSS). Demographic data were collected retrospectively. We then performed a MANCOVA test and a categorical regression analysis.
Results: We found a statistically significant difference in the means of the groups of NTRK2 rs1387923 regarding FSS scores ($p = 0.022$). Successively, we performed a follow-up categorical regression analysis, which showed a significant correlation between the A/G genotype and higher FSS scores compared to either the A/A genotype or G/G genotype ($p = 0.019$ and $p < 0.001$, respectively) only in patients with BDNF Val/Val or Val/Met genotype.

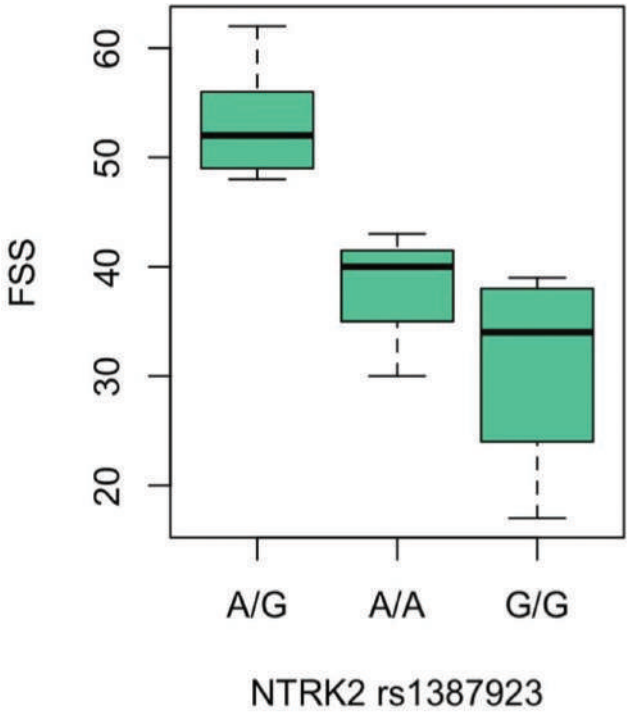

FIGURE 1 Boxplot representing averaged values of Fatigue Severity Scale (FSS) scores corresponding to A/G, A/A, and G/G genotypes of NTRK2 rs1387923 polymorphism in the subgroup of patients with BDNF Val/Val or Val/Met genotype.

Conclusion: BDNF has been linked to fatigue in cancer and chronic fatigue syndrome. To our knowledge, this is the first study to suggest that BDNF and NTRK2 polymorphisms may be associated with an increased susceptibility to fatigue in pwMS. Further studies on a larger number of patients are needed to corroborate this hypothesis.
Disclosure: Nothing to disclose.

EPO-597 | User perspectives on digital health applications for people with multiple sclerosis: A focus group investigation

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Background and Aims: Digital health applications (DHA) are software tools designed to assist in healthcare management. They are particularly relevant for people with chronic diseases such as multiple sclerosis (MS). Despite advances in clinical use, further strategies are needed to facilitate DHA implementation and maintain adherence of its users. This study aimed to analyse patient perspectives on the feasibility of DHA and identify key criteria for potential clinical implementation.
Methods: People with MS (pwMS) with prior DHA interaction were recruited through the Department of Neurology, Medical University of Vienna. Semi-structured interviews, guided by WHO digital health principles, were transcribed from two focus groups and subsequently analysed using reflexive thematic analysis.
Results: Thirteen pwMS (9 female) were interviewed in two focus groups. Participants' median age was 43 years (range 25–60), median disability on the Expanded Disability Status Scale was 1.5 points (1–6). Key findings include the need for a user-centred design of DHA ensuring interfaces are intuitive and tailored to the specific needs of pwMS. The integration of DHA into existing clinical workflows was seen as an opportunity to improve communication on an equal footing between pwMS and neurologists. Robust data protection measures, transparent data policies and autonomous data management were considered essential for a sustained use of DHA.
Conclusion: This study elaborates on attributes of DHA that may enhance their feasibility as an addition to standard care for pwMS. Recognizing individual patient needs and incorporating an intuitive design emerged as critical factors in DHA adherence.
Disclosure: This study was funded by Roche Austria by a research grant awarded to the corresponding author (PA). The form says I have to enter less than 1500 characters but disclosures for all authors make up 2200 characters.

EPO-598 | Autoimmune diseases associated with neuromyelitis optica spectrum disorder: Population-based registry data

T. Pekmezovic[1]; V. Jovicevic[2]; M. Andabaka[2]; N. Momcilovic[2]; N. Veselinovic[2]; O. Tamas[2]; M. Budimkic[2]; S. Todorovic[3]; M. Jeremic[2]; E. Dincic[4]; S. Vojinovic[3]; S. Mesaros[2]; J. Drulovic[2]
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Background and Aims: The aim of our study was to estimate the frequency of autoimmune comorbidities in NMOSD patients from the national Serbian NMOSD Registry. Additionally, analysis of the frequency of related pathogenic organ-specific and not organ-specific autoantibodies was analyzed.
Methods: Our study comprises 136 patients with NMOSD, diagnosed according to the NMOSD criteria 2015. At the time of the study, in the Registry were collected demographic and clinical data, including those related to the coexisting comorbidities and pathogenic autoantibodies.
Results: Among 136 NMOSD patients, 50 (36.8%) had at least one associated autoimmune disorder. The most frequently reported diseases were autoimmune thyroid disease (15.4%), Sjogren's syndrome (11.0%), systemic lupus erythematosus (5.1%), myasthenia gravis (4.4%), and primary antiphospholipid antibody syndrome (2.9%). Aquaporin (AQP) 4-IgG was present in the sera from 106 patients (77.9%) and in this subgroup, autoimmune comorbidities were statistically significantly more frequent than in the AQP4-IgG negative subjects ($p=0.002$). In the total cohort of our NMOSD patients, out

of 106 tested patients, at least one pathogenic autoantibody was detected in 76 subjects (71.7%). Antinuclear antibodies (ANAs) were the most frequently detected antibodies (54.3%). ANAs and anti-extractable nuclear antigen antibodies were statistically significantly more frequent in AQP4-IgG positive vs. AQP4-IgG negative patients ($p=0.006$, and $p=0.033$, respectively).

Conclusion: NMOSD patients, especially AQP4-IgG seropositive ones, are rather frequently associated with wide spectrum of autoimmune diseases, including both organ-specific and systemic autoimmune disorders, and related pathogenic autoantibodies, in our defined cohort with European ethnical background.

Disclosure: Nothing for disclose.

EPO-599 | Comparison of ocrelizumab and ofatumumab: Examining clinical characteristics within the first year of market availability

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Background and Aims: The number of treatment options for relapsing multiple sclerosis (RMS) has considerably increased in recent years. Onlabel anti-CD20 monoclonal antibodies (anti-CD20) ocrelizumab (OCR; introduced: 2018) and ofatumumab (OFA; introduced: 2021) are highly effective disease-modifying therapies (HE-DMTs). This study aims comparing the clinical characteristics of people with MS (pwMS) initiating treatment with OCR/OFA within the first year of German market availability.

Methods: We analysed data from the German MS Registry as of 1-Nov-2023, focusing on OCR/OFA-treated RMS patients. pwMS with DMT initiation within one year of German market availability (observation time: OCR 1-Feb-2018 to 1-Feb-2019; OFA 1-Sep-2021 to 1-Sep-2022) were characterized regarding clinical variables and DMT prescription before OCR/OFA.

Results: 452 pwMS received OCR and 175 OFA (Table 1). Age, disease duration and disability level (expanded disability status scale; EDSS) at OCR/OFA initiation were significantly lower in OFA patients than in OCR patients. Lower EDSS scores were identified to favor OFA initiation (Figure 1). OFA users were more often treatment-naïve than OCR users (29.7% vs. 25.7%; chi-square test $p=0.334$; Figure 2). S1P receptor modulators, natalizumab, and daclizumab were the most used pre-OCR treatments, whereas glatiramer acetate, anti-CD20, and cladribine were more frequently prescribed before OFA.

Table 1. Baseline comparison between initiation with ocrelizumab and ofatumumab patients with MS

Variables	Ocrelizumab (N=452)	Ofatumumab (N=175)	p-value
Female sex, N (%)	324 (71.7)	113 (64.6)	0.101
Age at MS onset [years], mean (± SD)	29.3 (9.7)	29.5 (9.6)	0.871
Time to MS diagnosis [years], median [25%;75%-quantiles]	0.2 [0.0;1.1]	0.1 [0.0;0.6]	0.075
Age at ocrelizumab/ofatumumab initiation [years], mean (± SD)	41.9 (11.0)	39.4 (11.8)	***0.020***
Disease duration at ocrelizumab/ofatumumab initiation [years], mean (± SD)	12.2 (8.8)	10.2 (8.8)	***0.013***
EDSS at ocrelizumab/ofatumumab initiation, median [25%;75%-quantiles]	3.0 [2.0;4.5]	2.0 [1.5;2.9]	***<0.001***
Annualised relapse rate (± SD)	0.28 (0.6)	0.20 (0.5)	0.063
Number of prior therapies, N (%)			0.942
Initial therapy	116 (25.7)	52 (29.7)	
1 prior therapy	1024(27.4)	43 (24.6)	
2 prior therapies	83 (18.4)	31 (17.7)	
≥ 3 prior therapies	129 (28.5)	49 (28.0)	

EDSS - expanded disability status scale; MS – Multiple sclerosis; N – number of patients; SD - standard deviation

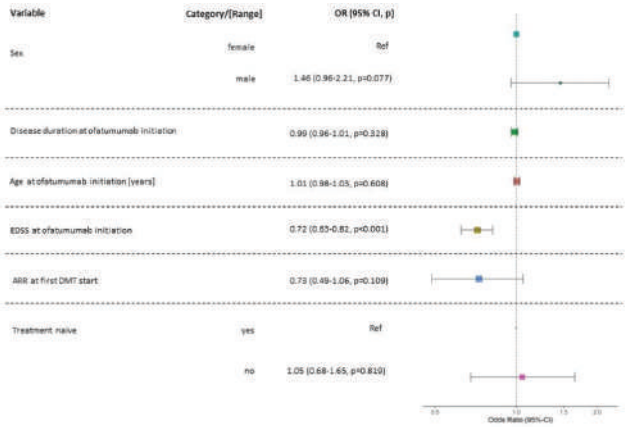

Figure 1 - Predictors for starting treatment with ofatumumab within the first year of market availability. A multivariable logistic regression model was used to identify variables associated with the initiation of ofatumumab among 175 MS patients. The forest plot contains colored boxes indicating the ORs of the variables analyzed for treatment with ofatumumab. Box sizes represent the number of patients included. Whiskers symbolize the 95% CIs of ORs. ARR - annualized relapse rate; CI - confidence interval; EDSS - expanded disability status scale ; MS - multiple sclerosis; OR - odds ratio; p - p-value; Ref - reference

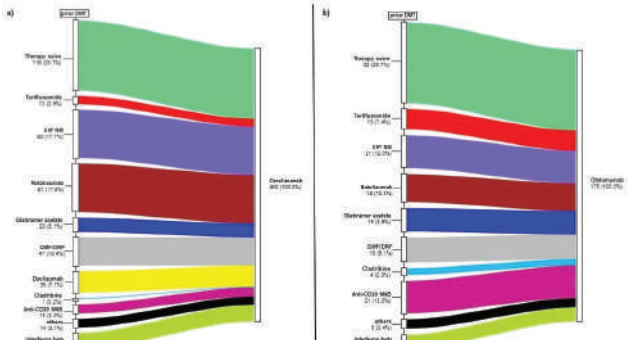

Figure 2. DMTs prescribed prior to patients with ocrelizumab (a) (N=452) and ofatumumab (b) (N=175). The boxes on the left side represent the proportion of patients, stratified by the prior DMT used. On the right side, the immediately following ocrelizumab (a) or ofatumumab (b) treatment is shown. The color line does correspond to the proportions of patients using the respective DMTs. Anti-CD20 MAB – anti-CD20 monoclonal antibodies; ocrelizumab/ofatumumab/rituximab; DMF – dimethyl fumarate; DMT – disease-modifying therapy; DRF – disease-free rate; MS – multiple sclerosis; N – number of patients; S1PRM – sphingosine-1-phosphate-receptor modulators; teriflunomide/leflunomide

Conclusion: Differences in clinical patient characteristics and pre-therapy may be explained by the market availability of additional HE-DMTs. PwMS were more often initiated with OCR as the first in-class medication compared to the subsequent OFA. The administration route of OCR (infusion) and OFA (injection) could also impact patient preferences and physician decisions in the future.

Disclosure: The authors have received speaking fees, travel support, honoraria from advisory boards, and/or financial support for research activities from pharmaceutical companies. None resulted in a conflict of interest.

EPO-600 | A phase 2 trial of tolebrutinib, a Bruton's tyrosine kinase inhibitor, for chronic active lesions in multiple sclerosis

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Background and Aims: In paramagnetic rim lesions (PRL), iron accumulates in activated microglia at the edge of chronic active multiple sclerosis (MS) lesions. PRL are associated with smoldering tissue degeneration and aggressive disease and are not resolved by approved disease-modifying therapies. Tolebrutinib, a brain-penetrant Bruton's tyrosine kinase (BTK) inhibitor, modulates B cells and microglia.

Methods: BRaKe-MS (NCT04742400), a single-site, open-label, rater-blinded, Phase 2a trial, assessed whether 48 weeks of tolebrutinib 60 mg resolved PRL on 7-tesla MRI in adults with no new white matter lesions or clinical relapses for ≥6 months, who were on anti-CD20 therapy at baseline. Radiological, clinical, and biological outcomes were measured at 24 and 48 weeks (primary outcome). Secondary outcomes included safety, tolerability, and other radiological outcomes.

Results: We enrolled a preplanned total of 7 participants. At baseline, the median number of PRL per participant was 9 (range: 6–46). The primary outcome (disappearance of ≥1 PRL in at least 2 participants) will be reported, together with changes in the CSF and blood proteome (Olink) and single-cell transcriptome (10×). No participant had a clinical or radiological relapse. The most common adverse events were COVID-19 (4), headache (3), and nausea (3). No safety-related discontinuations or treatment-related deaths occurred.

Conclusion: BRaKe-MS tested whether 48 weeks of BTK inhibition with tolebrutinib reduced radiological and biological markers of inflammation associated with chronic active white matter lesions in MS.

Disclosure: This study was supported and sponsored by the Intramural Research Program of NINDS (NIH), in part via a Cooperative Research and Development Agreement with Sanofi.

Muscle and neuromuscular junction disorder 3

EPO-601 | Comparison between IVIG and plasma exchange in the management of myasthenia crisis

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Background and Aims: Myasthenic crisis (MC) is characterized by type II respiratory failure needing mechanical ventilation (MV). Intravenous immunoglobulin (IVIg) or plasma exchange (PLEX) are used as a rescue treatment although there is paucity of information. We compare the efficacy of IVIg and membrane based PLEX in MC in an open labelled trial.

Methods: Patients with MC were included, and their clinical findings, precipitating causes and laboratory parameters were noted. Patients were either treated with IVIg (400 mg/kg/day for 5 days) or membrane based PLEX (40 ml/kg/alternate day for 5 sessions). Primary outcome was duration of MV, and secondary outcomes were duration of hospital stay, time to reach pre-worsening status, pyridostigmine dose at discharge, and adverse events.

Results: 44 episodes of MC occurred in 17 patients. IVIg was prescribed in 15 (34.1%) and PLEX in 8 (18.18%) episodes. Mean age was higher in IVIg group than the PLEX (49.53 ± 9.93 vs 40.25 ± 7.92; $p = 0.02$). Other baseline characteristics are comparable. Infection was the most frequent cause (61.4%) of MC. IVIg group required longer duration of MV compared to PLEX (17.47 ± 11.32 vs 7.38 ± 7.40 days; $p = 0.018$). However, there was no difference in the duration of hospital stay (30.33 ± 21.39 vs 24.12 ± 7.88 days; $p = 0.33$) and time to reach pre-worsening status (53.33 ± 22.25 vs 48.13 ± 31.27 days; $p = 0.68$). Allergic reaction (6.7%) and raise in creatinine (13.3%) were seen in IVIg group needing withdrawal in one. In PLEX group, 50% episodes were associated with transient fall in blood pressure, not required withdrawal.

Conclusion: Membrane based plasmapheresis reduced the duration of mechanical ventilation in MC compared to IVIg. Blood pressure monitoring is important during plasmapheresis.

Disclosure: Nothing to disclosure.

EPO-602 | Subcutaneous efgartigimod PH20 demonstrates improvements in gMG patients regardless of prior administration route

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Background and Aims: ADAPT-SC+ is an ongoing, open-label extension trial evaluating long-term efficacy/safety of subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) in generalised myasthenia gravis (gMG). Interim analyses (December 2022) demonstrated efficacy/safety of efgartigimod PH20 SC in gMG participants rolled over from ADAPT+/ADAPT-SC (Fig.1). Here we evaluate efgartigimod PH20 SC in gMG participants who received IV or SC formulations in antecedent studies.

Methods: Efgartigimod PH20 SC 1000 mg was administered in cycles of 4 once-weekly injections. Subsequent cycles were initiated ≥28 days from last dose based on clinical evaluation.

Results: As of December 2022, 179/184 participants received ≥1 efgartigimod PH20 SC dose; participants previously received efgartigimod IV (IV-SC: 127/179 [70.9%]) or efgartigimod PH20 SC (SC-SC: 52/179 [29.1%]). Mean (SD) study duration was 413.9 (107.9) days (136.9 patient-years follow-up) and 410.4 (96.7) days (56.5 patient-years follow-up) in the IV-SC and SC-SC subgroups, respectively. In AChR-Ab+ participants (IV-SC: $n=98$; SC-SC: $n=43$), mean [SE] total MG-ADL score improved from baseline to week 4, cycle 1 (IV-SC: −4.3 [0.33]; SC-SC: −3.6 [0.49]) and was consistent over subsequent cycles in both subgroups (Fig.2). Mean MG-QoL15r/EQ-5D-5L scores improved from baseline over multiple cycles in both subgroups, indicating improved QoL over time. Adverse events were predominantly mild/moderate and consistent between subgroups; most frequent were injection site erythema (IV-SC: 30.7%; SC-SC: 25.0%), COVID-19 (IV-SC: 23.6%; SC-SC: 19.2%), and headache (IV-SC: 17.3%; SC-SC: 26.9%). Four deaths were reported (IV-SC), with none efgartigimod-related, as per investigator.

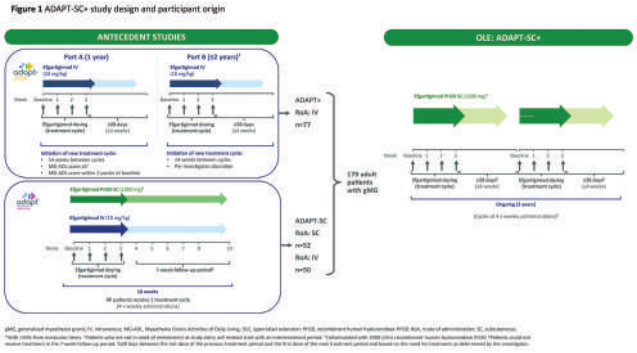
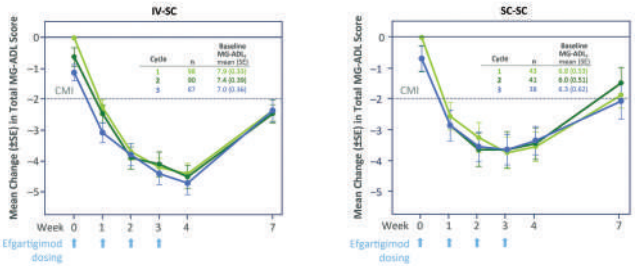


Figure 2 Mean change in MG-ADL total score from baseline (AChR-Ab+ participants)



AChR-Ab+, acetylcholine receptor antibody–positive; CMI, clinically meaningful improvement; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; SC, subcutaneous; SE, standard error.

Conclusion: Efgartigimod PH20 SC demonstrated comparable efficacy/safety in gMG participants previously treated with IV or SC formulations.

Disclosure: ECV: Alexion, argenx, Janssen, UCB. JV: Alexion, argenx, Health Holland, NMD Pharma, MuSK MG patent applications, MuSK antibody assays, member of the European Reference Network for Rare Neuromuscular Diseases (ERN EURO-NMD), Princes Beatrix Fonds. HW: Abbvie, Actelion, Alexion, Amicus, argenx, Biogen, Bristol Myers Squibb, CSL, Deutsche Forschungsgesellschaft (DFG), Deutsche Myasthenie Gesellschaft e.V., EMD Serono, Fondazione Cariplo, Genzyme, German Ministry for Education and Research (BMBF), Gossamer Bio, Idorsia, Immunic, Immunovant, Janssen, Lundbeck, Merck, Neurodiem AG, NexGen, Novartis, PSI CRO, Roche, Sanofi, Swiss Multiple Sclerosis Society, TEVA, UCB, WebMD Global and Worldwide Clinical Trials. LL, FG, SS, BVH, and JP: employees of argenx. KU: Alexion, argenx, Chugai, Horizon, Janssen, Japan Blood Products Organisation, Mitsubishi Tanabe, UCB, Viela Bio. JLDB: Alexion, Alnylam, argenx, CSL, Janssen, Sanofi Genzyme, UCB. RM: Alexion, argenx, Biogen, BioMarin, Catalyst, Merck, Roche, Teva, UCB.

EPO-603 | Cardiac organoids as in vitro model for myotonic dystrophy type 1

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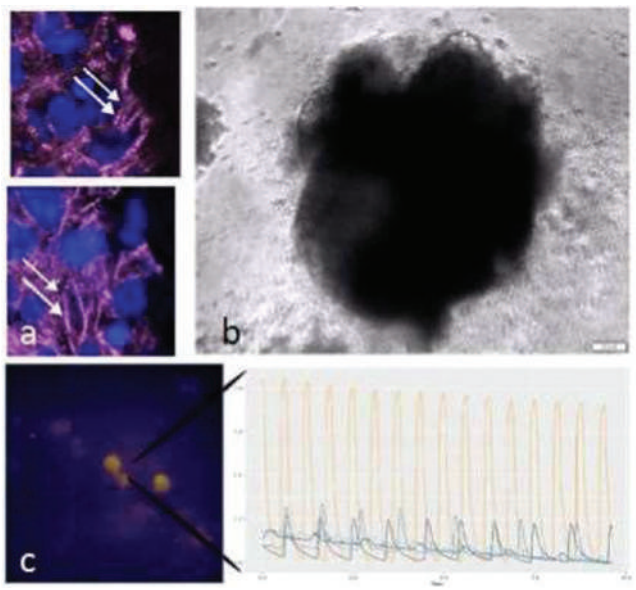
Background and Aims: Current animal models fail to faithful replicate the complexity of Myotonic Dystrophy. Organoids are self-organizing in vitro culture systems that acquire in vivo-like organ complexity, enabling them to recapitulate the architecture and functions of organs. Our aim is to generate cardiac organoids as in vitro model of DM1 to explore pathophysiology of the disease and as a preclinical model for testing candidate drugs.
Methods: Three iPSCs lines from distinct caucasian affected with myotonic dystrophy harbouring different expansion triplet numbers have been used. Cardiac organoids were generated using a published protocol by Lewis-Israeli (2021) and cultured until day 50 (Fig. 1).
Results: Patient-derived organoids (PdOs) showed similar contractile structures to controls (Fig. 1) and manifested different gene expression profiles. PdOs showed increased expression of COL1A1 ($p<0.01$) and calcium channel ($p=0.03$) and a decrease in insulin receptor ($p<0.01$) and IGF receptor ($p=0.03$). Of note, an increase of CACNA1C expression have been found also in vivo (Poulin, 2021), while the reduction in INSR and IGFR expression may, in part, explain the insulin resistance, We observed marked differences in PdOs and control organoids regarding the amplitude of calcium transients and conduction velocities, both reduced in DM1 organoids (Fig. 1).



1A: Both patient-derived and controls organoids shows characteristic contractile structures. 1B: Organoids at 50 days of culture. 1C: calcium analysis.

Conclusion: We generated PdOs that replicate certain features observed in vivo. Given their flexibility, organoids can serve as personalized disease models and may improve our understanding of pathophysiological mechanisms in DM1, as a tool to evaluate DMPK expansion effects in distinct aspects of cell physiology, as well as a test platform for candidate drugs.
Disclosure: Nothing to disclose.

EPO-604 | Safety and efficacy of amifampridine in Lambert-Eaton myasthenic syndrome patients – Real world data

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Background and Aims: Lambert-Eaton myasthenic syndrome (LEMS) is an ultrarare neurological disease with triad of symptoms: muscle paresis, dysautonomy and areflexia. Symptomatic treatment with amifampridine is available. Aim: To assess the effectiveness and safety of treatment in real-world.
Methods: 14 patients with non-neoplastic LEMS treated with amifampridine were enrolled in the study (F 42.9%, mean age 48.8 ± 11.4 years). The patients were assessed using Quantitative Myasthenia Gravis (QMG) scale, QMG limb domain (LD) score, spirometry, Hand Grip Strength (GRIP) test and repetitive nerve stimulation study (RNS) at baseline and end of follow-up. Diagnostic delay was 7–260 months. The patients were treated for 21.1 ± 12.0 weeks (13–48 weeks).
Results: All patients improved in QMG score. Mean improvement was 5.1 ± 2.0 (1–8) points ($p<0.001$). Clinically meaningful improvement ≥3 points achieved 85.7% of patients ($N=12$) Improvement in QMG LD was seen in 78.6% of the patients (mean 2.2 ± 1.6 points, $p<0.001$). Also, FVC improved on treatment ($p=0.031$). Mean improvement in GRIP test was 7.0 ± 7.1 kg in right and 5.2 ± 7.5 kg in left hand ($p<0.001$). In RNS before treatment, facilitation (>100%) was observed in 78.6% ($N=11$) of patients and was higher before treatment ($p<0.001$). Mean increase of CMAP amplitude was 2.1 ± 1.6 times. CMAP amplitude increased on treatment ($p<0.001$). In 64.3% ($N=9$) of patients lowering of corticosteroid dose was achieved.
Conclusion: Amifampridine is an effective treatment in non-neoplastic LEMS patients. Treatment is well-tolerated and allows to lower dose of corticosteroids in the majority of patients.
Disclosure: Nothing to disclose.

EPO-605 | From phenotype to genotype: Diagnosis pitfalls in atypical FSHD cases

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Background and Aims: Facioscapulohumeral muscular dystrophy (FSHD) is the third most common dystrophy, in which different

phenotypes can be observed, showing different disease progression and/or implying distinct genetic mechanisms. To date, the diagnostic criteria are based on the detection of the genetic signature (reduced D4Z4 allele, permissive haplotype, hypomethylation, mutations in modifiers genes as SMCHD1, LRF1 or DNMT3B). Still, the interpretation of the genetic test cannot ignore a careful correlation with the phenotype.

Methods: We present data of a cohort of 43 patients from 24 families selected by phenotypic features, characterized by incomplete penetrance/atypical phenotypes according to the Comprehensive Clinical Evaluation Form (CCEF), in which a short D4Z4 allele segregated. The molecular characterization included the assessment of 4q subtype, DNA methylation levels, Whole Exome Sequencing (WES) and segregation analysis.

Results: In our cohort, methylation levels displayed high variability in relation to the disease phenotype. In more than half of the atypical phenotypes, despite the detection of the FSHD genetic signature, WES analysis identified VUS or likely pathogenic/pathogenic variants in other genes associated with neuromuscular disorders, compatible with the observed phenotype, or known FSHD-modifying genes. A definitive alternative diagnosis was obtained in 5 families.

Conclusion: Our results further support the need to perform a detailed phenotypic characterization of patients with a suspect of FSHD, and, in cases of atypical phenotypes, to combine the D4Z4 sizing with other procedures such as WES. In this regard, methylation analysis represents a valuable tool to provide preliminary evidence for FSHD to be confirmed by further testing.

Disclosure: The authors have no conflicts of interest to disclose.

EPO-606 | The METMYD Study: Early results on efficacy and safety of metformin in myotonic dystrophy type 1 (DM1)

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Background and Aims: DM1 is still orphan of a cure or disease-modifying treatment. While gene therapy and antisense-oligonucleotide treatments are under investigation, recent studies showed that metformin can modify the aberrant alternative splicing causative of DM1. The aim of this study is to evaluate the superiority of a 24 month-treatment with the biguanide drug metformin over placebo, on mobility and strength parameters in adult DM1 patients.

Methods: METMYD is a multi-center, randomized, triple-blind, two-arm, placebo-controlled, phase III clinical trial. The primary endpoint is a better performance at the 6MWT at the end of study as compared to baseline. Secondary clinical endpoints explore muscle quantitative testing of upper and lower limbs, dexterity, fatigue. In addition, quantitation of circulating alternative splicing products deficient in DM1 and of markers of oxidative stress is performed before and after treatment.

Results: Enrolment started in January 2020 and the study ended in December 2023. One-hundred and forty-nine patients were enrolled and 146 were randomized either to metformin or placebo. The two arms at baseline did not differ for sex, age, BMI, HOMA index and 6MWT. Fifty-four (37%) patients (29 on metformin, 25 on placebo) dropped out for various reasons, mainly non-compliance, consent withdrawal and diarrhea and 92 patients completed the protocol.

Conclusion: The METMYD study shows that a long-term pharmacological intervention is feasible in DM1 patients, even during the COVID-19 pandemics. Metformin showed to be safe when administered in non-diabetic DM1 patients, the only common AE being diarrhea, as in general population. The analysis of clinical and laboratory efficacy measures is underway.

Disclosure: Nothing to disclose.

EPO-607 | Anti-HMGCR necrotizing myopathy: Characterization and therapy management in 17 patients over a 10 years follow-up

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Background and Aims: Antibodies against 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) myopathy represents an immune-mediated necrotising myopathy (IMNM) typically associated with statin use, with a variable onset. In this retrospective study we examined 17 patients diagnosed with anti-HMGCR IMNM according to 2017 EULAR criteria, followed at our Center in the years 2013–2014.

Methods: Medical records, encompassing clinical, histological, instrumental, and laboratory data (table 1–2), were systematically reviewed.

Results: Clinical onset manifested as a progressive proximal muscle weakness in 70.5% of patients. 29.5% of cases were only mildly symptomatic but 80% of them developed remarkable weakness within two years, before starting IVIg treatment, with only one remaining slightly symptomatic. 88% of patients had prior statin exposure; elevated serum creatine kinase (CK) levels (600–27000 UI/L) and positive anti-HMGCR antibodies were observed in all cases. In 16/17 patients, immunomodulant/suppressive therapy was administered with steroids and/or intravenous immunoglobulin (IVIg); five patients also received azathioprine or methotrexate. IVIg yielded

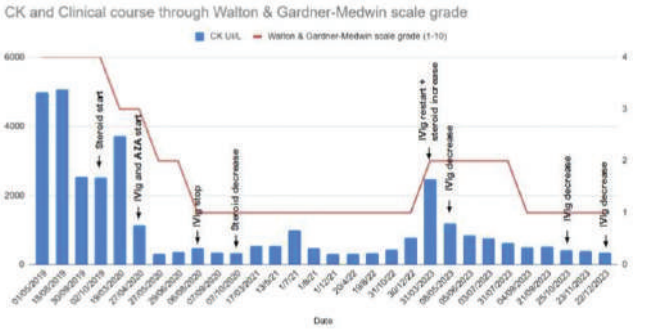
optimal responses in 88% of patients. Immunotherapy was gradually tapered for all patients throughout the years. Of nine patients ceasing IVIg after achieving clinical-biochemical remission, six of them had to resume treatment, leading to rapid improvement.

Gender		Age at onset	
M	10 (59%)	Mean (SD)	63.8 yrs
F	7 (41%)	Range	17 - 79
Dysphagia		**Dyspnoea**	
N	12 (70.6%)	N	15 (88.2%)
Y (occasional, solved with treatment)	5 (29.4%)	Y	2 (11.8%)
Skin lesions		**Interstitial lung disease**	
N	14 (82%)	Y	2 (12%)
Y	3 (18%)	N	15 (88%)
Neoplasia		**Anti-HMGCR Ab titre (n.v. < 19 CU)**	
Y (prostate ca., in remission at IMNM diagnosis)	2 (12%)	Median*	142
N	15 (88%)	IQR*	85, 200
*2 pts were anti-HMGCR Ab positive but we couldn't collect the value			
Statins		**Months of treatment with statins**	
Y	15 (88.2%)	12	2 (15%)
N	2 (11.8%)	24	4 (31%)
		36	3 (23%)
		120	4 (31%)
		NA	4
Associated MSA/MAA		**Muscle biopsy alterations**	
None	13 (76%)	Y	11 (65%)
PL-12	1 (5.9%)	NP	6 (35%)
M2	1 (5.9%)	**Muscle MRI alterations**	
Anti-tRNA synthetase	1 (5.9%)	Y	11 (65%)
Mi2b, EJ	1 (5.9%	NP	6 (35%)
CK at onset (n.v. < 145 UI/L)		**Last CK (n.v. < 145 UI/L)**	
Median	5,000	Median	346
IQR	4000, -7118	IQR	196, 606

TABLE 1 Ab anti-HMGCR-IMNM. Clinical, serological, instrumental and histological information.

First Line Treatment		Ongoing Steroid	
Steroid therapy	11 (64.7%)	Y	15 (88.2%)
Steroid therapy + IVIg	3 (17.6%)	N	5 (29.4%)
IVIg	2 (11.8%)	NA (follow-up not available	1 (5.9%)
N	1 (5.9%)		
Second Line Treatment		**Ongoing IVIg**	
IVIg	6 (35.3%	Y	10 (58.8%)
Azathioprine	1 (5.9%)	N	4 (23.5%)
Azathioprine + IVIg	1 (5.9%)	N, but is waiting for subcutaneous Ig	1 (5.9%)
IVIg + increase steroid	4 (23.5%))	NA (1 no treatment at all, 1 lost FU)	2 (11.8%)
Third Line Treatment			
N	13 (76.5%)		
Azathioprine	2 (11.8%)		
Methotrexate	1 (5.9%)		
IVIg	1 (5.95%)		

TABLE 2 Ab anti-HMGCR-IMNM. Treatment management.



GRAPHIC 1 Ab anti-HMGCR-IMNM. Clinical course (calculated with Walton and Gardner-Medwin scale grade, y axis on the right), serological course (based on CK levels, y axis on the left) and treatment modifications thorough the years of one patient.

Conclusion: Anti-HMGCR IMNM seems to produce a persistent dysimmune process; chronic immunomodulant treatment appears to be the most suitable to maintain clinical and biochemical remission. In our cohort, 67% of patients relapsed after IVIg treatment suspension, although still well responded to IVIg reintroduction. This highlights the need for recurring treatment cycles and vigilant clinical and serological monitoring.

Disclosure: Nothing to disclose.

EPO-608 | Facioscapulohumeral muscular dystrophy (FSHD) type 1 mimics: Review of 60 cases with normal size D4Z4 alleles

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Background and Aims: Analysis of D4Z4 alleles is indicated in patients with facial-shoulder girdle weakness and in FSHD1 patients' relatives. Our research focused on carriers of D4Z4 alleles with ≥11 repeats, reviewing their phenotypes according to the Comprehensive Clinical Evaluation Form (CCEF) Clinical Categories, and identifying alternative genetic diagnoses.

Methods: We examined 510 patients referred for 4q35-D4Z4 analysis to the Miogen Laboratory (Modena) in the last 15 years.

Results: Excluding 356 cases (69.8%) showing a D4Z4-reduced allele, 154 (30.2%) carried D4Z4 alleles with ≥11 repeats: 94 (61%) were unaffected relatives (Category C), and 60 (39%) represented sporadic symptomatic patients. Among the latter group, 9 (15%) presented a full phenotype (Category A), 3 (5%) an incomplete one (Category B), and 48 (80%) an atypical involvement (Category D). Subsequent genetic analyses identified damaging variants in the following genes and Clinical Categories: 3 SMCHD1 (FSHD2) and 1 COL6A (Category A); 1 EMD (Category B1); in Category D, 4 CAPN3 (2 recessive and 2 dominant), 2 COL6A, 1 MYH7, 1 DMPK, 1 RYR1, 1 GAA, 1 DMD (Becker phenotype), 1 FKRP, and 1 SGCG. In 1 atypical

case, a variant on PMP22 already described in Charcot-Marie-Tooth (CMT)-like distal weakness was found. In the remaining 41 patients further genetic analyses are ongoing.

Conclusion: The study of 4q35 region is justified in FSHD-like phenotypes and in FSHD1 patients' relatives for segregation. In our cohort, alternative diagnoses were found in 32% of FSHD1-mimicking phenotypes, making it a varied group needing thorough phenotyping and extensive genetic investigations.

Disclosure: Nothing to disclose.

EPO-609 | Safety and efficacy of tofacitinib in patients with refractory myasthenia gravis: A pilot study

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Background and Aims: Myasthenia gravis is one of the most common autoimmune neuromuscular disorders. About 10 percent MG patients still are refractory and there still is an unmet need for effective, well tolerated, and convenience treatment options for these patients. We aimed to assess the safety and efficacy of tofacitinib, an inhibitor of JAK kinases with oral administration.

Methods: This registered open-label, single-arm pilot study was conducted from June 2020 through December 2023 (NCT04431895). Refractory gMG patients received tofacitinib (5mg, twice a day) as the only IS in combination with corticosteroids. Clinical scales, including QMG score, MG-ADL, MG-QoL15, and MGC were assessed prospectively from the baseline to 24 weeks after Tofacitinib initiation. The phosphorylation level of STAT3 in peripheral blood CD4+T cells for MG patients were detected by multi-color flow cytometry.

Results: We enrolled 19 anti-AChR antibody-positive gMG cases. By week 24 after tofacitinib administration, a significant reduction was observed in MG-ADL (6.0 vs 1.5 at baseline; $p=0.0004$) and QMG (14 vs 11 at baseline; $p=0.0391$), respectively. Corticosteroids dose were significantly reduced from 20 mg to 15 mg ($p=0.0074$). Tofacitinib induced the elevation of triglycerides in some patients. Phosphorylation flow cytometry revealed that tofacitinib inhibits the phosphorylation levels of STAT3 protein in Th17.1 cells in MG who received tofacitinib.

Conclusion: The study provided preliminary evidence of the safety and efficacy profile of tofacitinib in treating patients with refractory gMG. The therapeutic effect of Tofacitinib was probably associated with the inhibition of pro-inflammatory Th17.1 cells.

Disclosure: Nothing to disclose.

EPO-610 | Germinal centers are associated with the prognosis of thymoma-associated myasthenia gravis

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Background and Aims: Some studies have observed that the presence of germinal centers (GCs) in the non-neoplastic thymic tissues play a part in the pathogenesis of thymoma-associated myasthenia gravis (TAMG). The aim of this study is to analyze whether the presence of GCs in the thymus of patients with TAMG are associated with clinical outcome of myasthenia gravis after removal of thymoma.

Methods: We conducted a retrospective analysis of TAMG patients who underwent surgical removal of the thymoma. Clinical characteristics were collected and thymic tissue slides were rereviewed by a pathologist. Patients were classified into GC-positive and GC-negative groups based on the presence of GC.

Results: Preoperative use of prednisolone is known to reduce the number of GCs, and the proportion of patients who were on preoperative prednisolone treatment was lower in the GC-positive group (Table 1) After excluding the patients with preoperative prednisolone use, a total of 83 patients with 37 (44.6%) in the GC-positive group and 46 (55.4%) in the GC-negative group were analyzed. The clinical differences between the two groups are presented in Table 2. Multivariate analysis using cox regression revealed a negatively significant between minimal manifestation and the presence of GCs (Table 3).

Table 1. Clinical and perioperative data of patients with thymoma associated myasthenia gravis with and without germinal centers in thymic tissue adjacent to the thymoma

	GC-positive (n = 41)	GC-negative (n = 70)	p
Age at onset (y)	41.4 ± 12.0	47.9 ± 11.8	0.006*
Sex, male (%)	15 (36.6%)	38 (54.3%)	0.080
MGFA clinical classification			0.062
I	7 (17.1%)	18 (25.7%)	
II	11 (26.8%)	31 (44.3%)	
III	18 (43.9%)	15 (21.4%)	
IV	2 (4.9%)	1 (1.4%)	
V	3 (7.3%)	5 (7.1%)	
MGFA clinical classification ≥ III	23 (56.1%)	21 (30.0%)	0.007*
Preoperative AChR-Ab (nmol/L)	11.1 ± 4.3	9.6 ± 3.9	0.063
Postoperative AChR-Ab (nmol/L)	10.3 ± 5.0	8.1 ± 3.9	0.042*
Reduction in AChR-Ab (nmol/L)	0.7 ± 4.0	1.6 ± 3.3	0.312
Preoperative prednisolone use	4 (9.8%)	24 (34.3%)	0.004*
Onset to thymectomy (m)	6.8 ± 14.0	18.3 ± 50.6	0.157
Size of thymoma			0.129
< 3cm	9 (22.0%)	25 (35.7%)	
≥ 3cm	32 (78.0%)	45 (64.3%)	
WHO histology classification			0.267
A	1 (2.4%)	6 (8.6%)	
AB	3 (7.3%)	12 (17.1%)	
B1	6 (14.6%)	11 (15.7%)	
B2	23 (56.1%)	26 (37.1%)	
B3	8 (19.5%)	15 (21.4%)	
WHO histology type B (B1+B2+B3)	37 (90.2%)	52 (74.3%)	0.042*
Masaoka stage			0.136
I	14 (34.1%)	16 (22.9%)	
II	23 (56.1%)	51 (72.9%)	
III	1 (2.4%)	2 (2.9%)	
IV	3 (7.3%)	1 (1.4%)	
Invasive thymoma (Masaoka stage III+IV)	4 (9.8%)	3 (4.3%)	0.252
Postoperative chemotherapy and radiotherapy	25 (61.0%)	50 (71.4%)	0.256
Thymoma recurrence	4 (9.8%)	7 (10.0%)	0.967
Follow-up duration after thymectomy (m)	86.2 ± 45.5	76.0 ± 35.5	0.225

Table 2. Clinical and perioperative data of thymoma associated myasthenia gravis patients with no preoperative prednisolone use with and without germinal centers in thymic tissue adjacent to the thymoma

	GC-positive (n = 37)	GC-negative (n = 46)	*p*
Age at onset (y)	42.1 ± 12.3	49.0 ± 11.8	0.012*
Sex, male (%)	13 (35.1%)	25 (54.3%)	0.081
MGFA clinical classification			0.054
I	7 (18.9%)	16 (34.8%)	
II	11 (29.7%)	20 (43.5%)	
III	15 (40.5%)	7 (15.2%)	
IV	1 (2.7%)	1 (2.2%)	
V	3 (8.1%)	2 (4.3%)	
MGFA clinical classification ≥ III	19 (51.4%)	10 (21.7%)	0.005*
Preoperative AChR-Ab (nmol/L)	11.3 ± 4.1	9.0 ± 4.0	0.013*
Postoperative AChR-Ab (nmol/L)	9.9 ± 5.1	8.4 ± 4.3	0.0219
Reduction in AChR-Ab (nmol/L)	0.9 ± 4.1	1.1 ± 3.1	0.830
Onset to thymectomy (m)	5.8 ± 12.3	9.3 ± 30.1	0.488
Size of thymoma			0.189
< 3cm	8 (21.6%)	16 (31.8%)	
≥ 3cm	29 (78.4%)	30 (65.2%)	
WHO histology classification			0.214
A	0	1 (2.2%)	
AB	3 (8.1%)	11 (23.9%)	
B1	5 (13.5%)	8 (17.4%)	
B2	21 (56.8%)	19 (41.3%)	
B3	8 (21.6%)	7 (21.6%)	
WHO histology type B (B1+B2+B3)	34 (91.9%)	34 (73.9%)	0.034*
Masaoka stage			0.147
I	13 (35.1%)	9 (19.6%)	
II	20 (54.1%)	35 (76.1%)	
III	1 (2.7%)	1 (2.2%)	
IV	3 (8.1%)	1 (2.2%)	
Invasive thymoma (Masaoka stage III+IV)	4 (10.8%)	2 (4.3%)	0.258
Postoperative chemotherapy and radiotherapy	22 (59.5%)	34 (73.9%)	0.162
Thymoma recurrence	4 (10.8%)	5 (10.9%)	0.993
Follow-up duration after thymectomy (m)	89.3 ± 45.7	74.4 ± 37.0	0.112

Table 3. Cox regression analysis of prognostic factors for MM in patients with TAMG (Tx to MM, GC 33%)

Variable	Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*
Age at onset	1.003	0.982-1.025	0.761			
Sex (male)	1.560	0.884-2.754	0.125			
MGFA clinical classification ≥ III	0.702	0.387-1.276	0.246			
Preoperative AChR-Ab	0.929	0.862-1.002	0.055	1.014	0.911-1.130	0.796
Postoperative AChR-Ab	0.929	0.869-0.993	0.030*	0.925	0.845-1.014	0.093
Reduction in AChR-Ab	1.062	0.977-1.153	0.156			
Onset to thymectomy	1.003	0.991-1.015	0.609			
Size of thymoma (≥3cm)	0.803	0.429-1.505	0.494			
WHO (B type)	0.462	0.226-0.947	0.035*	0.760	0.318-1.815	0.536
Masaoka stage (III, IV)	1.544	0.607-3.924	0.362			
Postoperative therapy	1.023	0.562-1.862	0.941			
Thymoma recurrence	0.433	0.154-1.221	0.113			
Germinal center	0.466	0.265-0.855	0.014*	0.479	0.237-0.968	0.040*

Conclusion: Presence of GCs in the nonthymomatous tissue of TAMG patients was associated with greater disease severity and worse clinical outcome after thymectomy. The presence of thymic GCs could be used as a predictor of clinical outcome in patients with TAMG.
Disclosure: Nothing to disclose.

EPO-611 | Real world experience of Efgartigimod in a single UK centre – A 17 month follow up study

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Background and Aims: We present our experience of treating patients with generalised Myasthenia Gravis (gMG) with the neonatal Fc receptor (FcRN) antagonist Efgartigimod under the UK Early Access to Medicine Scheme (EAMs) in single centre over a 16 month period.
Methods: Data regarding all patients receiving Efgartigimod in the National Hospital for Neurology and Neurosurgery were collected prospectively. Efgartigimod was given as per the ADAPT protocol. Response to Efgartigimod was measured with MG-ADL scores, change in prednisolone dose and need for rescue therapies.
Results: 18 patients with gMG were treated with Efgartigimod over the 17 month period, 12 were female and the average disease duration was 14.6 years (range 1–40). 66% had required IVIG/PLEX regularly and 22% had required intermittent rescue treatment prior to starting Efgartigimod. All patients had previously received prednisolone and non-steroidal immunosuppressant therapies (NSITs). The average NSITs tried was 2.4. 50% had received Rituximab. The mean MG-ADL at baseline was 11.3. Following the first treatment cycle 89% were defined as MG-ADL responders with an average reduction of 7 points. Two patients stopped taking Efgartigimod due to lack of efficacy. 89% remained on it with a mean inter-cycle interval of 6.5 weeks. 83% of patients reduced their steroid doses. Rescue IVIG and PLEX were required in the two patients that stopped treatment but otherwise no rescue treatments were required Efgartigimod was well tolerated with only minor side effects reported.
Conclusion: Efgartigimod is an effective and well tolerated treatment in patients with refractory gMG.
Disclosure: JS received speakers fees, and travel support from UCB and argenx and has served on UCB advisory boards.

EPO-612 | Cyclic and continuous dosing of intravenous Efgartigimod for generalised myasthenia gravis: Part A of ADAPT NXT

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Background and Aims: Individualised cyclic administration of efgartigimod, a human immunoglobulin G1 Fc-fragment that blocks the neonatal Fc receptor, was well tolerated and efficacious in the ADAPT/ADAPT+ phase 3 trials in generalised myasthenia gravis (gMG). In an effort to evaluate additional dosing regimens, the phase 3b ADAPT NXT study (NCT04980495) is investigating the efficacy, safety, and tolerability of 10 mg/kg intravenous efgartigimod administered in a cyclic (4 once-weekly infusions, 4-week intertreatment period) or continuous dosing regimen [every 2 weeks (Q2W)].

Methods: Adult participants with acetylcholine receptor antibody positive gMG who had MG-ADL total score ≥5 (with >50% of the score due to nonocular symptoms), and on a stable dose of ≥1 concomitant gMG treatment were recruited. Sixty-nine participants were randomised 3:1 on Day 1 to either continuous or cyclic dosing regimens for the initial 21-week comparison period (Part A; Figure). In Part B, participants in the cyclic arm received a final cycle before being rolled over to continuous Q2W dosing, while participants in the continuous dosing arm maintained Q2W dosing. Participants were followed for an additional 105-week extension period, and participants who maintained clinical improvement had the option to reduce dosing frequency to every 3 weeks.

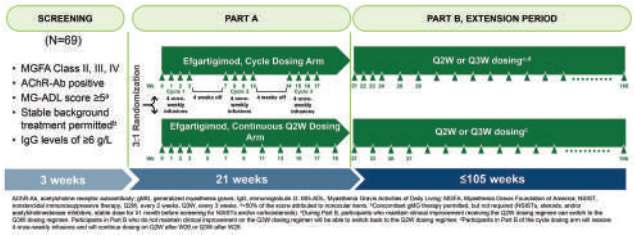

FIGURE ADAPT NXT study design.

Results: The primary endpoint is mean (SD) of the average change in MG-ADL total score from study baseline to Week 21 for each regimen. Safety, tolerability, and pharmacokinetic/pharmacodynamic effects are also being assessed; results will be presented at the congress.

Conclusion: ADAPT NXT will provide important efficacy and safety data on different treatment regimens in patients with gMG.

Disclosure: Multiple relationships financial and non-financial nature for authors KGC, VB, YH, KG, GS, AAH, ECV, EB, DG, AS, RHJ, DH, RM, AM, and SA stated at point of presentation.

EPO-613 | Danon disease in Japan: A phenotype-genotype correlation

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Background and Aims: Danon disease, an X-linked dominant vacuolar cardiomyopathy and skeletal myopathy, is caused by primary deficiency of lysosome-associated membrane protein-2 (LAMP-2). However, the clinical and genetic characteristics of Danon disease have not been well established.

Methods: We conducted a nationwide, questionnaire-based survey on Danon disease to 2,617 hospitals in Japan. We reviewed clinical histories, muscle specimens, and genetic analyses of the LAMP-2 gene in patients. We added patients newly found and reported since the national survey in Japan.

Results: As a result, we identified 47 Danon disease patients (23 men and 24 women) from 26 families. Hypertrophic cardiomyopathy and ECG abnormalities were documented in most patients with Danon disease. Among the 20 patients who had died, 19 (95%) died of cardiac failure or sudden cardiac arrest. Heart transplantation, the most effective therapy, was performed in only one woman and is just now required by 5 patients. Pathologically, all patients showed autophagic vacuoles with sarcolemmal features in muscles. In this study, 22 different LAMP-2 mutations were identified in 26 families with Danon disease. Half of the probands showed de novo mutations. The distribution of mutations widely ranged from exon 1 to 9. Four families with mutations in exon 9B (c.1097_1098 delAA) that encodes LAMP-2B showed markedly mild or no cardiomyopathy.

Conclusion: Cardiomyopathy is the most important prognostic factor and the main cause of death among Danon disease patients. However, clinical phenotypes of only mutations in exon 9B were markedly mild, suggesting that this particular mutation causes an exceptionally mild phenotype.

Disclosure: Nothing to disclose.

EPO-614 | Ventilatory function and sleep-disordered breathing in patients with facioscapulohumeral muscular dystrophy type 1

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Background and Aims: Facioscapulohumeral muscular dystrophy type 1 (FSHD1) is rarely associated with ventilatory dysfunction. The prevalence of sleep-disordered breathing (SDB) is thought to be high but remains poorly characterized and likely underestimated.

Methods: Observational study on demographic and clinical characteristics of adult FSHD1 patients.

Results: Twenty-nine patients were included, 52% males, with a mean current age of 49.6±15.7 years. The mean duration of disease was 26.8±16.4 years, with 5 (17%) patients showing childhood onset. The median Clinical Severity Score (CSS) was 3 (IQR=2.25–3). Twenty-four patients (83%) were able to walk unaided, 2 with unilateral support, 1 with bilateral support, and 2 were wheelchair-bounded. Respiratory function tests were conducted in 28 patients. Spirometric curves were normal in 20 (69%) patients, with a restrictive pattern in 4 (14%), and obstructive in another 4 (2 with a history of asthma). Patients with mild to moderate symptoms (CSS ≤3) showed higher mean forced vital capacity (FVC) than those with severe disease (CSS ≥3.5) ($p=0.01$). No correlation was found between respiratory function parameters (FEV1, FVC) and disease duration. Nine patients underwent maximal respiratory pressure studies, with altered results in 4, showing a tendency for greater compromise in expiratory pressures. Sleep studies were conducted in 27 patients, with 13 (48%) presenting sleep apnea syndrome, 6 of which requiring nocturnal non-invasive ventilation.

Conclusion: Our results support previous studies suggesting a high prevalence of SDB in FSHD1 patients. We would also like to emphasize the importance of an active search for ventilatory dysfunction in these patients, especially in more severe motor presentations.

Disclosure: Nothing to disclose.

EPO-615 | Clinical outcome measures in a prospective cohort of myasthenia gravis patients

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Background and Aims: Clinical assessment of myasthenia gravis (MG) relies on validated patient-reported outcome (PRO) and physician reported outcome (PhyRO) measures, coupled with post-intervention status (PIS) or the recently proposed "PASS question". The aim of this study is to validate the PASS question and assess PIS and PASS cut-off values for PRO and PhyRO scales in a prospective cohort.

Methods: The clinical status of AChR-MG patients was assessed with MG-ADL, MG-QOL15r and QMG scores over a 1 year-period. Favourable outcomes were defined by a positive response to the PASS question and a PIS of minimal manifestation (MM)-or-better. ROC curve analysis was used to determine cut-off values of the QMG, MG-ADL and MG-QOL15r in relation to PASS and PIS.

Results: 107 AChR-MG patients were included, of whom 42% females, with a median age at onset of 46 years. Patients with a favourable PASS and in MM-or-better status had a lower median QMG, MG-ADL, MG-QOL15 scores than symptomatic patients ($p<0.0001$). A QMG ≤9, MG-ADL ≤2 and MG-QOL15r ≤6 identified patients with a favourable PASS status. Same cut-offs for the QMG and MG-ADL scores were found to identify patients in MM-or-better, while the cut-off for the MG-QOL15r was much lower (≤4). In the multivariable logistic regression both MG-ADL ($p=0.025$) and MG-QOL15r ($p=0.043$) were independently associated with "PASS=yes", while QMG score was not.

Conclusion: PASS and PIS provide complementary information on the MG clinical status. The PASS cut-off values found for the most common MG scales support the use of the PASS question in clinical practice and clinical trials.

Disclosure: Work supported by: (1) #NEXTGENERATIONEU (NGEU) and funded by the Ministry of University and Research (MUR), National Recovery and Resilience Plan (NRRP), project MNESYS (PE0000006) – A Multiscale integrated approach to the study of the nervous system in health and disease (DN. 1553 11.10.2022); (2) Myasthenia Gravis Rare Disease Network–MGNet, a member of the Rare Disease Clinical Research Network Consortium (RDCRN) NIH U54 NS115054. All RDCRN consortia are supported by the network's Data Management and Coordinating Center (DMCC) (U2CTR002818). Funding support for the DMCC is provided by the National Center for Advancing Translational Sciences (NCATS) and the National Institute of Neurological Disorders and Stroke (NINDS).

Tuesday, July 02, 2024

Ageing and dementia 4

EPO-616 | Alzheimer disease prognostic from early clinical assessment: A two-year follow-up study

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Background and Aims: Alzheimer Disease (AD) evolution is characterized by high heterogenicity. Some patients show fast evolution, and further research is required. The aim of this study is to develop a prognostic model using clinical variables to detect patients at high risk of fast AD progression.

Methods: This observational study has been carried out in the Cognitive Disorders Unit in the Neurology Service of the Hospital Universitari i Politècnic La Fe (HULAFE). Participants were patients diagnosed with mild cognitive impairment (MCI) due to Alzheimer's

disease (AD) at time-1 (T1). For this, CSF biomarkers, and neuropsychological evaluation (CDR sum of boxes, MMSE, and RBANS) were obtained atT1. Two years after diagnosis (T2) the neuropsychological evaluation was repeated. From these data, a prognosis model for the probability of fast AD progression was developed using neuropsychological and CSF variables at T1 as predictor variables; and neuropsychological score (sum of the 3 tests) difference (T2-T1), as response variable.

Results: The developed model predicted the probability of fast progression, with an AUC of 0.79 (sensitivity 63.6% (95% CI 35.4–84.8); specificity 85.4% (95% CI 71.6–93.1); positive predictive value 53.8% (29.1–76.8); negative predictive value 89.7% (95% CI 76.4–95.9). Among the predictor variables, sex, CSF NfL and RBANS (language, immediate memory and visuospatial/constructional) could be relevant.

Conclusion: Some variables obtained from the MCI-AD diagnosis time (neuropsychology, CSF) could be helpful for detecting patients with a high risk of fast AD progression.

Disclosure: Nothing to disclose.

EPO-617 | Role of pro-inflammatory S100A9 protein in amyloid-neuroinflammatory cascade in neurodegenerative diseases

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Background and Aims: The amyloid cascade and neuroinflammation are central to onset of Alzheimer's and other neurodegenerative diseases. S100A9 may serve as a critical link in the amyloid-neuroinflammatory cascade in these diseases, as this protein possesses both amyloidogenic properties and acts as alarmin, triggering inflammatory responses.

Methods: The kinetic analysis of amyloid aggregation by thioflavin-T fluorescence, microfluidic analyses, charge-detection mass-spectroscopy, AFM, molecular dynamic simulation and gamma-oscillation were used in synergy. The level of S100A9 in CSF was measured by ELISA and dot-blots.

Results: We found that S1009 is intrinsically amyloidogenic and forms amyloids in vitro, in cells and in the brain tissues during Alzheimer's, Parkinson's and traumatic brain injury. We showed that S100A9 co-assembles with Aβ42 fibrils, forming new type of hetero-amyloid complexes. In these complexes the autocatalytic surfaces of Aβ42 fibrils template S100A9 amyloids. The formation of Aβ42-S100A9 complexes may sequestrate smaller toxic species, which is consistent with finding that their co-aggregation mitigates amyloid cytotoxicity. Small molecules, regulating S100A9 amyloid aggregation, including cell penetrating NCAM1 peptides, oleuropein aglycone, Nb10 and TiNb9 polyoxometalates, cyclin and DOPA derivatives, are viewed in the light of their prospective therapeutic applications in blocking amyloid formation. We have shown also that the levels of S100A9 follow those of Aβ in CSF during the development of Alzheimer's and S100A9 together with Aβ can serve as a biomarker for early stages of Alzheimer's disease.

Conclusion: The finding of S100A9 involvement in neurodegenerative diseases may open a new avenue for therapeutic interventions targeting S100A9 primarily and via this pathway affecting the whole amyloid-neuroinflammatory cascade.

Disclosure: There is no conflict of interest in presented data.

EPO-618 | Effects of frailty on hospital outcomes among patients with neurological disorders: A cohort study

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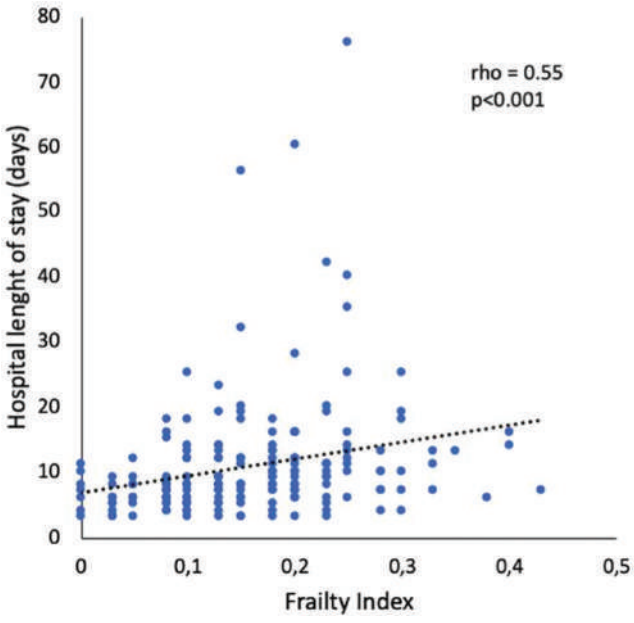
Background and Aims: Patients acutely presenting with neurological disorders exhibit highly heterogeneous clinical courses. We explored whether baseline frailty predicts adverse hospital outcomes among patients admitted to neurological wards.

Methods: All patients consecutively admitted to the neurology wards of the Policlinico Umberto I University Hospital of Rome (Italy) were considered. A 40-item Frailty Index (FI) was calculated from the emergency department assessment. Hospitalization outcomes were prospectively collected. Linear and logistic regression models were conducted to test the association between FI and adverse hospital outcomes.

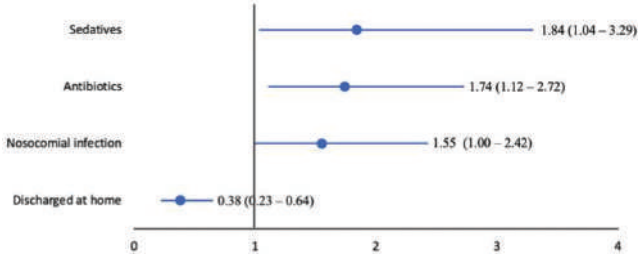
Results: Overall, 185 participants (women 50.3%; mean age 68.6, SD 18.6 years) were enrolled. FI scores ranged between 0 and 0.43, with a median value of 0.15 (IQR 0.10–0.20), and were positively correlated with age (Spearman's rho 0.55, $p < 0.001$). In multivariate regression models adjusted by age, sex, and neurological diagnosis, the FI was significantly associated with the number of days spent in the neurological ward (B 2.19, 95% CI 0.36–4.02, per 0.1 increase; $p = 0.02$), with a lower likelihood of being discharged at home (OR 0.38, 95% CI 0.23–0.64, per 0.1 increase; $p < 0.001$), with higher odds of nosocomial infections (OR 1.55, 95% CI 1.00–2.42 per 0.1 increase; $p = 0.05$), prescription of antibiotics (OR 1.74, 95% CI 1.12–2.72, per 0.1 increase; $p = 0.01$) and sedatives (OR 1.84, 95% CI 1.04–3.29 per 0.1 increase; $p = 0.04$).

40 - ITEM FRAILTY INDEX			
	DEFICT	Presence = 1	Absence =0
COMORBIDITIES			
1.	Hypertension		
2.	Arrythmias		
3.	Ischemic heart disease		
4.	Heart failure		
5.	Diabetes mellitus		
6.	Chronic kidney disease		
7.	Previous stroke		
8.	Cognitive impairment/Dementia		
9.	Psychiatric disease		
10.	Malignancy		
11.	Autoimmune Disorders		
12.	Chronic obstructive pulmonary disease		
13.	Endocrinopathies		
14.	Chronic Infections		
15.	Obesity or Malnutrition		
SIGN AND SYMPTOMS			
16.	Abnormalities in cardiac examination		
17.	Abnormalities in chest examination		
18.	Abnormalities in abdominal examination		
19.	Abnormalities in cutaneous examination		
20.	Focal neurological signs		
21.	Consciousness impairment		
22.	Agitation		
23.	Headache		
PARAMETERS			
24.	Systolic Blood Pressure <90 mmHg or >140mmHg		
25.	Diastolic Blood Pressure <50 mmHg or >90mmHg		
26.	Heart Rate <50 bpm or >100 bpm		
27.	Respiratory rate >20 bpm		
28.	Saturation <90%		
29.	Temperature >37.5°C		
30.	Haemoglobin <12 g/dL or >17 g/dL		
31.	Platelets <50x103 or >450x10		
32.	White Cell Count <4x103 or >10x103		
33.	INR <0,8 or >1,2		
34.	ALT <12 UI/L or >41 UI/L		
35.	Troponins >0,014 µg/L		
36.	CRP >0,5 mg/dL		
37.	Glycemia <74 mg/dL or >200 mg/dL		
38.	Creatinine >1,2 mg/dL		
39.	Sodium <136 mEq/L or > 145 mEq/L		
40.	Potassium <3,5 mEq/L or > 5,1 mEq/L		
TOTAL			
FRAILTY INDEX (range 0-1)			

40-item Frailty Index.



Correlation between Frailty Index and hospital length of stay (days).



Bivariate logistic regression model adjusted by age, sex, and neurological diagnosis exploring the factors associated with the 40-item Frailty Index (dichotomized dependent variable of interest). Data are shown as odds ratios (95% confidence intervals).

Conclusion: Assessing the frailty status of patients with acute neurological conditions can improve prognostication. This can have relevant implications for care planning and allocation of healthcare resources.

Disclosure: Nothing to disclose.

EPO-619 | Cross-sectional and longitudinal associations between sTREM2 and synapses-related biomarkers in healthy individuals

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Background and Aims: We aimed to study the association between TREM2-dependent microglial activation and synaptic dysfunction, and whether this relationship is influenced by AD core biomarkers in asymptomatic volunteers.

Methods: We studied cross-sectional ($n=239$) and longitudinal ($n=117$) associations between cleaved sTREM2 (cTREM2) and synapse-related biomarkers (neurogranin, alpha-synuclein and s100b) in cerebrospinal fluid (CSF) from asymptomatic volunteers. cTREM2 was measured by an in-house MSD-based immunoassay, while synapse-related and AD core markers were quantified by the Elecsys® platform (Neurotoolkit). We defined subgroups according to the AT classification, and medians of *p*-tau and Aβ42/Aβ40 ratio. We used R program (v-4.3.1) for statistical analysis.

Results: Cross-sectional associations are shown in table 1. Higher s100b levels were associated with higher cTREM2 levels independently of AD core biomarkers in participants with Aβ42/Aβ40 ratio < median, and in participants with *p*-tau levels >median. Higher

cTREM2 levels were also independently associated with higher alpha-synuclein levels in the T+ group, with a trend for an association in A+ participants. Higher baseline s100b levels independently predicted a larger longitudinal increase of cTREM2 (beta = 0.28, *p*-value = 0.03). Baseline cTREM2 levels were not associated with any synaptic biomarker longitudinally.

	Total sample n=[illegible]		< Aβ42/Aβ40 median n=119		> Aβ42/Aβ40 median n=120		Positive Aβ42/Aβ40 n=[illegible]		Negative Aβ42/Aβ40 n=[illegible]		< P-tau median n=119		> P-tau median n=120		Negative P-tau n=214		Positive P-tau n=25	
	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
Neurogranin																		
Model 1	0.37	[illegible]	0.38	[illegible]	0.35	[illegible]	0.40	[illegible]	0.39	[illegible]	0.25	[illegible]	0.27	[illegible]	0.39	[illegible]	0.69	[illegible]
Model 2	-0.04	[illegible]	0.13	[illegible]	-0.37	[illegible]	-0.05	[illegible]	-0.05	[illegible]	-0.04	[illegible]	-0.06	[illegible]	0.07	[illegible]	0.32	[illegible]
Alpha-synuclein																		
Model 1	0.38	2.01e-12	0.365	[illegible]	0.39	[illegible]	0.48	[illegible]	0.37	[illegible]	0.30	[illegible]	0.29	[illegible]	0.37	[illegible]	0.79	[illegible]
Model 2	0.16	[illegible]	0.15	0.25	0.20	[illegible]	0.37	[illegible]	0.12	[illegible]	0.11	[illegible]	0.19	[illegible]	0.11	[illegible]	0.83	[illegible]
S100b																		
Model 1	[illegible]	[illegible]	0.41	[illegible]	0.15	[illegible]	0.29	[illegible]	0.28	[illegible]	0.11	[illegible]	0.32	[illegible]	0.22	[illegible]	0.74	[illegible]
Model 2	0.16	0.06	0.26	[illegible]	0.06	[illegible]	0.23	[illegible]	0.15	[illegible]	0.05	[illegible]	0.28	[illegible]	0.10	[illegible]	0.70	[illegible]

Model 1 adjusted by age and sex. Model 2 adjusted by age, sex, Aβ42 and PTAU.
Aβ42/Aβ40 median = [illegible]. The cut-off for amyloid (A) positivity according to the Aβ42/Aβ40 ratio is < [illegible].
P-tau median = [illegible] pg/mL. The cut-off for tau (T) positivity according to P-tau is > 24.8 pg/mL.

TABLE 1 Beta-coefficients and *p*-values for cross-sectional associations between synaptic biomarkers and cleaved TREM2 (cTREM2) in linear regression models.

Conclusion: cTREM2 is associated with s100b and alpha-synuclein in asymptomatic participants with a biomarker profile suggestive of first stages of Aβ-aggregation and tau pathology. Higher baseline levels of s100b predicts a larger longitudinal increase of cTREM2 in asymptomatic volunteers. Our findings suggest an early influence of synaptic dysfunction on the TREM2-dependent microglial response in neurodegenerative processes.

Disclosure: Nothing to disclose.

EPO-620 | Association of *Helicobacter pylori* infection and Alzheimer's disease risk – A meta-analysis of case-control studies

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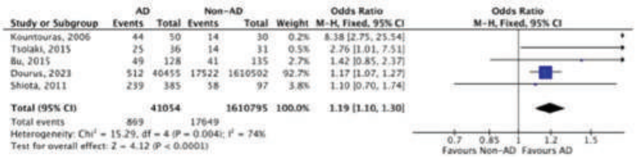
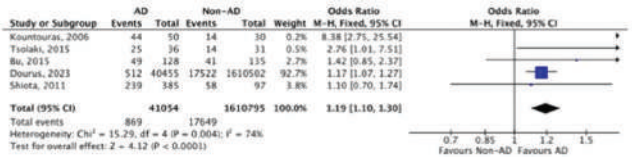
Background and Aims: Alzheimer's disease (AD) remains a challenge in public health due to the aging of the global population. The potential link between bacterial infections, specifically by Helicobacter pylori (HP), and the pathogenesis of AD is still unclear. Hence, we sought to explore the association between HP infection and AD.

Methods: MEDLINE, Embase, and Cochrane databases were systematically searched. Data were examined using the Mantel-Haenszel method, with Odds Ratio (OR) as the primary measure of association and 95% confidence intervals (CI). Heterogeneity was assessed using I^2 statistics. Statistical analysis were performed using Review Manager software, version 5.4.1.

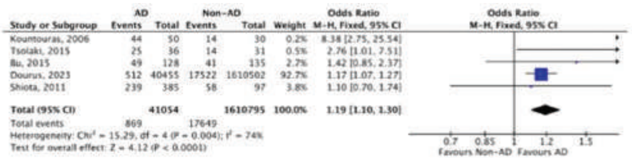
Results: A total of 1,651,849 patients from 5 population-based case-control studies were included in this analysis. Within these patients, 41.054 composed the case group of patients previously diagnosed with AD. In the AD group, 869 individuals were found to be positive for HP infection, meanwhile, in the non-AD group, this number was 17,649 individuals. Comparing the incidence of HP infection between both groups, statistically significant correlation was observed between AD and HP infection (2.11% vs 1.09%, OR. 1.19, 95% CI 1.10–1.30, $p < 0.01$, $I^2 = 74\%$).



Odds Ratio – Forest Plot.



Odds Ratio – Forest Plot.



Odds Ratio – Forest Plot.

Conclusion: In this meta-analysis, consistent results suggest that HP infection is associated with an increased odds for AD.

Disclosure: All authors declare no conflicts of interest and assume responsibility for data reliability and freedom from bias in presentation and interpretation.

EPO-621 | Combining a semantic cued recall paradigm with blood-based biomarkers in the detection of Alzheimer's disease pathology

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Background and Aims: Episodic memory impairment defined by the Free and Cued Selective Reminding test (FCSRT) is a reliable marker

of the early involvement of medial temporal structures in AD. Blood-based biomarkers (BBM) (*p*-tau181, NfL and GFAP) were developed for the diagnosis and prognosis of AD. We aim to study the association between FCSRT and BBM in detecting prodromal AD.

Methods: We included 70 non-demented individuals (66 years of median age, 67% female) with memory complaints and available cerebrospinal fluid (CSF)-AD biomarkers. Baseline and longitudinal neuropsychological evaluation were performed. Median follow-up duration was 8 months. BBM were determined using Single Molecule Array (SiMoA). Amyloid pathology was determined by amyloid status (A) using CSF Abeta42/40 ratio.

Results: In the comparison between A+ ($n=28$) and A- individuals ($n=42$), we observed significant differences in all the FCSRT-selected measures ($p<0.05$), except for FCSRT cued-delayed recall. Longitudinally, significant differences in the change of normative *z*-scores for MoCA and MPCR were shown ($p<0.001$). A+ individuals had significantly higher levels of serum GFAP and plasma *p*-Tau181. Additionally, multinomial logistic regression model, adjusted for age, identified blood *p*-Tau181 (B = 1.8, $p=0.002$), GFAP (B = 0.02, $p=0.008$) and NfL (B = −0.2, $p=0.01$) as independent significant predictors of amyloid status, particularly in relation to FCSRT free-delayed recall (B = −0.4, $p=0.006$).

Conclusion: This study shows the utility of a semantic and cued recall paradigm (FCSRT) for detecting AD at its prodromal stage, supporting its use as a valid clinic marker together with BBM. These results can now be used to develop individual predictive models of disease progression.

Disclosure: Nothing to disclose.

EPO-622 | Association between frailty and neurophysiological measures of peripheral nerve conduction

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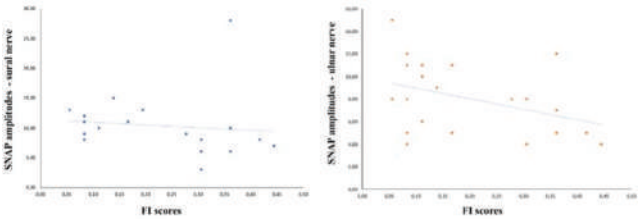
Background and Aims: Frailty is a marker of biological age and has been associated with a higher risk of adverse neurological outcomes. The present study aimed at investigating the association between frailty and neurophysiological measures of nerve conduction.

Methods: Patients with no peripheral nervous system disorders were subjected to a nerve conduction study at the Department of Human Neuroscience, Sapienza University of Rome. Frailty was assessed through a Frailty Index (FI), designed on the model of deficit accumulation and constituted by 36 items including symptoms, signs, disabilities, and laboratory findings. Spearman's correlations were used to conduct the statistical analysis.

Results: Overall, 25 participants (mean age 59.9, standard deviation [SD] 16.1; 64.7 % women) were recruited. SNAP amplitudes were significantly, inversely correlated with age (ulnar: rho = −0.48, $p=0.03$; sural: rho = −0.73, $p<0.001$). A negative correlation was also observed between SNAP amplitudes and FI scores (ulnar: rho = −0.09, $p=0.03$; sural: rho = −0.73, $p=0.06$). In partial correlations adjusted by FI, age was no longer correlated with the SNAP amplitude of the ulnar nerve (rho = −0.35, $p=0.18$); the correlation coefficient between age and the SNAP amplitude of the sural nerve decreased to −0.54, $p=0.03$.



Correlation between SNAP amplitude and sural and ulnar nerve.

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Conclusion: The negative correlation between increasing age and measures of SNAP amplitudes seems to be partly moderated by frailty. The FI may be useful to explore the impact of the ageing process on peripheral nerve conduction, beyond chronological age.

Disclosure: Nothing to disclose.

EPO-623 | Quantitative T1-mapping changes in the gray matter of patients with Alzheimer's disease

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Background and Aims: Structural MRI plays an important role in the diagnosis of Alzheimer's disease (AD) so that it is included in the A/T/N classification. However, structural changes occur late in the course of the disease and lack of a specific correlation with the underlying pathogenetic process. The purpose of our study is to analyze the role of brain quantitative T1-mapping as a possible index of AD pathology.

Methods: 27 AD patients and 22 healthy controls underwent an MR scan on a clinical 3T MR scanner with a protocol including an MP2RAGE sequence whose output include a set of 3D structural T1-weighted images and a coupled quantitative T1 map. 3D T1 images were then segmented using FreeSurfer obtaining segmentation masks of the brain that were used to extract regional quantitative T1 (qT1) values of the subjects' gray matter.

Results: Statistical analysis performed with a volume-corrected model (so corrected for regional atrophy) demonstrated a significant increase in qT1 values in regions known to be involved in AD. For example, hippocampi demonstrated significantly increased qT1 values ($p=0.0055$). Moreover, we found a significant difference in overall cortical values ($p=0.028$) primarily driven by parietal lobe ($p=0.0197$).

Conclusion: Our results demonstrate the presence of alterations in qT1 values in AD that do not seem to be justified by atrophy alone, suggesting in this way that other changes in the microscopic composition of the brain of these subjects can influence this MR-derived metric.

Disclosure: Nothing to disclose.

EPO-624 | Cerebral amyloid angiopathy in the basal ganglia and brainstem in routine autopsies

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Background and Aims: Previously, we confirmed that cerebellar CAA was observed in 29 cases (48.3%), and the severity of cerebellar CAA was relatively mild compared with 60 cases with CAA-positive occipital lobe. On the other hand, CAA are said a few in the basal ganglia and brainstem, but the frequency and severity of CAA in the basal ganglia and brainstem are obscure.

Methods: We selected 54 cases with CAA observed in the occipital lobe. Analyses were performed on the occipital lobe, cerebellum, basal ganglia, and brainstem. Brain sections were mainly immunostained with monoclonal amyloid β (Aβ) peptides 17–24 (4G8) and monoclonal anti-phosphorylated tau (AT8) antibodies.

Results: Of the 54 cases, CAA was observed in the basal ganglia and brainstem in 13 cases (24.1%). In the basal ganglia, CAA was rarely or slightly observed in the claustrum, putamen, and thalamus in 10 cases, with no evidence of CAA in the pallidum. In the putamen and thalamus, Aβ deposits were mainly located in the abdominal portions of the tunica media and adventitia of the vessels. In the brainstem, two cases showed rare CAA in the midbrain. In five cases, CAA was only rarely observed in the meningeal vessels of the brainstem.

Conclusion: These findings suggest that CAA initially develops in the leptomeningeal and cortical vessels of the neocortex, followed by the vessels of cerebellum, and then vessels of the putamen, thalamus, and brainstem.

Disclosure: Nothing to disclose.

EPO-625 | Performance and concordance of plasma versus CSF biomarkers of Alzheimer's disease: A single center Memory Clinic cohort

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Background and Aims: Cerebrospinal fluid (CSF) for Alzheimer's disease (AD) comes with several limitations, namely relative invasiveness, restricted access and high costs, hence the recent focus on plasma biomarkers. Previous studies identified a good accuracy of plasma phosphorylated-tau181 (plasma/*p*-tau181) and plasma amyloid ratio (plasma/amyR, Aβ42/Aβ40) to identify patients with biologically-defined AD. We addressed their use in clinical practice, verifying their performance accounting for possible confounders, such as renal function (serum creatinine) and blood-brain barrier permeability (Albumin Quotient), and concordance with CSF biomarkers.

Methods: We enrolled 99 patients with CSF and plasma AD biomarkers, measured using fully-automized CLEIA (Fujirebio LUMIPULSE® G1200). Patients were stratified into CSF/A+T+ ($n=45$, CSF Aβ42/Aβ40 < 0.06, CSF/*p*-tau181 > 55 pg/ml) or CSF/non-A+T+ ($n=54$). We evaluated accuracy, sensitivity and specificity of pathological plasma/*p*-tau181 (>2.01 pg/ml), plasma/amyR (<0.083) and these combined (plasma/A+T+) in differentiating CSF/A+T+ vs CSF/non-A+T+, as well as inter-test reliability (Cohen's K).

Results: Plasma/*p*-tau181 showed good sensitivity (82.22%), specificity (87.041%) and agreement with CSF/A+T+ status ($K=0.694$); plasma/amyR had lower sensitivity (57.78%), good specificity (81.48%) and modest agreement ($K=0.399$); plasma/A+T+ had the overall best sensitivity (94.44%), but low specificity (51.11%) and moderate agreement ($K=0.472$). The multivariate logistic regression highlighted that both pathological plasma/*p*-tau181 and plasma/amyR are strongly associated with CSF/A+T+ (respectively OR = 31 and OR = 6; $p<0.001$), additionally when adjusting plasma/*p*-tau181 for creatinine levels (OR = 32) and amyR for Albumin Quotient (OR = 7.7).

Conclusion: Our findings confirm plasma/*p*-tau181 as the most reliable stand-alone predictor of AD. Moreover, renal function and measures of blood-brain barrier permeability should be considered in order to improve the consistency of plasma biomarkers in clinical practice.

Disclosure: Nothing to disclose.

EPO-626 | Synthesis and evaluation of ketoamide derivatives in modulating amyloid beta aggregation for Alzheimer's disease therapy

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Background and Aims: The prevalence of Alzheimer's disease (AD), a multifactorial disorder, is on the rise, and the absence of effective therapies necessitates the discovery of novel treatment options. Previous attempts at target-based therapeutics for AD have faced challenges, but recent successes in amyloid beta-targeted immunotherapies have inspired new approaches. Motivated by recent advancements, in this study, we aimed to design and develop amyloid beta aggregation inhibitors with an α-ketoamide scaffold. Specifically, we synthesized a series of piperazine and piperidine-substituted ketoamide derivatives and further evaluated them for their potential in modulating amyloid beta aggregation.
Methods: The piperazine and piperidine-substituted ketoamide derivatives were synthesised in high purity and high yield using an appropriate chemical methodology and structurally characterized using NMR spectroscopy and mass spectrometry. Further, the synthesized compounds were subjected to in vitro evaluation for their potential to modulate the aggregation of amyloid beta 42 (Aβ42) using ThT-based aggregation kinetic assays.
Results: The percentage purity for all the compounds was >95. Among all the synthesized compounds, three compounds demonstrated a significant delay in amyloid beta aggregation, as evidenced by the aggregation kinetics assay.
Conclusion: Our findings highlight the potential of the α-ketoamide derivatives as promising hit compounds for further development into lead candidate for modulating the Aβ42 aggregation activity which is relevant to Alzheimer's disease treatment.
Disclosure: The authors declare no conflict of interest.

EPO-627 | Survival analysis in patients with early-onset frontotemporal lobar degeneration

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Background and Aims: The survival rate of patients with early onset FTLD is still undefined. The aim of this study is to determine the survival rates of FTLD behavioral variant (FTLDbv) and primary progressive aphasia (FTLDppa), and to identify clinical and demographic factors that influence it.
Methods: We included 82 patients, 61 with FTLDbv and 21 FTLDppa, observed from 2012 to 2019. Kaplan-Meier curve and Cox proportional hazard models were used for survival analysis with time from diagnosis to outcome (death or 2019y.) as independent variable.
Results: The mean age at diagnosis in the FTLDbv group was 55.36 ± 7.34 y, with 55.7% males, and 58.3 ± 5.8 y in FTLDppa group, with 47.6% men. In total 53 patients died (32 FTLDbv, 21 FTLDppa). The median survival in the FTLDbv group was 7 y. Age, age at onset, time from symptoms to diagnosis, MMSE and FAB scores were estimated, none of which influenced survival in these patients. Only the presence of motor symptoms (oculomotor disorders, dysphagia) shortened the lifespan of these patients ($p = 0.002$, median survival 3.75 y in group with, and 8 y without motor symptoms). Median survival in the FTLDppa group is 4.5 y, and older age ($p = 0.03$, median survival 5.5 y for younger, and 4 y for older patients) as well as older age at onset ($p = 0.03$, median survival 5.5 y in group below 60, and 3.75 y in group beyond 60) influenced survival in these patients.
Conclusion: Presence of motor symptoms is a clear indicator of faster progression of FTLDbv patients, while older age at onset shortens lifespan of FTLDppa early onset patients.
Disclosure: Nothing to disclose.

EPO-628 | MRI-guided brain stimulation with TPS ameliorates cognitive deficits and depressive symptoms in Alzheimer's disease (AD)

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Background and Aims: No effective long-term treatment has been found for the treatment of AD so far. MRI-guided TPS (Transcranial Pulse Stimulation) offers new perspectives to ameliorate AD-deficits. Pilot studies show beneficial effects on learning and memory of TPS.
Methods: 21 out-patients with AD (with light to moderate symptoms) received MRI-guided 6.000 pulses of TPS (0.2 mJ/mm^2 per single pulse, with a frequency of 4 Hz) per session bilaterally into the frontal, parietal and temporal cortex with Neurolith by Storz Medical. TPS-pulses were administered. Pulses were applicated over a period of 2 weeks (3 sessions per week). Cognitive capabilities (especially executive functions) of the patients were tested using the Stroop-Test (colour-word-interference-test) and the CERAD. Patients were tested using a pre – post design (t0 pre stimulation: t1 after 6 sessions, two weeks later).
Results: TPS-stimulation over a period of two weeks (6 sessions) showed ameliorating effects on performance in the Stroop-Test (pre vs. post; $p < 0.05$ – paired *T*-test). Single patients showed extraordinary improvements by shortening completer times in the Stroop-Test by half. Depressive symptoms of the patients were also

ameliorated. The BDI measured before and after the treatment diminished form 18.1 to 12.4 in the mean. No significant side-effects occurred during all the sessions in none of the patients.

Conclusion: The results of this pilot-trial show that cognitive impairments of executive functions and depressive symptoms in Alzheimer's disease may be ameliorated using TPS as a noninvasive brain stimulation method. No severe side-effects were observed.

Disclosure: The authors have no conflicts of interests to disclose.

EPO-629 | Disentangling empathy impairment along Alzheimer's disease continuum

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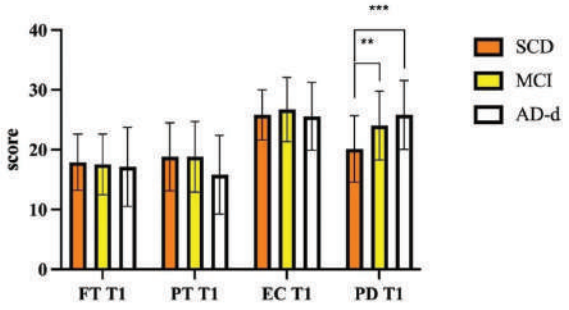
Background and Aims: Little is known about empathy changes from the early stages of Alzheimer's Disease (AD). The aim of this study is to investigate empathy from Subjective Cognitive Decline (SCD) to Mild Cognitive Impairment (MCI) and AD dementia (AD-d).

Methods: Forty-five SCD, 83 MCI and 80 AD-d patients were included. Empathy was assessed by Interpersonal Reactivity Index (IRI) rated by caregivers before (T0) and after (T1) cognitive symptoms' onset. IRI was also self-administered to SCD patients. Facial emotion recognition was assessed by Ekman-60 Faces Test. Patients underwent CSF biomarkers analysis and cerebral FDG-PET SPM analysis.

Results: PD scores significantly increased from T0 to T1 in SCD, MCI and AD-d ($p<0.001$), while PT scores decreased in MCI and in AD-d ($p<0.001$). SCD AP+ showed a greater increase in PD scores over time (ΔPD T0-T1) than SCD AP- ($p<0.001$). SCD self-reported PT scores were lower than those of general Italian population (14.94±3.94, 95% C.I. [13.68–16.20] vs 17.70±4.36, 95% C.I. [17.30–18.10]). In AD continuum (SCD AP+, MCI AP+, AD-d), a positive correlation was detected between PT-T1 and brain metabolism in left posterior cingulate gyrus, precuneus and right frontal gyri; a negative correlation was found between ΔPT and brain metabolism in bilateral posterior cingulate gyri.

	SCD n = 45	MCI n = 83	AD-d n = 80
Sex (F/M)	36/9*	50/33	44/36*
Age at onset (years)	55.73±9.46^{ac}	64.13±9.67^{c}	66.26±6.56†
Age at empathy evaluation (years)	64.94±8.40^{ab}	71.36±8.29^{a}	70.95±7.01^{a}
Disease duration (years)	8.13±7.32‡§	6.27±3.64‡	4.01±1.76§
Family history of AD	34/43 (79.06%)	41/74 (55.40%)	37/68 (54.41%)
Years of education	13.56±3.12	11.56±4.48	11.53±4.63
MMSE	28.93±1.33§	26.74±2.36§	19.29±5.84§§
APOE ε4+	8/32 (25%)	19/55 (34.54%)	29/60 (48.33%)

Values are reported as mean and standard deviation or frequencies or percentages for continuous variables and categorical variables respectively. Statistically significantly different values among groups are reported as underlined character. M: males; F: females; MMSE: Mini Mental State Examination. * $\chi^2=7.81$, $p=0.006$; ^{a} $p<0.001$; ^{c} $p<0.001$; § $p<0.001$; §§ $p<0.001$; ‡ $p=0.001$; † $p<0.001$; § $p<0.001$; §§ $p<0.001$. Statistical significance after Bonferroni correction $p=0.0062$.



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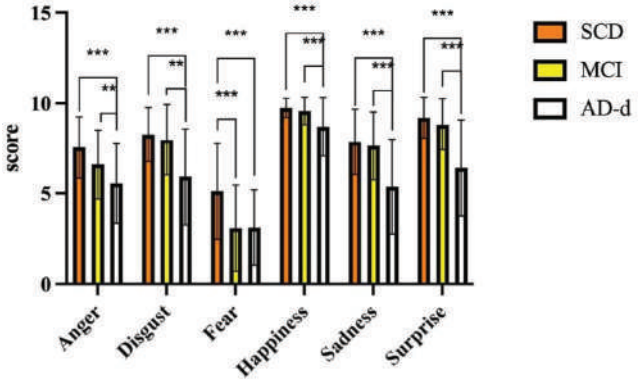

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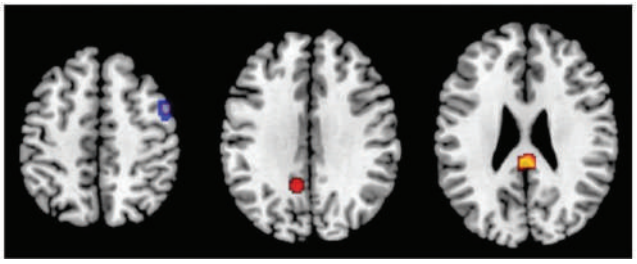

SPM analysis.

Conclusion: PT may be subtly involved since the preclinical phase of AD. Changes over time of PD are influenced by the underlying

Alzheimer's pathology and could potentially serve as an early AD neuropsychological marker.
Disclosure: Nothing to disclose.

EPO-630 | Brexpiprazole for agitation in Alzheimer's disease: A systematic review and meta-analysis of randomized controlled trials

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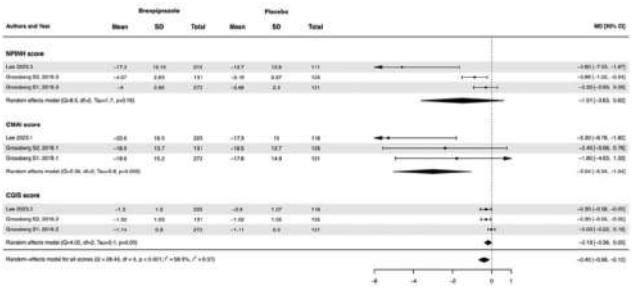
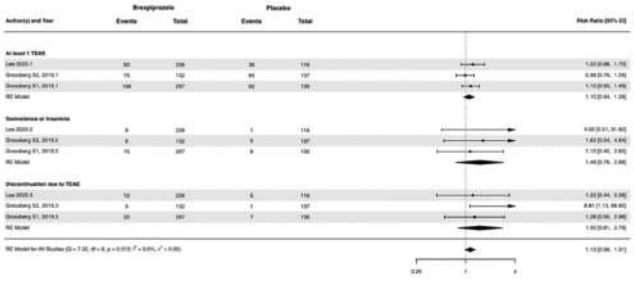
Background and Aims: Agitation in Alzheimer's disease (AD) requires effective and well-tolerated interventions. Recently, Brexpiprazole has emerged as a promising therapeutic avenue.
Methods: We systematically searched ClinicalTrials.gov, PubMed, Embase, and Cochrane Library for randomized controlled trials (RCT) comparing Brexpiprazole to placebo in patients with AD presenting with agitation. A random-effects model was employed to compute mean differences and risk ratios using R software 4.3.1. The results were reported following the PRISMA guideline.
Results: A total of 3 double-blind RCTs were included, comprising 1,028 patients with an average age of 74 years. Throughout a 12-week mean follow-up period, Brexpiprazole was associated with no changes in Clinical Global Impression-Severity of illness (MD −0.19; 95% CI −0.38 to 0.00; $p=0.05$) and Neuropsychiatric Inventory-Nursing Home scores (MD −1.51; 95% CI −3.63 to 0.62; $p=0.16$). However, there was a notable improvement in Cohen-Mansfield Agitation Inventory score (MD −3.04; 95% CI −5.04 to −1.04; $p<0.01$). Additionally, no difference was observed for the incidence of at least 1 treatment-emergent adverse events (TEAE) (RR 1.10; 95% CI 0.94 to 1.28; $p=0.52$), discontinuation due to TEAE (RR 1.50; 95% CI 0.81 to 2.78; $p=0.20$), dizziness (RR 1.04; 95% CI 0.52 to 2.11; $p=0.86$), extrapyramidal disorders (RR 2.60; 95% CI 0.44 to 15.40; $p=0.99$), and all-cause death (RR 1.51; 95% CI 0.25 to 8.94; $p=0.48$)



Change in the Agitation Scores.



Adverse Events.

Conclusion: In this systematic review and meta-analysis of 3 RCTs and 1,028 patients, Brexpiprazole was associated with a modestly favorable modulation in agitation score, concurrent with a positive safety profile.
Disclosure: Nothing to disclose.

Child neurology/developmental neurology

EPO-631 | Neuroplasticity in children post-war trauma: A critical review of prefrontal, amygdaloid, and hippocampal alterations

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Background and Aims: This literature review endeavors to amalgamate current understanding of the impact of war trauma on neuroplasticity in children, with a specific focus on the prefrontal cortex, amygdala, and hippocampus. It examines the intricate interplay between these brain regions and their role in the cognitive, emotional, and behavioral development of traumatized children, elucidating how trauma-induced alterations in these areas contribute to various psychological disorders.
Methods: A comprehensive analysis of peer-reviewed journals was conducted, emphasizing neuroimaging studies (MRI and fMRI) that reveal changes in brain volume, activity levels, and functional connectivity in the prefrontal cortex, amygdala, and hippocampus. Attention was given to studies showcasing the effects of trauma on the developmental trajectory of these brain regions, including both adaptive and maladaptive neuroplasticity.
Results: The review delineates significant neuroplastic changes in the prefrontal cortex, amygdala, and hippocampus of children exposed to war trauma. It highlights a reduction in prefrontal cortex volume, associated with impaired decision-making and emotion regulation; amygdala hyperactivation, linked to increased anxiety and stress responses; and hippocampal volume reduction, correlated with memory impairments and altered stress regulation. Additionally, it discusses variations in neuroplastic responses based on the age at which trauma was experienced.
Conclusion: This review integrates diverse findings to provide a nuanced understanding of the neuroplastic changes in children

following war trauma, underscoring the critical need for specialized therapeutic interventions. These insights are pivotal for developing strategies to mitigate the long-term psychological and neurobiological impacts of such trauma, with a view towards fostering resilience and recovery in affected children.

Disclosure: Nothing to disclose.

EPO-632 | Clinical, humanistic, and economic burden of Rett syndrome: A systematic review

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Background and Aims: Rett syndrome is a rare neurodevelopmental disorder characterized by severe functional impairment. A systematic literature review was conducted to examine the clinical, humanistic, and economic burden associated with Rett syndrome and its treatment.

Methods: Literature from relevant databases (through June 2023), recent congress proceedings, and clinical trial registries was reviewed. References were independently screened by two authors. Predefined outcomes from highly relevant publications were extracted and validated.

Results: Data were extracted from publications reporting on clinical ($n = 40$), humanistic ($n = 32$), and cost/healthcare resource use ($n = 11$) outcomes (Figure 1). Only 7 trials designed to assess treatment effect on clinical severity or other key components of Rett syndrome specified a primary endpoint (Table 1). Trofinetide led to significant improvement of the co-primary endpoints. Dextromethorphan polistirex led to a significant improvement in some clinical outcomes though the primary endpoint was not met. Mixed findings, including life-threatening safety concerns, were reported with glatiramer acetate. Mecasermin was associated with symptom worsening. Across humanistic outcomes, physical functioning and physical component quality of life scores were generally low while caregiver burden was high. Direct costs and healthcare resource utilization were high in the few studies reporting these outcomes.

Conclusion: Rett syndrome is associated with significant challenges including limited functional abilities for those affected, substantial cost, and caregiver burden. Several potential treatments have been studied but only trofinetide has been evaluated in a phase 3 trial and been approved in the US. Future research should consider the impact of this approval on the burden associated with Rett syndrome.

Disclosure: DM is employed by Acadia Pharmaceuticals Inc. MG, MA, and SC are employed by Cencora which received funds from Acadia Pharmaceuticals to support this research.

Table 1. Key results from studies designed to assess treatment effect on clinical severity or other key components of Rett syndrome with a specified a primary endpoint

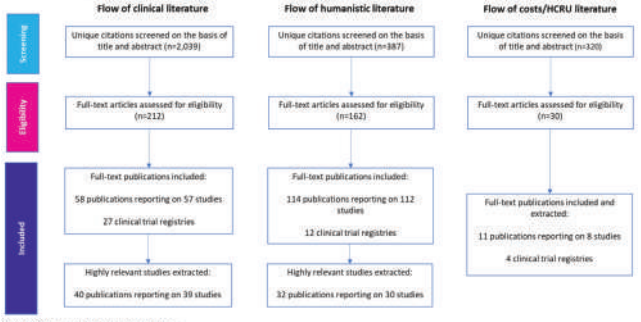
Intervention vs comparator	Trial phase	N	Primary outcome	Primary results reported by authors	Key clinical findings[a]
Trofinetide vs placebo	Phase II	82	Safety and PK	No significance testing reported; "All dose levels were well tolerated and generally safe"	Significantly improved Rett-specific global function and general global function
Trofinetide vs placebo	Phase III	187	Co-primary endpoints: RSBQ total score (change from baseline to week 12) and CGI-I score at week 12	Significant improvement for both co-primary endpoints	Significantly improved Rett-specific global function, general global function, and cognition/communication/psychosocial outcomes
Mecasermin vs placebo	Phase II	30	ADAMS Social Avoidance subscale, RSBQ Fear/Anxiety subscale, PTSVAS top three concerns, CGI-EI, PGI-EI, and the Kerr (overall) severity scale	The Kerr severity scale, ADAMS Depressed Mood subscale, Visual Analog Scale Hyperventilation, and delta average power change scores significantly increased, implying worsening of symptoms	Significantly worse Rett-specific global function and cognition/communication/psychosocial outcomes
Glatiramer acetate vs baseline	Phase II	10	Gait velocity	Gait velocity improved significantly from baseline.	Significantly improved ADLs and cognition/communication/psychosocial outcomes
Glatiramer acetate (no comparator)	Phase II	14	Safety and tolerability of the treatment as well as decrease in epileptiform activity as recorded in a 24-hour electroencephalograph	Terminated due to life-threatening safety concerns; prespecified outcomes not assessed	
Fingolimod vs baseline	Phase I/II	6	Efficacy: change in levels of BDNF in serum/CSF (cerebrospinal fluid) and change in deep gray matter volumes (thalamus, caudate, putamen, pallidum, hippocampus, amygdala and accumbens) measured by MRI. Safety: white blood cell/lymphocyte counts, liver enzymes, and occurrence of any (serious) adverse events	Primary outcome measures were not met	No significant changes
Dextromethorphan polistirex vs baseline	Phase II	38	Spike activity	There was no difference in the distribution of spike counts across doses for either visit 1 or 2 and no significant changes in spike count between the 2 visits for each dose	Significantly improved cognition/communication/psychosocial outcomes

Key: ADAMS – Anxiety, Depression, and Mood Scale; ADLs – activities of daily living; BDNF – brain-derived neurotrophic factor; CGI-EI – Clinical Global Impressions – Efficacy Index; CGI-I – Clinical Global Impressions – Improvement; CSF – cerebrospinal fluid; MRI – magnetic resonance imaging; N – sample size; PGI-EI – Parent Global Impression – Efficacy Index; PK – pharmacokinetics; PTSVAS – Parent Targeted Symptoms Visual Analog Scale; RSBQ – Rett Syndrome Behavior Questionnaire

[a] Key clinical findings summarizes primary outcomes as well as other clinical outcomes including Rett-specific function, general global function, activities of daily living, and cognition/communication/psychosocial outcomes

Blue – Significant benefit for intervention assessed compared to control/placebo or baseline; Grey – No significant differences for treatment compared to control/placebo or baseline; Red – Significantly worse results for the intervention assessed compared to control/placebo or baseline; No shading – Significance not assessed.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow of literature diagrams for clinical, humanistic, and costs/HCRU outcomes.



Key: HCRU – healthcare resource use.

All publications meeting the population, interventions, comparators, outcomes, study design (PICOS) criteria were included. Data extraction was completed for highly relevant studies defined as clinical studies evaluating treatment effect as the primary objective and humanistic studies reporting utility values, lost work productivity due to caregiving, or validated QoL measures.

EPO-633 | Parsonage-Turner disease due to SEPTIN9 mutation: First report of an Italian family

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[1]*Neurology Unit, E.O. Ospedali Galliera, Genoa, Italy;* [2]*Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health Department of Neuroscience (DINOGMI), University of Genoa, Italy;* [3]*Child Neuropsychiatry Unit, IRCCS G. Gaslini Institute, Genoa, Italy;* [4]*Neurology Clinic, IRCCS, Ospedale Policlinico San Martino, Genova, Italy;* [5]*Central Laboratory of Analysis, IRCCS G. Gaslini Institute, Genoa, Italy;* [6]*UOC Medical Genetic, IRCCS G. Gaslini Institute, Genoa, Italy*

Background and Aims: Parsonage Turner disease is a neuralgic amyotrophy (NA) of the brachial plexus including idiopathic and rare hereditary forms (HNA). SEPTIN9-associated mutations have been involved. We report a HNA Italian family carrying a missense variant and reviewed related literature.

Methods: We provide clinical, electrophysiologic and genetic data of an 8-year-old girl with an HNA heterozygous pathogenic variant of SEPTIN9-gene and her affected father. A PubMed search was performed for cases of neurological diseases associated with SEPTIN9-mutations.

Results: A 6 years Italian girl with normal development came to our institute for pain in both shoulders with scapular girdle asymmetric hypotrophy, hyposthenia and hypotonia and dysmorphic features (hypotelorism, neck skin folds). No abnormalities were detected on NCS (nerve-conduction-study). After two years no more episodes of limbs pain were reported. NCS/EMG were repeated showing only chronic denervation signs. A closer look at the family history revealed that the child's father suffered from two episodes of transient upper-limbs pain/weakness in the past. Genetic test showed a heterozygous SEPTIN9-gene variant (c.262C>T;p.Arg88Trp) inherited from her father. We reviewed 107 subjects (49M, 58F)

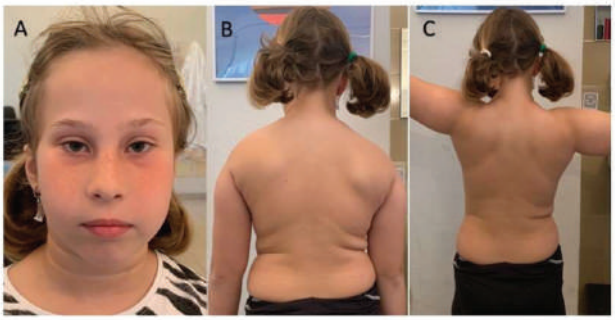

Figure 1: A: dysmorphic features, hypotelorism, shortened palpebral fissures, epicanthal fold , long nasal bridge and neck skin folds; B,C: neuromuscular clinical finding, winged scapula, sloped shoulder and reduction of muscle strength in the right upper girdle.

Dysmorphic features.

General Data		
	Mean	Range
Age disease onset (years)	13	8 - 40
Age disease diagnosis (years)	35	03 - 2,5
Male	49	
Female	60	
HNA diagnosis	107/109	
CMT diagnosis	2/107	
Clinical Data		
Monophasic disease course	3/22	
Relapsing-remitting disease course	19/22	
Progressive disease course	1/22 (included CMT)	
Acute motor signs (upper limbs)	24/31	
Acute pain (upper limbs)	18/31	
Acute sensitive sings (upper limbs)	12/31	
vocal cords involvement	7/31	
Lower limbs involvement	1/31 (included CMT)	
Residual neurological sign	13/20	
NCS/EMG		
Axonal and demyelinating neuropathy	7/14	
Denervation	1/14	
Axonal neuropathy	1/14	
Brachial plexopathy (unclear whether diagnosed by NCS or EMG)	1/14	

Table 1: General, clinical and neurophysiological findings of the 109 SEPTIN9 patients included in our literature review.

with SEPTIN9-mutations (Three missense mutations and several SEPTIN9-gene duplications); symptoms onset 13 years, time onset-diagnosis 22 years. Typical NA features were founded.

Dysmorphic Features	
	N. of Subjects
Hypotelorism	32
Skin folds of the neck or arms	11
Short stature	10
Microstomia	7
Epicanthal folds	5
Small and shaped ears	3
Cleft palate	2
Nasal cysts	2
Blepharophimosis	2
Thin, downward sloping eyebrows	2
Ptosis	2
Low-positioned ears	2
Micrognathia	1
Finger furrows	1
Cleft uvula	1
Narrow face	1
Pectus excavatum	1
SEPTIN9 finding	
c.262C>T (p.Arg88Trp)	68/109
Gene Duplications	29/109
c.278 C>T (p.Ser93Phe)	1/109
c.-121G>C	2/109
c.140C>C (p.Val48Ala)	2/109 (CMT)

Table 2: Dysmorphic and genetic features of the SEPTIN9 cohort included in our review.

Conclusion: To the best of our knowledge, this is the first case of SEPTIN9-gene mutation associated with an HNA phenotype in an Italian family. The reported subjects' phenotypes don't appear related to the mutation type. Clinicians should consider HNA diagnosis in children with family history of upper-limbs neuralgia and dysmorphic features in order to improve long-term clinical outcome.

Disclosure: No disclosure.

EPO-634 | Sex-specific gut microbiome changes in a novel mouse model of autism

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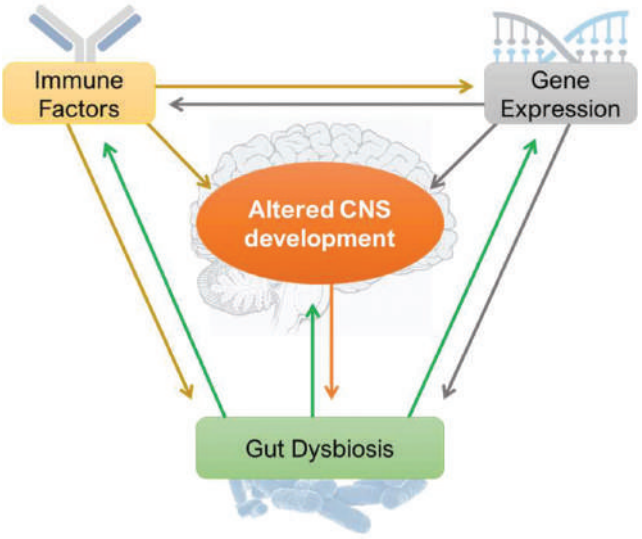
[1]Cell Signalling Laboratory, Department of Psychiatry, University of Saskatchewan, Saskatoon, Canada; [2]Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Canada

Background and Aims: A bidirectional relationship has been demonstrated between the gut microbiome and the central nervous system. Though this field of study is still nascent, the so-called 'Gut-Brain Axis' (GBA) has been implicated as a major factor in neurological and psychiatric disease. TgsAPPα mice, which carry the transgene for human soluble amyloid precursor protein alpha, exhibit behavioral, neurochemical, and immunological phenotypes analogous to Autism Spectrum Disorder (ASD).

Methods: To further investigate the relationship between ASD and the GBA, we profiled the gut microbiomes of 3-month old heterozygous TgsAPPα mice and age- and sex-matched wildtype littermates, using cpn60 barcode sequencing.

Results: Pooled male and female data revealed differences in the proportional abundances of Bacteroides coprophilus, Pseudoflavonifractor capillosus, Bacteroides caecimuris, and Akkermansia muciniphila between TgsAPPα and wildtype groups. Stratifying the data for sex revealed a decrease in the proportional abundance of Prevotella dentalis, Lachnoanaerobaculum umeaense, and Clostridium amygdalinum in TgsAPPα males (cf. wildtype males) and an increase in the abundance of Flavonifractor sp. in TgsAPPα females (cf. wildtype females). The proportional decrease of Akkermansia muciniphila observed was maintained in TgsAPPα mice, regardless of sex.



Role of the Gut-Brain-Axis in Autism Spectrum Disorder.

Conclusion: Our observations reinforce established links between Akkermansia muciniphila and ASD, and support the future use of TgsAPPα mice as a translational model for the development of microbiota-bases therapies for ASD.
Disclosure: Nothing to disclose.

EPO-635 | Rotational vertebral artery syndrome in a pediatric patient

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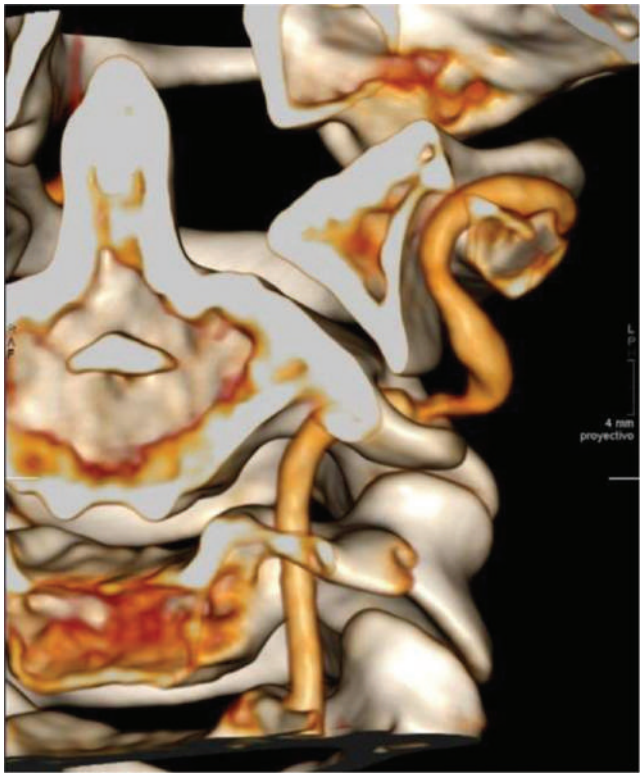
[1]*Neurology, Donostia University Hospital;* [2]*Radiology, Donostia University Hospital;* [3]*Pediatrics, Donostia University Hospital;* [4]*Neurosurgery, Donostia University Hospital*

Background and Aims: Rotational vertebral artery syndrome is an uncommon cause of vertebrobasilar stroke. Literature concerning pediatric patients is scarce.
Methods: We report a rare pediatric case of bow hunter's syndrome with illustrative neuroimaging findings.
Results: A 10-year-old patient, without relevant medical or family history, presented with cerebellar ataxia and nystagmus due to his third stroke since age 6. In previous episodes, etiologic studies were negative. Brain-MRI (image 1) showed multi-territory acute and chronic ischemic strokes. Brain-MRI showed an acute ischemic stroke in the cerebellum on Diffusion-WI (A), as well as contralateral lacunar chronic ischemic lesions on T2-WI (B). The previous episode presented as an acute right thalamic lesion with an intense restriction on Diffusion-WI (C) which initially misguided us towards metabolic and mitochondrial diseases. Cardiologic and hematologic tests were normal. His brain-CTA, brain-MRA, metabolic tests, vasculitis panel and exome for mitochondrial pathology were reported as normal. He underwent an angiography and CTA reconstruction (image 2). Angiography (A) revealed a basilar artery embolism, suggesting a proximal active embolic source, and a pseudo-aneurysmatic dilation of the vertebral artery. CTA reconstruction showed the left vertebral artery compressed by a protrusion of the inferior facet of the atlas (B), known as rotational vertebral artery syndrome or bow hunter's syndrome. Following excision, the patient has remained asymptomatic.



CTA reconstruction shows the left vertebral artery compressed by a protrusion of the inferior facet of the atlas.

Conclusion: Rotational vertebral artery syndrome must be ruled out in pediatric patients with vertebrobasilar strokes.
Disclosure: Nothing to disclose.

EPO-636 | Epidemiology of autism spectrum disorder in children in Kazakhstan: Data from UNEHS 2014–2021

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Background and Aims: We aimed to describe incidence and prevalence of Autism Spectrum Disorder (ASD) and examine factors associated with all-cause hospitalizations in children registered in the Unified National Electronic Healthcare System (UNEHS) in 2014–2021 in Kazakhstan.
Methods: Cohort comprised of patients less than 18 years old with ASD defined according to the International Classification of

Diseases, 10th revision (ICD-10) as codes: F84.0-F84.1, registered in the UNEHS from 2014 to 2021. Socio-demographic factors were analyzed using descriptive, bivariate and multivariable statistical analyses. ASD incidence and prevalence were calculated per 100,000 population. Cox proportional hazard regression analysis was performed to examine factors associated with all-cause hospitalizations. **Results:** Cohort consisted of 8,660 children with ASD, 6,834 (78.9%) were males and 6,384 (73.7%) were urban residents. The mean age at diagnosis was 6.0±2.2 years. The majority of hospitalizations were due to psychiatric/neuropsychiatric cause (73%). Number of hospitalized children with ASD increased from 305 to 1053 patients from 2014 to 2021. Median follow-up was 2.8 (1.2–4.9) years. Pediatric ASD incidence rate increased from 9.0 to 25.8 per 100 000 from 2014 to 2021. Period prevalence rate significantly raised from 6.7 to 130.2 per 100 000 from 2014 to 2021. Age specific ASD incidence was highest for 6–10 years age group. Younger age, having GI disorders, anemia, epilepsy, hydrocephalus and cerebral palsy are significantly associated with all-cause hospitalizations.

	ASD	Hospitalized	Non-Hospitalized	p-value
Socio-Demographics	**Total n=8,660**	**n=4,718 (54.5)**	**n=3,942 (45.5)**	
Age at diagnosis, mean±SD	6.0±2.2	6.2±2.4	5.8±1.9	<0.001
Age at the end of follow-up, mean±SD	9.2±3.3	9.0±3.3	9.4±3.2	<0.001
Age categories, n (%)				<0.001
0-5	4,204 (48.6)	2,154 (45.7)	2,050 (52)	
6-10	4,057 (46.8)	2,266 (48)	1,791 (45.4)	
11-17	399 (4.6)	298 (6.3)	101 (2.6)	
Gender, n (%)				0.665
Males	6,834 (78.9)	3,715 (78.7)	3,119 (79.1)	
Females	1,826 (21.1)	1,003 (21.3)	823 (20.9)	
Residency, n (%)				<0.001
Urban	6,384 (73.7)	3,755 (79.6)	2,629 (66.7)	
Rural	1,495 (17.3)	963 (20.4)	532 (13.5)	
Missing	781 (9.0)	0 (0)	781 (19.8)	
Median follow-up, years, IQR	2.8 (1.2-4.9)	2.7 (1.2-4.8)	2.9 (1.4-5.0)	<0.001
Comorbidities				
GI disorders	3,194 (36.9)	3,014 (63.9)	180 (4.6)	<0.001
Anemia	1,883 (21.7)	1,337 (28.3)	546 (13.9)	<0.001
Epilepsy	1,695 (19.6)	1,457 (30.9)	238 (6.0)	<0.001
Cerebral palsy	1,188 (13.7)	1,101 (23.3)	87 (2.2)	<0.001
Hydrocephalus	458 (5.3)	440 (9.3)	18 (0.5)	<0.001
Attention-deficit hyperactivity disorders (ADHD)	174 (2)	162 (3.4)	12 (0.3)	<0.001

ASD, autistic spectrum disorder; GI disorders, gastrointestinal disorders; ADHD, attention-deficit hyperactivity disorders;

TABLE 1 Socio-demographic characteristics of pediatric patients (0–17 years old) by hospitalizations registered in UNEHS with ASD between 2014–2021 in Kazakhstan.

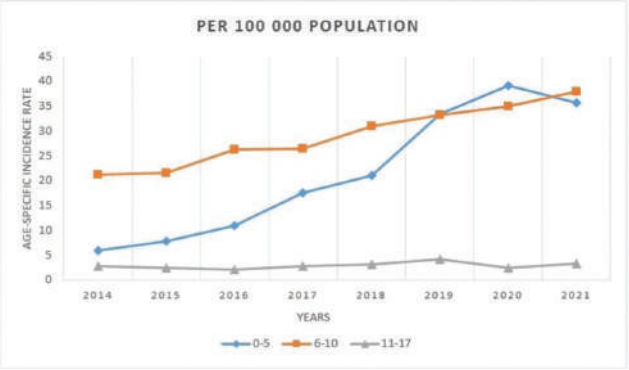

FIGURE 1 Age-specific incidence rate of pediatric ASD cohort in Kazakhstan for the period 2014–2021.

Variable	ASD			
	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Demographics				
Age groups				
0-5	1.14 [1.07; 1.21]	<0.001	1.13 [1.06; 1.2]	<0.001
6-10	Ref.		Ref.	Ref.
11-17	1.18 [1.05; 1.34]	0.006	0.97 [0.86; 1.1]	0.652
Gender				
Male	Ref.		Ref.	
Female	1.03 [0.96; 1.11]	0.347	1.0 [0.94; 1.09]	0.733
Residence				
Urban	Ref.		Ref.	
Rural	1 [0.94; 1.08]	0.870	0.96 [0.9; 1.03]	0.266
Comorbidities				
GI disorders				
No	Ref.		Ref.	
Yes	4.24 [3.99; 4.5]	<0.001	2.33 [2.18; 2.5]	<0.001
Anemia				
No	Ref.		Ref.	
Yes	2.13 [2.00; 2.28]	<0.001	1.33 [1.24; 1.42]	<0.001
Epilepsy				
No	Ref.		Ref.	
Yes	2.06 [1.93; 2.19]	<0.001	1.14 [1.06;1.22]	<0.001
Hydrocephalus				
No	Ref.		Ref.	
Yes	2.81 [2.55; 3.1]	<0.001	1.31 [1.18;1.45]	<0.001
Cerebral palsy				
No	Ref.		Ref.	
Yes	2.42 [2.26; 2.59]	<0.001	1.24 [1.16;1.34]	<0.001
ADHD				
No	Ref.		Ref.	
Yes	1.56 [1.33;1.82]	<0.001	0.97 [0.82;1.13]	0.703

ASD, autistic spectrum disorder; GI disorders, gastrointestinal disorders; ADHD, attention-deficit hyperactivity disorders; The model adjusted for demographics (age, gender, residence) and for comorbidities (GI disorders, anemia, epilepsy, hydrocephalus, cerebral palsy, ADHD);

TABLE 2 Cox PH regression analysis on predicting association between socio-demographic factors and all-cause hospitalization among pediatric ASD patients from 2014–2021.

Conclusion: The incidence and prevalence rates increased significantly during the study period. Younger age and comorbidities such as GI disorders, anemia, epilepsy, hydrocephalus and cerebral palsy are significantly associated with all-cause hospitalizations.

Disclosure: Nothing to disclose.

EPO-637 | Early but not delayed cannabinoid treatment augments hypothermic neuroprotection after neonatal asphyxia

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Background and Aims: Neonatal hypoxic-ischemic encephalopathy is one of the main causes of adverse neurological disabilities in newborns. Therapeutic hypothermia (TH) is the standard treatment used in clinics; unfortunately, it is not efficient in all cases. Promising new treatments are being investigated and cannabinoids have gained importance due to their neuroprotective properties. In a preclinical model of hypoxia-ischemia (HI), we aimed to establish the treatment window of the cannabinoid URB447 combined with TH.

Methods: On postnatal day 7, 101 Sprague Dawley rats were subjected to ischemia (left common carotid artery ligation) followed by hypoxia (120 min, 8%oxygen/92%nitrogen). The experiment included sham-operated controls ($n=10$). After HI, rats were cooled at 32.5–33°C for 3 h (TH-only; $n=32$). URB447 administration (i.p. 1 mg/kg) was before (URB447 + TH, $n=13$) or after (TH + URB447 $n=33$) the TH. The neuroprotective effect of the combined therapy was analyzed by histopathology.

Results: Animals that received URB447 before TH showed augmented hemispheric neuroprotection (95.08%) compared to TH-only (72.93%) and TH + URB447 (50.93%). This was further confirmed in the hippocampus, with percentage values of 98.54%, 45.49% and 40.29%, respectively. The tissue loss was also reduced when administering the compound before TH: URB447 + TH animals showed 9.51% of tissue loss, significantly lower ($p<0.05$) than those for TH-only (27.56%) and TH + URB447 (29.70%).

Conclusion: These results suggest that the administration of the cannabinoid URB447 before TH, but not after cooling, exerts adjuvant neuroprotective effects in a rat model of neonatal hypoxia-ischemia.

Disclosure: Acknowledgments: Grant MINECOR20/P66 funded by MCIN/AEI/10.13039/501100011033 and by "ERDF A way of making Europe", UPV/EHU predoctoral grant (PIFBUR22/03).

EPO-638 | URB447 reduces white matter demyelination and cerebral asymmetry and improves motor function after hypoxia-ischemia

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Background and Aims: Perinatal hypoxia-ischemia may cause white matter injury, leading to newborn morbidities. Although therapeutic hypothermia (TH) is efficient, a substantial number of babies suffer from behavioral impairments. Here, we wanted to assess white matter demyelination and long-term outcomes after the administration of the CB1-antagonist/CB2-agonist drug URB447 combined with TH in a model of neonatal asphyxia.

Methods: 117 Sprague Dawley rats were subjected to hypoxia-ischemia (HI) by left common carotid artery electrocoagulation + 2 h at 8%oxygen/92%nitrogen on postnatal day 7 (P7). TH-treated rats were maintained at 32.5–33°C for 3 h. URB447 was administered immediately after HI. Resulting groups were: Sham ($n=18$), HI ($n=34$), HI+TH ($n=44$) and HI+URB447+TH ($n=21$). White matter was assessed at P14 by immunohistochemistry for myelin basic protein (MBP) and motor impairments evaluated at P40-P42 and P90.

Results: HI+URB447+TH obtained the best results on protecting white matter, with higher MBP ratios (1.01; $p<0.05$) than HI (0.34) and HI+TH-only (0.69), and similar to Sham (1.00). The cylinder test revealed no signs of hemiparesis or cerebral asymmetry in the combined therapy group (−5.57%; $p<0.05$), unlike HI (43.37%) or HI+TH-only (43.17%). Motor coordination was also better in the combined therapy group: Sham (190.5), HI (120.3), HI+TH-only (111.8) and URB447+TH (171.3).

Conclusion: CB1-antagonist/CB2-agonist drug URB447 enhanced hypothermia by ameliorating both white matter injury and long-term motor function in a preclinical model of neonatal encephalopathy.

Disclosure: Acknowledgments: Grant MINECOR20/P66 funded by MCIN/AEI/10.13039/501100011033 and by "ERDF A way of making Europe", UPV/EHU predoctoral grant (PIFBUR22/03).

EPO-639 | Motor ability and neural correlates in children with aromatic L-amino acid decarboxylase deficit

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Background and Aims: Aromatic L-amino acid decarboxylase deficit (AADCD) is a rare, autosomal recessive neurometabolic disorder resulting in impaired or delayed motor development. Traditional motor assessment tools were unsuitable for AADCD children due to variable motor ability among individuals. Cortical neural activity and connectivity are associated with the maturation of the motor system in typically developed children. This study aims to use EEG to explore the relationship between motor ability and cortical neural activity in children with AADCD.

Methods: Children with definitive diagnosis of AADC deficiency and were older than 24 months were recruited. Cortical activity (32-channel EEG system, ANT Neuro, Netherlands) was collected during the resting and the execution of arm reaches. The arm reach

performance was graded by the Grasping and Reaching Assessment of Brisbane (GRAB). The EEG data were divided into motor preparation and execution segments. Power spectral densities of the C3, Cz, and C4 channels were calculated in the alpha and beta frequency range. The Spearman correlation test measured the correlation between reaching abilities and power spectral density. The significant level is established at $p < 0.05$.

Results: Eight individuals who underwent gene therapy were enrolled; one participant demonstrated a GRAB score of 1, while the remaining participants all scored GRAB 3. Our preliminary results showed that AADC individuals with lower GRAB scores exhibited lower alpha power spectrum density in the resting phase.

Conclusion: Our findings provide a preliminary observation of the relationship between cortical neural activities and motor ability in AADCD children.

Disclosure: Nothing to disclose.

EPO-640 | Understanding lived experiences with KCNQ2-development and epileptic encephalopathy (KCNQ2-DEE) – Parent interviews

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Background and Aims: While quantitative descriptions of KCNQ2-DEE have been provided from in-depth survey data, limited qualitative interview-based data exists describing the patient-caregiver experiences with KCNQ2-DEE and the burden of disease. We performed this study to develop KCNQ2-DEE conceptual models to illustrate the disease- and quality of life (QoL)-related experiences and identify its most burdensome aspects.

Methods: One-on-one interviews were conducted with US-based parental caregivers of children (1–18 years-old, September through November 2023) with mild, severe, and profound KCNQ2-DEE phenotypes. Parents were recruited via a patient advocacy group (KCNQ2 Cures Alliance). Semi-structured interviews were audio recorded, transcribed, coded and analysed by ATLS.TI, following established qualitative research methods. Concept saturation was assessed, and 4 models were derived – one for each phenotype severity level and one overall model. The most burdensome disease aspects were discussed (rated on a 0–10 scale).

Results: Based on interviews with 53 parents, the most common concepts reported were communication difficulties, gross and fine motor problems, and chewing/eating difficulties; each worsening with increasing phenotype severity and with age. Communication challenges was the most burdensome symptom (mean = 8.6/10, $n = 47$, 87% participants). Epileptic seizures were a key concern in infancy, but once adequately controlled were rated as one of the least burdensome symptoms post-infancy (mean = 5.0/10, $n = 23$, 43% participants).

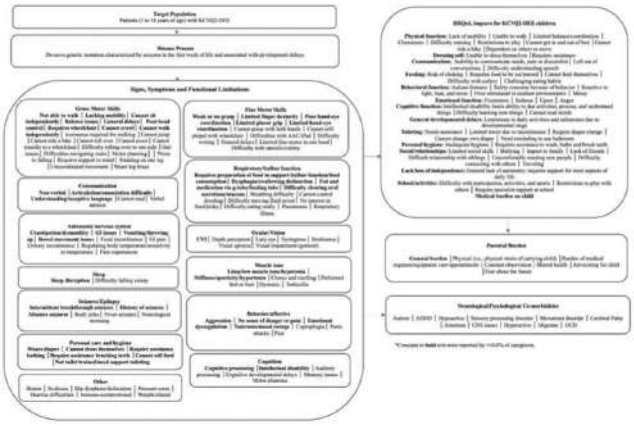

FIGURE 1 Parent-informed conceptual model (inclusive of all phenotypes and ages).

Conclusion: KCNQ2-DEE is a multifactorial condition that manifests through numerous symptoms, resulting in significant impacts on the child and parent. These findings identify the outcome domains important to families and patients that could inform measurement tools and endpoint selection in future therapeutic trials.

Disclosure: This study was sponsored by Biohaven Pharmaceuticals, Inc. ATB has received consulting fees from Biogen, Biohaven Pharmaceuticals Inc, and Encoded Therapeutics; Speakers bureau for Biomarin Pharmaceuticals. JL, GL, and MHP have received personal compensation for serving as an employee of Biohaven Pharmaceuticals. JM has received royalties or licenses from UpToDate; received consultancy fees from Biohaven, Eisai, Neurocrine, and Xenon; received speaker honoraria from Biomarin and Greenwich; has participated in a Data Safety Monitoring Board for Praxis; and serves on the board of directors for Child Neurology Foundation (unpaid). Parexel International has conducted the study on behalf of Biohaven Pharmaceuticals, Inc. LAW received compensation from Parexel International for serving as a pediatric clinical outcomes assessments expert on the project.

EPO-641 | Identification of neonates through prospective newborn screening for metachromatic leukodystrophy

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Background and Aims: Metachromatic leukodystrophy (MLD) is a lysosomal storage disorder caused by arylsulfatase A (ARSA) deficiency, leading to toxic sulfatide accumulation. Symptom onset varies, causing neurological deterioration. Pre-symptomatic interventions like autologous hematopoietic stem cell gene therapy (arsa-cel) for early-onset and hematopoietic stem cell transplantation (HSCT) for late-onset show success. This study details the first prospective newborn screening (NBS) for MLD, focusing on management and treatment experiences.

Methods: First-tier dried blood spot (DBS) samples from 109,259 newborns in the German NBS program were analyzed using electrospray ionization tandem mass spectrometry for sulfatide levels. Next-generation sequencing of the ARSA gene in samples with elevated sulfatides was conducted in the second tier. Confirmation involved assessing ARSA enzyme activity in blood, urinary sulfatides, and genetic sequencing. Identified neonates followed a standardized care pathway for management and treatment.

Results: Elevated sulfatide levels were found in 386 neonates, and genetic sequencing revealed ARSA gene variants in three samples. Conventional diagnostic testing confirmed MLD in all three cases. Two predicted with early-onset MLD underwent successful pre-symptomatic arsa-cel treatment at 9 months, while the third, predicted with late-onset MLD, was scheduled for allogeneic HSCT between 2 and 5 years.

Conclusion: This study highlights NBS for MLD's technical feasibility and high efficiency, emphasizing specificity and sensitivity. Disease onset prediction in three neonates allows timely treatment or monitoring following a standardized care pathway.

Disclosure: Lucia Laugwitz, Nils Janzen, E. Teunissen6, Friedericke Buerger, Joachim Janda, Michaela Döring, Marcus Weitz, Pascal Martin, Stefanie Beck-Woedl, Samuel Gröschel, hendrik Rosewich: Nothing to discolose Thomas P. Mechtler, Petra Oliva, Berthold Streubel, David Kasper are Archimedlife employees. Charlotte 0, Charlotte Chanson, Mirko M. Essing are Orchard employees.

EPO-642 | Neuroimmunological indicators of children with autism spectrum disorders

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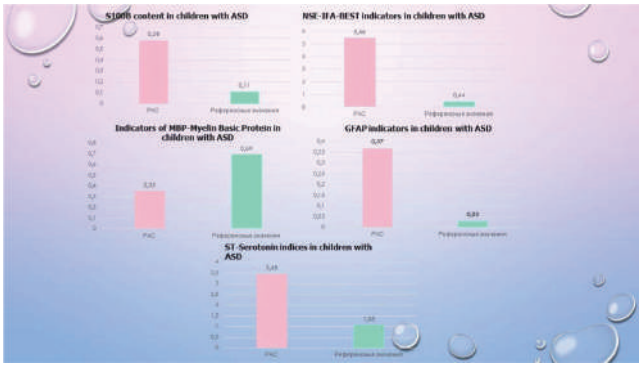
Tashkent Pediatric Medical Institute

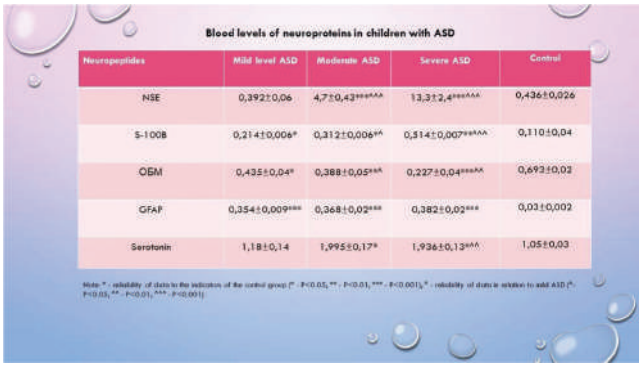
Background and Aims: Various neurochemical systems (glutamatergic, GABAergic, etc.) play an important role in the activity and maturation of the central nervous system. This makes it necessary to clarify and revise the existing hypotheses of the pathogenesis of neuropsychiatric diseases in children with ASD.

Methods: 45 children with ASD (main group; MG) were examined. Determination of neurotropic autoantibodies (NAAB) was performed using standard procedures of solid-phase immunoassay ELI-N-Test and test kits "Immunculus". The control group consisted of 20 practically healthy children of similar age (control group, CG).

Results: when assessing the average content of S100B protein in serum of the children of the MG children, a significant increase was observed in comparison with that of the CG children ($p = 0.005$). In 14 (31%) children with ASD, S100B values were slightly higher or at the upper limit of the norm in contrast to CG children. In children with ASD, there was a 12.4-fold increase in NSE relative to normal values (5.46 ± 0.84 vs. 0.44 ± 0.03; $p < 0.001$). The appearance of decreased indices of antibodies to OBP in serum testifies to the disruption of the blood-brain barrier, most significant in patients with ASD (0.69 ± 0.02 vs. 0.35 ± 0.03; $p < 0.05$). There was a 12.3-fold increase in GFAP values relative to normal values (0.37 ± 0.008 versus 0.03 ± 0.002; $p < 0.001$).



The content of neuroproteins in children with ASD was analyzed.



Blood levels of neuroproteins in children with ASD

Neuropeptides	Mild level ASD	Moderate ASD	Severe ASD	Control
NSE	0,392±0,06	4,7±0,43***^^^	13,3±2,4***^^^	0,436±0,026
S-100B	0,214±0,006*	0,312±0,006**^	0,514±0,007***^^^	0,110±0,04
OBM	0,435±0,04*	0,388±0,05*^^	0,227±0,04***^^^	0,693±0,03
GFAP	0,354±0,009***	0,368±0,02***	0,382±0,02***	0,03±0,002
Serotonin	1,18±0,14	1,995±0,17*	1,936±0,13*^^	1,05±0,03

Note: * - reliability of data in the indicators of the control group (* - P<0.05, ** - P<0.01, *** - P<0.001), ^ - reliability of data in relation to mild ASD (^ - P<0.05, ^^ - P<0.01, ^^^ - P<0.001)

Blood levels of neuroproteins in children with ASD.

Conclusion: Thus, in children with ASD, there is an imbalance in neuroimmunological status, so there is an increase in the level of S100B, NSE, GFAP, and a decrease in OBP.

Disclosure: To investigate the role of neuroproteins in the blood of children with autism spectrum disorders.

EPO-643 | Deriving reference limits for visual evoked potentials from historical data

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Background and Aims: Neurophysiological methods, including visual evoked potentials (VEP), rely on valid and accurate reference limits. VEP variables vary between laboratories, and may change over time because of changes in equipment and procedures. Therefore, there is a need for laboratory specific and updated reference limits. The traditional method for development of reference limits from healthy subjects has several ethical, practical, and economical challenges. We attempt to bypass these challenges by generating reference limits for VEP from historical data using the extrapolated norms (e-norms) method.

Methods: In the Norwegian DIGMINE project we have collected data from 1500 adult patients examined with pattern-reversal VEP at the section of Clinical Neurophysiology at St. Olavs University Hospital in Trondheim. VEP for 1138 and 362 patients were recorded on a Keypoint-Classic system (2006–2018) and a TruTrace-system (2018–2023) respectively. VEPs were recorded with a standardized procedure. Using e-norms we calculated reference limits for VEP variables, including P100 latency and N70-P100 amplitude.

Results: The resulting reference limits (+3SD) for P100 latency were 111 ms for both systems combined, 110 ms for the TruTrace-system and 112 ms for the Keypoint-system. The resulting reference limits (−3SD) for N70-P100 amplitude were 2.5, 2.7 and 2.3 μV respectively.

Conclusion: Historical data can efficiently be used to calculate reference limits for VEP. The resulting reference limits were similar but slightly stricter than those currently used in clinical practice at our laboratory. Our results indicate that historical data can be useful for developing and maintaining reference limits, and for monitoring data quality and effects of changes in equipment and procedures.

Disclosure: Nothing to disclose.

EPO-644 | Quality care for people with CDKL5 deficiency disorder: An expert panel opinion on the European patient journey

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Background and Aims: Introduction: CDKL5 deficiency disorder (CDD) is a rare genetic disorder characterised by seizures and neurodevelopmental delays from infancy. To address the lack of evidence-based guidelines for standardised care of CDD in Europe, clinical experts and patient advocacy group (PAG) representatives from Europe convened to map the patient journey and provide

consensus on how to ensure quality care in routine clinical practice within the European setting.

Methods: Methods: Semi-structured one-to-one interviews were conducted by a third-party agency. Insights were collated into a visual representation of the Europe-specific clinical journey in CDD. Workshops followed to reach consensus, and validate the journey, and to identify challenges and provide expert opinion on potential solutions.

Results: Results: The CDD patient journey has three elements: clinical presentation/diagnosis, seizure management and multidisciplinary care. Clinical criteria for CDD diagnosis include seizure semiology and age at epilepsy onset. Genetic testing is crucial for diagnosis, allowing for appropriate seizure management, multidisciplinary care and outcomes. When planning pharmacotherapy, the refractory and variable seizure semiology, comorbidities, effects of polypharmacy and safety profiles of concomitant medications should be considered. Multidisciplinary collaboration and specialist access are essential for long-term care, support and improved quality of life, each adapting with the changing needs of the patients. The expert group highlighted disparity in management approaches and available resources; therefore, cross-country knowledge-sharing is key.

Conclusion: Conclusion: To achieve quality care of people with CDD, European practice recommendations are required that align on realistic treatment goals, diagnostic criteria and management approaches, and are adaptable.

Disclosure: Editorial support was provided by AXON Communications, supported by Orion Corporation.

Education & history of neurology

EPO-645 | Abstract withdrawn

EPO-646 | Abstract withdrawn

EPO-647 | Optimising continuing medical education: Exploring learning trends and preferences among European and US neurologists

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PeerVoice, Luxembourg, Luxembourg

Background and Aims: To optimise continuing medical education (CME) tailored for neurologists, this study investigates neurologists' CME participation patterns and preferences.

Methods: In 2023, a 20-minute electronic survey was administered to practicing neurologists in Europe and the United States. Recruitment employed the LiMA network of validated healthcare professionals. Question sequences were randomised to mitigate response bias. Each clinician was remunerated in their local currency for participating.

Results: Data were collected from 50 neurologists. Peer-reviewed journal articles (92%) and CME websites (70%) are the top two channels that neurologists used frequently to acquire medical information. Measured using a 5-point scale, content credibility (4.18) and clinical applicability (4.16) were rated as being notably more important than interactivity (2.96) and format novelty (2.84) in driving neurologists' CME participation. Most neurologists reported spending ≤20 minutes per online CME engagement (72%), and identified "having to complete assessment questions to access the education" as a barrier to their CME participation (80%). Linear regression analysis demonstrated a positive correlation ($b = 0.16$, $p < 0.05$) between neurologists' CME participation and increased frequencies of self-reported clinical practice change implementation. Primary changes implemented occurred in treatment plan management (59%), screening and/or diagnosis (51%), and patient monitoring (41%).

Conclusion: CME design needs to prioritize content over format. The identified barriers, notably the time constraints and compulsory assessment questions, highlight the importance of eliminating roadblocks to CME participation. The alignment between clinical practice change and CME participation amongst neurologists validates the effectiveness of CME in driving critical clinical behaviour to improve patient care.

Disclosure: Nothing to disclose.

EPO-648 | PhD and clinician-scientist pathway among neurology residents and junior neurologists in Europe – A survey from the RRFS

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Background and Aims: The decreasing number of clinician-scientists in neurology underscores the urgency of understanding the challenges encountered by early-career professionals to safeguard the future of academia in neurology. Our aim is to explore the characteristics of Ph.D. programs across Europe and the main challenges faced when embarking on an academic career.

Methods: From September to December 2023, an online survey was sent through email to EAN-RRFS members.

Results: We obtained 297 valid responders. 49% were residents, 43% had completed training, and 85% aspired to become a clinician-scientist. Of the 82% who were doing research, 39%

were enrolled in a Ph.D. programme and 15% already completed one. Ph.D. access and graduation criteria varied significantly and 74% of the respondents believed that better harmonization of PhD programs could be beneficial. Less than half of the Ph.D. were fully funded, with universities (31%) and governmental bodies (20%) being the most frequent funding sources. The most commonly perceived challenges included combining clinical activities with research (59%) and finding funding (52%). Among Ph.D. students, over 60% experienced stress, struggled with time management and maintaining a work/life balance, with around one-third expressing concerns about lack of supervision/communication from their supervisor.

Conclusion: We provide insight into the structure, content, perceived benefits, and challenges of doing a Ph.D. in Europe, as well as the difficulties perceived by early career neurologists entering research. Future measures could address these challenges to reduce the barriers for trainees to access a career in Academia.

Disclosure: Nothing to disclose.

EPO-649 | Assessing the digital care pathways unmet needs for rare brain diseases: The case of phenylketonuria

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Background and Aims: Digital Care Pathways for Rare Brain Diseases research project (2023–2024) is coordinated by the European Brain Council. The study is looking at unmet needs while using digital care pathways and aims to assess benefits of digital tools from patient's perspective after COVID-19 pandemic, presenting the phenylketonuria (PKU) case-study.

Methods: A survey was co-designed with PKU patients' representatives, translated into German and Spanish, and anonymously launched in EU Survey platform. The survey contained demographic questions, 13 questions about patient unmet needs on information, communication and education, 8 questions regarding patients' experience on access to care pathways during the COVID-19, and 13 questions on the role of digital tools in supporting PKU management.

Results: 75 respondents (59% patients, 41% parents) participated to the survey. Information about PKU and communication between patient and healthcare professionals are extremely important (44% and 60%), and education on digital platforms for the management of PKU is very important (47%). Digital tools are needed for sharing information and for communicating before the clinic visit (75%) and enhance understanding the information provided for treatment or monitoring (90%). On day-to-day PKU management, Apps, wearables, e-mail, telephone call could help in understanding information received from center and for communication (90%).

Conclusion: Treatment management and care delivered to PKU patients demonstrated benefits and interest for more use of digital tools in management and follow-up. Preliminary results provided valuable insight into understanding needs of PKU patients and defining best channels to engage and communicate with them. While looking at patient perspective, clinician perspective is equally important.

Disclosure: The study received financial support from Pfizer.

EPO-650 | Persistent postural perceptual dizziness (PPPD) in the neurology clinic

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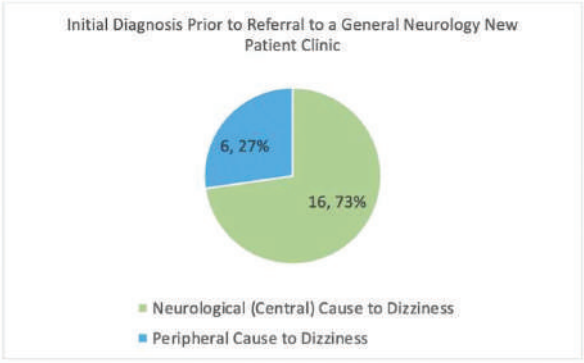
Background and Aims: Persistent postural perceptual dizziness (PPPD) is a recently introduced diagnosis which may be underrecognized. The Bárány Society has defined the condition as persistent dizziness/unsteadiness for ≥3 months causing significant functional impairment. Diagnosis is made clinically and vestibular diagnostic tests and neuroimaging are typically negative. The objectives of the study were to determine the proportion of referrals to a General Neurology New Patient Clinic which met the diagnostic criteria of PPPD and to determine response to treatment.

Methods: In this retrospective review, referral letters of 1315 patients to a General Neurology New Patient Clinic from 2021–2023 were screened for terms 'dizziness', 'vertigo', 'unsteadiness' and 'vestibular'. A chart review was performed to establish the group that met the diagnostic criteria for PPPD. Follow-up correspondences was reviewed to establish response to treatment.

Results: 202 (15.4%) patients were referred with 'Dizziness', 'Vertigo' or 'Unsteadiness'. 22 (1.7%) patients fulfilled the diagnostic criteria of PPPD. 10 (45.5%) were treated with Venlafaxine, conferred ≥50% subjective improvement of symptoms for 8 (80%) patients. Vestibular physiotherapy improved symptoms by ≥25% in 7 (100%) patients. CBT and effective communication of the diagnosis alone alleviated symptoms by 50% in 3 (14%) patients respectively.

Age, Mean (SD)	47.8 (9.96)
Males (%)	10 (45.5%)
Females (%)	12 (54.5%)
Co-morbidities:	
Peripheral Vestibular Conditions	7 (31.8%)
Neurological Conditions	7 (31.8%)
General Medical Conditions	3 (13.6%)
Head Trauma	1 (4.5%)
Psychiatric Conditions	4 (18.3%)
Mean Duration of Symptoms (Months), (SD)	33.5 (12.2)
Subjective Treatment Response to Venlafaxine:	
Number of patients tried Venlafaxine	10 (45%.5)
At least 50% Improvement with Venlafaxine	8 (80%)
25% Improvement with Venlafaxine	1 (10%)
No response To Venlafaxine	1 (10%)
Subjective Treatment Response to Vestibular Physiotherapy:	
Number of patients tried Vestibular Physiotherapy	7 (31%)
At least 25% Improvement with Vestibular Physiotherapy	7 (100%)
Subjective Treatment Response To CBT:	
Number of patients tried CBT	3 (14%)
At least 50% Improvement with CBT	3 (100%)

Subjective Treatment Response To Effective Communication of Diagnosis :	
Number of Patients who had the diagnosis of PPPD Explained to them	22 (100%)
At least 50% Improvement with Effective Communication of Diagnosis	3 (14%)



Conclusion: PPPD is a relatively common neurological condition, should be considered in patients with chronic vestibular symptoms which result in significant functional morbidity. In this cohort, treatment with Venlafaxine and vestibular physiotherapy resulted in significant improvement in symptoms.

Disclosure: Nothing to disclose.

EPO-651 | Online education improves specialists' knowledge and competence on management of depression in people with epilepsy

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Background and Aims: To evaluate whether an online educational programme directed at European-based specialists, could improve knowledge on identification of depression in people with epilepsy and competence relating to management of depression in people with epilepsy.

Methods: The educational activity was a 15-minute online video with 2 European experts in Epilepsy. Educational effect was assessed using a 3-question repeated pairs, pre/post assessment survey. A paired-samples *t*-test was conducted to assess overall number correct and confidence change. p values < 0.05 (McNemar's test) are statistically significant. Cohen's d test was used for magnitude of effect of education on the overall outcomes (knowledge). The activity launched on 29 September 2023 and data analysed as of 11 December 2023.

Results: 461 neurologists and 196 psychiatrists participated in the programme, of which 54 neurologists and 39 psychiatrists completed pre- and post-assessment tests. Significant improvements were seen for both groups, with an average correct response rate of 33% and 27% pre-assessment, which increased to 69% and 64% post-assessment, for neurologists ($p < 0.001$; Cohen's $d = 1.12$) and psychiatrists ($p < 0.001$; Cohen's $d = 1.11$) respectively. Table 1 provides further results for each learning objective. Based on a self-reporting question, neurologists expressed a 61%, and psychiatrists expressed a 59%, increase in confidence following the education in managing depression in people with epilepsy.

Table 1

		Mean % of responses correct	Relative % change	P value	%*Improved on this learning objective	% #Reinforced on this learning objective
Increased knowledge regarding the identification of depression in people with epilepsy	Neurologists pre-	31	116	P <.001	57	30
	Neurologists post-	67				
	Psychiatrists pre-	31	116	P <.001	59	23
	Psychiatrists post-	67				
Greater competence related to managing depression in people with epilepsy	Neurologists pre-	35	111	P <.001	39	35
	Neurologists post-	74				
	Psychiatrists pre-	21	181	P <.001	38	21
	Psychiatrists post-	59				

*Improved: answers at least one more question correctly
#Reinforced: answers the same number of questions correctly pre/post

Table expressing knowledge and competence changes for neurologists and psychiatrists before and after education.

Conclusion: This study demonstrates the positive effect of online medical education on specialists' knowledge, competence and confidence in managing comorbid depression in people with epilepsy in Europe.

Disclosure: Lionel Thevathasan, Katherine Carpenter and Camille Scott-Smith are employed by Medscape LLC. An unrestricted educational grant for this programme was provided by Angelini Pharma. Marco Mula and Ley Sander have nothing to disclose.

EPO-652 | Online medical education improves specialists' knowledge on selecting antiseizure medications in people with epilepsy

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Background and Aims: Post-pandemic education is variable, so we evaluated whether an online educational programme directed at European-based specialists, could improve knowledge on appropriate selection of antiseizure medications (ASMs) for people with focal epilepsy, particularly relating to mechanisms of action and latest clinical trial data.

Methods: The educational activity was a 29-minute online video with 1 European expert in Epilepsy. Educational effect was assessed using a 3-question repeated pairs, pre/post assessment survey. A paired-samples *t*-test was conducted to assess overall number correct and confidence change. p values < 0.05 (McNemar's test) are statistically significant. Cohen's d test was used for magnitude of effect of education on the overall outcomes (knowledge). The activity launched on 15 June 2023 and data analysed as of 20 October 2023.

Results: 2,214 neurologists and 769 psychiatrists participated in the programme, of which 218 neurologists and 38 psychiatrists completed pre- and post-assessment tests. Significant improvements were seen for both groups, with an average correct response rate of 49% and 31% pre-assessment, which increased to 72% and 47% post-assessment, for neurologists ($p < 0.001$; Cohen's $d = 0.80$) and psychiatrists ($p < 0.001$; Cohen's $d = 0.63$) respectively. Table 1 provides further results for each learning objective. Based on a self-reporting question, neurologists expressed a 43%, and psychiatrists expressed a 34%, increase in confidence following the education in knowledge on antiseizure medication selection.

Table 1

		Mean % of responses correct	Relative % change	P value	% Improved* on this learning objective	% Reinforced# on this learning objective
Increased knowledge regarding the latest clinical trial data for newer ASMs	Neurologists pre-	48	54	P <.001	44	45
	Neurologists post-	74				
	Psychiatrists pre-	33	52	P <.001	32	42
	Psychiatrists post-	50				
Increased knowledge regarding the mechanism of action of ASMs	Neurologists pre-	50	36	P <.001	19	49
	Neurologists post-	68				
	Psychiatrists pre-	26	62	P <.05	18	24
	Psychiatrists post-	42				

*Improved: answers at least one more question correctly
#Reinforced: answers the same number of questions correctly pre/post

Table of results expressing changes in knowledge on mode of action and clinical trial data before and after education.

Conclusion: This study demonstrates the positive effect of online medical education on specialists' knowledge and confidence in selection of antiseizure medications for people with focal epilepsy in Europe.

Disclosure: Lionel Thevathasan, Katherine Carpenter and Camille Scot-Smith are employed by Medscape LLC. Rhys Thomas has nothing to disclose. This educational programme was supported by an unrestricted educational grant by Angelini Pharma.

EPO-653 | Online medical education improves specialists' knowledge and confidence on sudden unexpected death in epilepsy

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Background and Aims: To evaluate whether an online educational programme directed at European-based specialists, could improve knowledge and confidence relating to SUDEP, specifically the risks of SUDEP and desire among patients and caregivers to receive this information.

Methods: The educational activity was a 36-minute online video with 3 European experts in Epilepsy. Educational effect was assessed using a 3-question repeated pairs, pre/post assessment survey. A paired-samples *t*-test was conducted to assess overall number correct and confidence change. p values < 0.05 (McNemar's test) are statistically significant. Cohen's d test was used for magnitude of effect of education on the overall outcomes (knowledge). The activity launched on 3 August 2023 and data analysed as of 9 October 2023.

Results: 598 neurologists and 326 psychiatrists participated in the programme, of which 76 neurologists and 39 psychiatrists completed pre- and post-assessment tests. Significant improvements

were seen for both groups, with an average correct response rate of 32% and 22% pre-assessment, which increased to 76% and 58% post-assessment, for neurologists ($p < 0.001$; Cohen's d = 1.22) and psychiatrists ($p < 0.001$; Cohen's d = 1.04) respectively. Table 1 provides further results for each learning objective. Based on a self-reporting question, neurologists expressed a 54%, and psychiatrists expressed a 51%, increase in confidence following the education in discussing SUDEP with patients/caregivers.

Table 1

		Mean % of responses correct	Relative % change	P value	% *Improved on this learning objective	% #Reinforced on this learning objective
Increased knowledge regarding the need for clear communication around SUDEP with people with epilepsy	Neurologists pre-	12	450	P <.001	54	12
	Neurologists post-	66				
	Psychiatrists pre-	13	254	P <.001	36	10
	Psychiatrists post-	46				
Increased knowledge regarding the risk of SUDEP	Neurologists pre-	43	88	P <.001	58	32
	Neurologists post-	81				
	Psychiatrists pre-	27	137	P <.001	59	28
	Psychiatrists post-	64				

*Improved: answers at least one more question correctly
#Reinforced: answers the same number of questions correctly pre/post

Table of results expressing changes in knowledge relating to need for communication and risk associated with SUDEP before and after education.

Conclusion: This study demonstrates the positive effect of online medical education on specialists' knowledge and confidence in risks associated with and communication on SUDEP in Europe.

Disclosure: Lionel Thevathasan, Katherine Carpenter and Camille Scot-Smith are employed by Medscape LLC. Rohit Shankar, Philippe Ryvlin and Torbjörn Tomson have no disclosures. This educational programme was supported by an unrestricted educational grant by Angelini Pharma.

EPO-654 | Abstract withdrawn

EPO-655 | Antiseizure prophylaxis in routine neurosurgery practice: Urgent need for training

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Background and Aims: Prophylactic antiseizure medications (ASMs) to prevent early and late seizures after craniotomy is not currently recommended, yet it is a common practice among neurosurgeons. This study investigates decision-making strategies regarding post-craniotomy ASM prescription in Italian Neurosurgery Units.

Methods: An online cross-sectional survey was conducted (November 2022-March 2023). The survey link was distributed via email to neurosurgeons of 110 Italian Pediatric and Adult Neurosurgery Units. The survey comprised 11 multiple-choice questions addressing ASM prescription for individuals without seizures or those experiencing early post-surgical seizures. Questions explored type and timing of prescribed ASMs, factors influencing decision, and drug withdrawal management.

Results: Eighty-two neurosurgeons from 64/110 Neurosurgery Units answered the survey. Forty-two out 82 (52.1%) neurosurgeons prescribed post-craniotomy ASMs for individuals without seizures: 9 routinely prescribed ASMs, 33 only under specific conditions (e.g., febrile seizures history, familiarity for epilepsy) or based on the surgical site. Levetiracetam was the most prescribed ASM (41/42; 97.6%). Thirty-one (73.8%) surgeons initiated ASMs before surgery. Thirty-two (39%) surgeons planned withdrawal within 6 months while 10 (10.2%) chose later suspension. Seventy-nine (96.3%) neurosurgeons prescribed ASM (mostly levetiracetam: 77/79; 97.5%) after an early post-surgical seizure. Only 4 (5.1%) surgeons routinely discontinued ASMs within 1 month, while 43 (54.4%) suspended them within 6 months and 32 (40.5%) continued beyond 6 months. Notably, 42 neurosurgeons managed ASM treatment independently, while 40 sought neurologist assistance.

Conclusion: This survey revealed widespread adoption of ASM prophylaxis after craniotomy in neurosurgery practice, despite lack of evidence about its usefulness, emphasizing the urgent need for training in this area.

Disclosure: Nothing to disclose.

EPO-656 | Gender disparities among neurology residents classifications in Portugal

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Background and Aims: Gender disparities in medical professions have long been a subject of concern, with research consistently pointing to the role of implicit bias in shaping differential career outcomes for men and women. This study endeavors to investigate whether gender-based differentials exist in the evaluation of Neurology residents in Portugal.

Methods: We collected publicly available data encompassing gender (as a social construct), grades and rankings from two pivotal assessments administered at the beginning and ending of Neurology Residency: the National Board Exam (NBE) and Neurology Exam (NE), respectively. The NBE is a multiple-choice gender-blinded

evaluation, whereas the NE involves an oral gender-unblinded evaluation.

Results: Our analysis revealed that 36.5% of women and 21.6% of male residents achieved the superior quartile of the NBE ranking, which reflects a similar representation among top classifications when accessed through a gender-blinded exam. On the contrary, the proportion of male residents on the top classification of NE, a gender-unblinded evaluation, was more than twice higher than women (37.8% vs. 18.3%, $p < 0.05$), indicating a statistically significant disparity in performance between genders in the oral examination setting (Table 1).

Conclusion: The findings of the present study may imply that there are nuanced disparities in women's career as a neurologist resident in Portugal. Although the recruitment seems relatively balanced between genders, the gender-unblinded assessments unveil significant discrepancies favoring men.

Disclosure: Nothing to disclose.

EPO-657 | Burnout, depression and anxiety among neurology residents in Türkiye: A preliminary report

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Background and Aims: Neurology residency is a long and difficult journey in which the physical and mental well-being of trainees are essential for their clinical and academic success. This ongoing study aims to determine the mental status and factors that affect mental health of neurology residents in Türkiye and therefore improve the quality of neurology training.

Methods: Neurology residents throughout Türkiye were invited to take part in an online survey by the support of Turkish Neurological Association. Additionally to demographic and institutional data of all participants; Minnesota Job Satisfaction Questionnaire, Maslach Burnout Inventory, Beck Anxiety Inventory and Beck Depression Inventory were assessed.

Results: Anxiety was found in 62%, depression in 63.3% and burnout in 44% of the participants (n: 79). In correlation analyses, an increase in the duration of neurology training was associated with lower levels of depression (r: −0.21, p: 0.05) and anxiety (r: −0.34, p: 0.002). Working long hours was associated with a decrease in job satisfaction (r: −0.22, p: 0.04) and an increase in depression (r: 0.24, p: 0.02). Job satisfaction scores increased with more time devoted to education (r: 0.28, p: 0.01) and research (r: 0.22, p: 0.04). The presence of depression was less in residents who were able to rest after night shift (p: 0.01).

Conclusion: Preliminary data from our ongoing study demonstrates a high prevalence of burnout, depression, and anxiety among neurology residents in Türkiye. To reduce these factors, it may be beneficial to decrease the daily working hours, increase the time allotted for education and research, and provide rest after night shifts.

Disclosure: The current results are preliminary and the study continues.

EPO-658 | Ethical and neurological dimensions of Dr. Robert G. Heath's deep brain stimulation experiments

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Background and Aims: This historical analysis revisits the pioneering yet ethically contentious deep brain stimulation (DBS) experiments of Dr. Robert Galbraith Heath. Heath's work in the mid-20th century focused on targeting limbic system components, such as the open-brain targeting of septal area, amygdala, and thalamus, aiming to unravel neurological foundations of psychiatric disorders. This retrospective study scrutinizes the specific neural circuits and neurotransmitter systems engaged in Heath's DBS trials, alongside their profound ethical implications.

Methods: A detailed examination of Heath's seminal publications and experiment records, particularly those documenting the septal stimulation for modulating depressive symptoms, the B-11 implant for psychiatric disorders, and interventions in schizophrenia and homosexuality, was conducted. The analysis involves a comprehensive review of limbic system circuitry, specifically the role of septal nuclei, amygdaloid complex, and thalamic connections, in conjunction with the dopaminergic and serotonergic pathways implicated in Heath's studies.

Results: Heath's DBS experiments revealed notable alterations in limbic circuitry functioning, particularly highlighting the role of septal and amygdaloid stimulation in modulating emotional and behavioral responses. The B-11 implant trials underscored the intricate interplay between deep brain regions in psychiatric symptomatology. Additionally, Heath's work raised pivotal ethical concerns regarding patient consent and the invasive nature of DBS, catalyzing a reevaluation of research protocols in neuropsychiatry.

Conclusion: Heath's forays into DBS epitomize a seminal yet polarizing epoch in neurology, spotlighting the nascent interplay between limbic neuromodulation and psychiatric therapeutics. This retrospection not only venerates his pioneering ethos but also subtly adumbrates the era's nascent ethical paradigms, affirming Heath's indelible imprint on the neurological vanguard.

Disclosure: An artifact supplementing this study is a book on psychosurgery, containing Heath's personal annotations and signature, providing a unique historical perspective.

EPO-659 | The history of Danish neuroscience

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Background and Aims: The history of Danish neuroscience dates back at the 17th century, and was from the start linked to clinical disciplines. This continued in the 19th and 20th century with new initiatives linking basic neuroscience to clinical neurology and psychiatry. From the middle of the 20th century, basic neuroscience was developing rapidly within the preclinical university sectors. Clinical neuroscience continued and was even reinforced during this period with important translational research.
Methods: Literature review.
Results: Some highlights: Steno (1638–1686) was active in many scientific fields. Among his main contributions to neuroscience was the investigation of the anatomy of the pineal gland. René Descartes had proposed how the pineal gland was the seat of the soul, acting by rotation to distribute animal spirits. Steno demonstrated that the pineal gland was merely grey matter with black spots. In the 19th century Carl Lange (1834–1900) had main contributions in neurology and psychiatry. He rode a book in Danish, "On emotions – Psycho-Physiological Study" in 1885, translated to German, French and English. Fritz Buchthal (1907–2003) had a main role in the Danish and international development of clinical neurophysiology and especially electromyography. Niels A. Lassen (1926–1997) main research field was the cerebral circulation. He, his group and collaborators were the first to demonstrate that activation led to blood flow increase – functional activation. Finally, Jens Christian Skou (1918–2018) received the Nobel Prize in 1997 for the discovery of the sodium-potassium pump.
Conclusion: Danish Neuroscience has a strong history.
Disclosure: Nothing to disclose.

Neuro-oncology

EPO-660 | Hemifacial spasm of central origin due to structural cause

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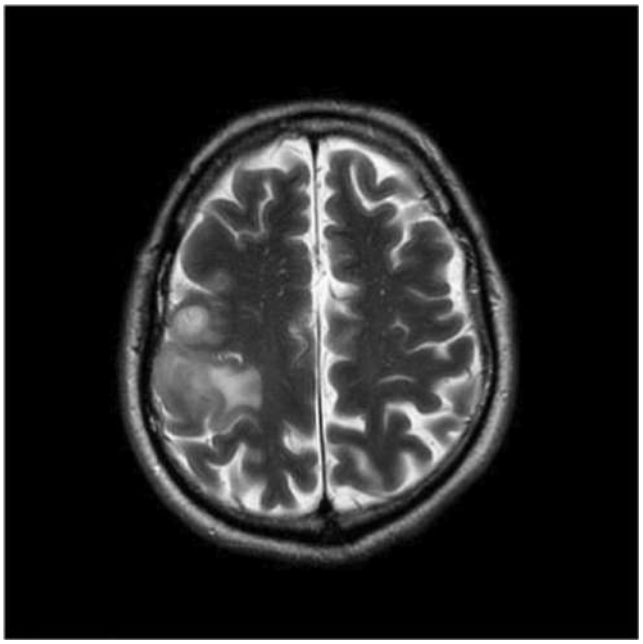
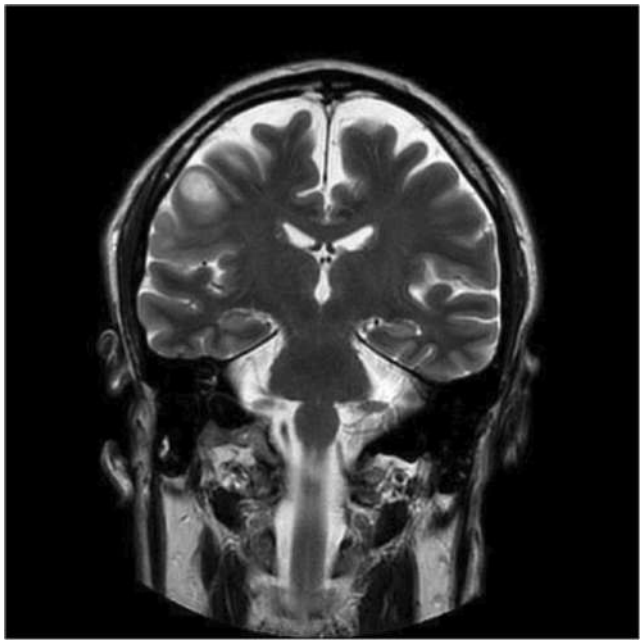
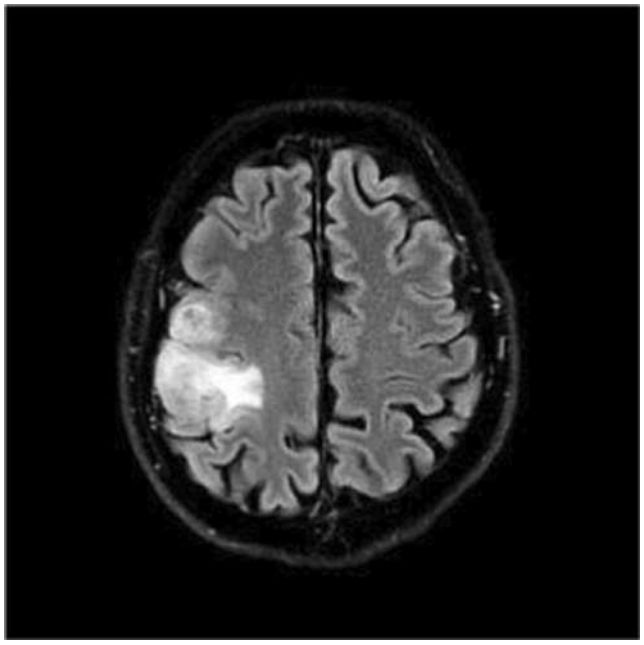
Background and Aims: Hemifacial spasm is a peripheral movement disorder consisting of irregular clonic/tonic involuntary movements of muscles innervated by the facial nerve. Its principal cause is an hyperexcitability of its nucleus or an abnormal transmission of the proximal nerve segment, usually of compressive origin due to a vascular structure; some atypical cases are caused by brain tumors, mainly infratentorial location. We present a case with central origin due to supratentorial lesion.
Methods: A 60-year-old male under neurology follow-up for epilepsy (motor focal aware seizures) of structural cause (right frontal SOL: non mutated IDH diffuse glioblastoma, TERT mutation, WHO CNS4), went to the emergency room because of arrhythmic spasmodic movements in bilateral frontal region (predominantly left), left orbicularis oculi and left hemiface. Thinking of continuous partial epilepsy, anti-seizure medication was increased, without any improvement. Asking again, these movements could be in relation to a distony: they improve during sleep and with sensory tricks and exacerbates with light, nervousness and speech, so infiltrations with botulinum toxin were performed, with marked improvement.
Results: Brain MRI: right fronto-parietal cortical thickening with obliteration of the sulci, hypertense on T2 / FLAIR and hypointense on T1, affecting opercular area and pre/post-central gyri; small subcortical pseudonodular area (12 × 5 mm) with subtle hypersignal in diffusion and a faint ring enhancement; stable compared to the previous one.



Brain MRI, axial T2.



Brain MRI, coronal T2.



Brain MRI, axial FLAIR.

Conclusion: Hemifacial spasm due to supratentorial tumors may be explained by affectation of the contralateral motor cerebral cortex (irritation of the lower motor unit of the facial nerve) based on anatomical investigation in veterinary medicine.
Disclosure: Nothing to disclose.

EPO-661 | A biopsy-verified case of CNS involvement of mycosis fungoides with positive RT-QuIC assay

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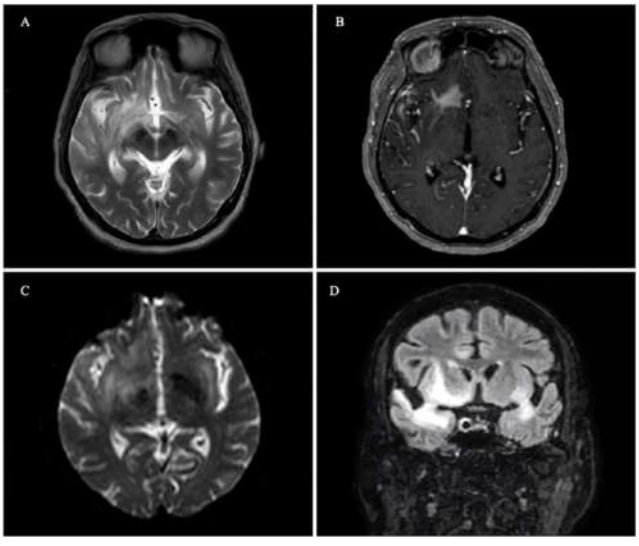
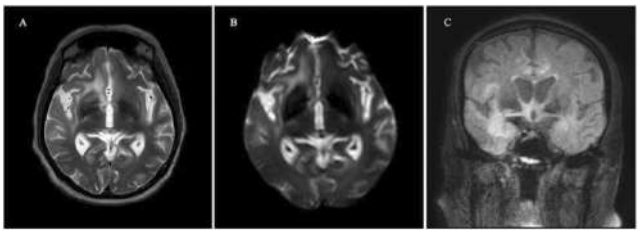
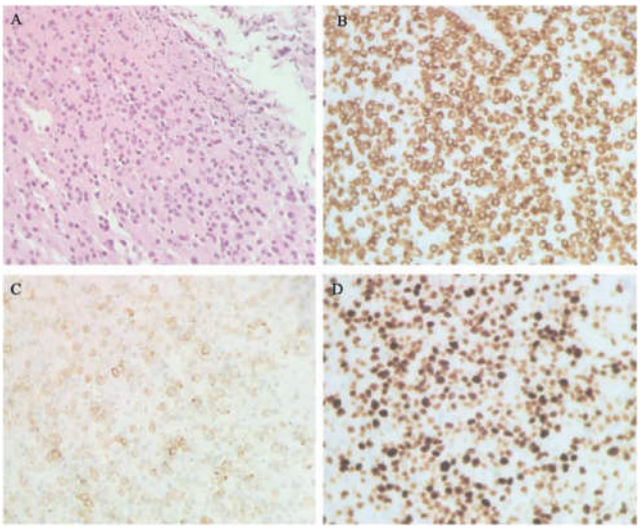
Background and Aims: We report a rare case of positive RT-QuIC assay in CNS involvement of mycosis fungoides.
Methods: A 73-year-old man presented with decreased consciousness and generalized convulsions. He had been formerly diagnosed with mycosis fungoides, which was in full remission. Clinical examination revealed profound cognitive deficits with fluctuating level of alertness during admission. A brain MRI showed multiple contrast-enhancing lesions in both hemispheres, while a first lumbar puncture indicated lymphocytic pleocytosis with elevated CSF protein.
Results: The rapidly progressive cognitive decline prompted investigations for Creutzfeldt-Jakob disease (CJD) with 14-3-3 and RT-QuIC assay, both of which came back positive. Meanwhile, flow cytometry analysis reported increased T-cell population, suggestive of CNS lymphoma. The RT-QuIC assay remained positive in the second, acellular, lumbar puncture. The CJD diagnosis was not further supported by imaging or EEG findings. A brain biopsy was performed, reporting brain infiltration by a highly malignant T-cell lymphoma, believed to represent large cell transformation of mycosis fungoides with CD30 expression. Treatment with pulsed steroids had some effect on the level of consciousness, although a degree of memory impairment remained.



Initial MRI scans of the brain. A. Axial T2 showing high signal in the right temporal lobe, B. Axial post-contrast scan, demonstrating an area of contrast enhancement in the right temporal lobe, C. Axial DWI, depicting a similar area of high signal in the right temporal lobe, D. Coronal FLAIR with high signal in both temporal lobes and extending to basal ganglia bilaterally.



Serial MRI scans of the brain after steroid treatment. A. Axial T2 and B. Axial DWI showing slight improvement of the high signal in the right frontotemporal area. C. Coronal FLAIR demonstrating bilateral temporal high signal to a lesser extent compared to the initial MRI; some areas of high signal are evident in the medial frontal lobes bilaterally. Image degraded my motion artefact.



Histological images from the patient's brain biopsy. A. Infiltration of brain parenchyma by medium-sized lymphocytes with dark chromatin and irregular nuclear membrane (Haematoxylin and eosin ×400 magnification), B. CD3 expression in medium-sized lymphocytes.

Conclusion: RT-QuIC assay is able to accurately detect the pathogenic agent (PrPSc), identified to be responsible for CJD occurrence. Positive RT-QuIC assay has been strongly linked to CJD, with specificity reaching 99%, although it has been suggested that high CSF white cell count and protein can affect the results. The brain biopsy has confirmed CNS involvement of the cutaneous lymphoma; however, a possibility of subclinical coexistence of CJD remains.
Disclosure: Nothing to disclose.

EPO-662 | Primary leptomeningeal sarcomatosis: An exceptional cause of chronic, aseptic meningitis

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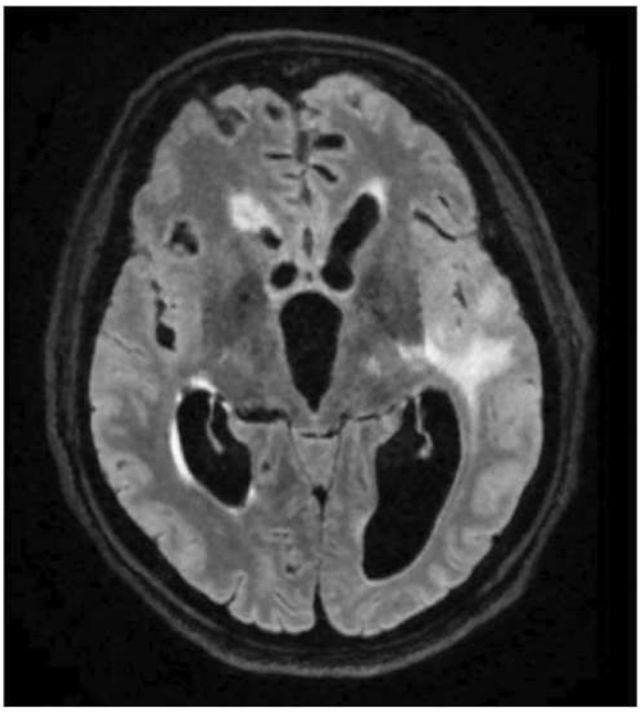
Background and Aims: Primary leptomeningeal sarcomatosis (PLS) represents less than 1% of primary intracranial tumors and is an even less frequent cause of non-infectious, chronic meningitis. Therefore, it should be taken into consideration when other causes of chronic meningitis have been dismissed.
Methods: We present the case of a 58-year-old man who presented a very suggestive granulomatous, subacute meningitis based on clinical findings. Nevertheless, every microbiological determination tested was negative and there were no specific findings in image tests.
Results: Our patient presented a wide range of symptoms: behavioral disorder, cognitive impairment, right hand drift, facial supranuclear partial palsy but no neck rigidity. Also, during hospitalization the patient developed seizures that required antiseizure medication. CT and MRI found digitiform edema in left parietotemporal lobes, meningeal thickening at that level and communicating hydrocephalus. Lumbar puncture resulted negative for every test underwent, as well as every other diagnostic procedure. Tuberculous meningitis was suspected at first, and antituberculous treatment was initiated. Due to poor evolution, brain biopsy was subsequently performed.



FLAIR-powered MRI showing digitiform left parietotemporal edema and meningeal thickening at that level.

Conclusion: PLS is an exceptional cause of chronic, aseptic meningitis which must be suspected when other more frequent etiologies are not present. Despite its fatal prognosis, holocranial radiotherapy showed little survival increasing, reaching up to 3 years in certain patients. Therefore, this diagnosis must be considered in certain scenarios.
Disclosure: Nothing to disclosure.

EPO-663 | The Last Bastion – 7 Cases of tectal gliomas with long follow up

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Background and Aims: Brainstem gliomas are an heterogenous group of gliomas that appear predominately during childhood. Mesencephalic gliomas are usually invasive; however, tectal gliomas are a subtype with a slow growth rate. These are low grade gliomas with a relatively benign course, that turn symptomatic when patients develop obstructive hydrocephalus. Permanent neurological deficits are rare.

Methods: This work will explore demographic, clinical and radiological features of 7 patients with tectal gliomas with active follow up at an oncological hospital in Lisbon.

Results: The median age of these patients was 14 years and 57.1% were female. In 4 of 7 cases, the clinical manifestation was supratentorial hydrocephalus demanding neurosurgical treatment – 3 had ventriculoperitoneal shunt placement and 1 had ventriculostomy. The diagnostic was incidental in the remaining. 28.6% of the tumors had a cystic-like appearance on brain magnetic resonance. The majority (85.7%) had no enhancement after gadolinium injection. Only 1 patient was submitted to neurosurgical biopsy and the histology showed grade II astrocytoma. More than half of the subjects (57.1%) have no neurological deficits. The remaining had pupillary or oculomotor abnormalities. All patients are under surveillance, without treatment, with radiologic stability for many years.

Conclusion: Tectal gliomas are indolent brain tumors whose main symptoms relate to obstructive hydrocephalus. Similarly to the literature, this cohort shows slow growth tumors, with few associated symptoms and sustained imagiologic stability. This entity is a rare case in Neuro-Oncology as brain biopsy may be dispensed due to the risk of worsening symptoms while not changing patient management.

Disclosure: Nothing to disclose.

EPO-664 | Prognostic impact of surgical resection versus biopsy in patients with primary central nervous system lymphoma (PCNSL)

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Background and Aims: Whether surgical resection, as compared to biopsy, may positively affect the outcome of Primary Central Nervous System Lymphoma (PCNSL) patients is controversial. In this study, we compared the clinical characteristics and outcome of PCNSL patients receiving either surgical resection or biopsy in our Institution.

Methods: We retrospectively collected clinical data of PCNSL patients, who underwent biopsy or surgical resection and were subsequently treated in our Institution from 2004 to 2023. Progression-free survival (PFS) and overall survival (OS) were defined as time from diagnosis and recurrence or death/censoring).

Results: We included 55 patients, with a median age of 66.0 years. 36 (65.5%) showed multifocal lesions at presentation. 32 (58.2%) underwent biopsy, whereas 23 (41.8%) surgical resection. 48 (87.3%) underwent adjuvant methotrexate-based chemotherapy. Unifocal vs multifocal lesions prevailed among patients undergoing surgical resection (20/23, 87.0%) vs biopsy (15/32, 46.9%), $p = 0.002$. Median PFS and OS of the whole cohort were 8.0 and 26.0 months. Surgical resection vs biopsy correlated with longer median PFS and OS both in a univariate (mPFS: 64.0 vs 7.0 months, $p = 0.031$; mOS: 68.0 vs 10.0 months, $p = 0.007$), and a multivariable analysis (HR 0.390, 0.168–0.907, $p = 0.029$). Conversely, unifocal vs multifocal presentation was the only variable with a favourable impact on the OS.

Conclusion: In our study, surgical resection, as compared to biopsy, was associated with longer PFS, but not OS, in PCNSL patients. Further studies on larger cohorts are needed to clarify whether surgical resection may be a feasible and safe option to improve survival in selected PCNSL patients.

Disclosure: Nothing to disclose.

EPO-665 | Progressive supra and infratentorial hypermetabolic white matter lesions non-typical of multiple sclerosis

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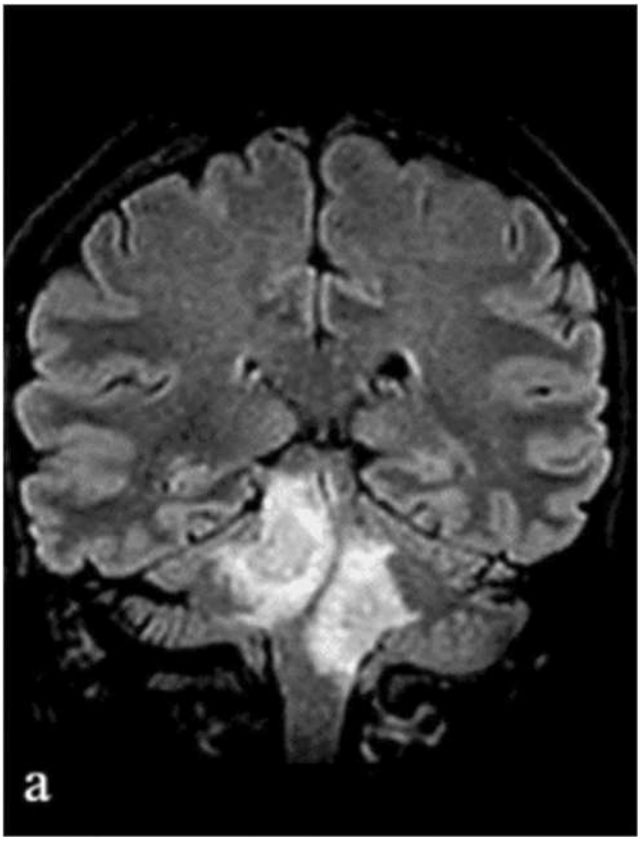
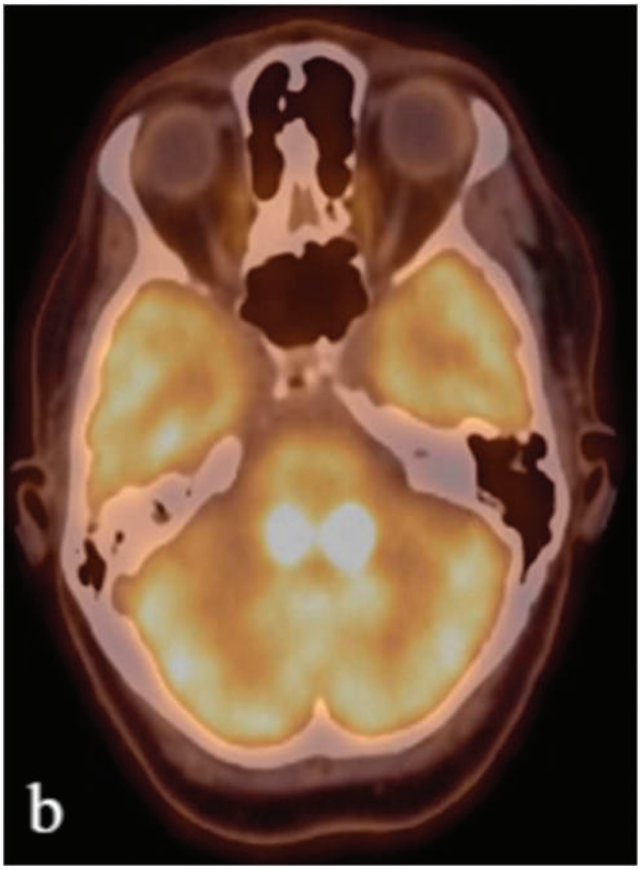
Background and Aims: A case report of a patient presenting progressive brainstem symptoms along with progressive supra and infratentorial white matter lesions (WML), hypermetabolic on Positron Emission Tomography-Computerized Tomography (PET-CT), mistakenly characterized as demyelinating.

Methods: Descriptive retrospective study of a case.

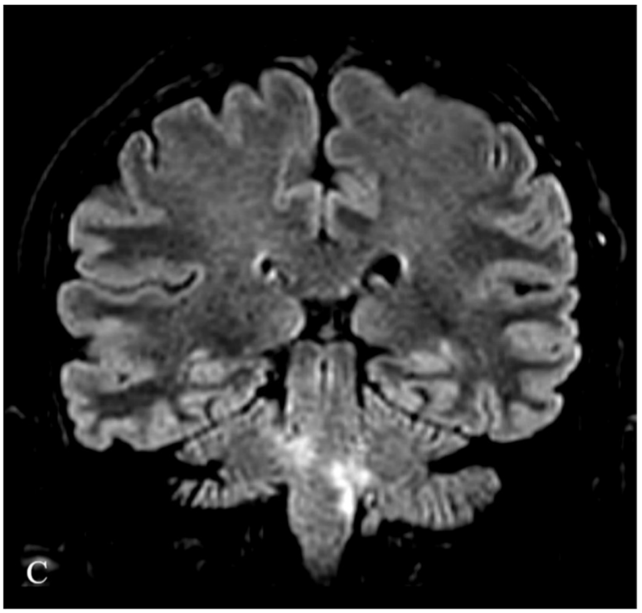
Results: a 43-year-old female presenting with progressive gait instability, paresthesia, left hemiparesis and left inferior facial palsy. Brain Magnetic Resonance Imaging (MRI) showed multiple supra and infratentorial WML, which were characterized radiologically as demyelinating. A total PET-CT showed hypermetabolic brainstem lesions, with no thoracoabdominal findings. Bloodwork, including tumor markers, autoimmunity serologies (antiMOG and AQ4 antibodies), as well as ophthalmologic slit-lamp examination and two cerebrospinal fluid (CSF) samples were all unremarkable. A course of intravenous corticosteroids resulted in slight clinical and radiological improvement. Further on, she presented signs of clinical worsening with multidirectional nystagmus, dysphagia, complete left facial and hypoglossal palsy with left hemianesthesia, and growth of the previous lesions in subsequent MRIs. A biopsy of the caudate lesion along with an intraventricular CSF sample were taken, showing findings suggestive of diffuse large B-cell lymphoma. MATRIX chemotherapy protocol was started, followed by autologous stem cell transplantation, with subsequent clinical and radiological improvement.



(a) T2-FLAIR weighted image showing hyperintense bilateral brainstem lesions.



(b) Brain PET-TC showing hypermetabolic activity in these lesions (calculated as SUV max 21, 8 [right] and 23.8 [left]).



(c) T2-FLAIR weighted image after 3rd chemotherapy cycle (MATRIX scheme) showing noticeable decrease in the size of the infratentorial lesions.

Conclusion: Primary central nervous system lymphoma is a rare cause of WML, with less than 10% showing infratentorial lesions. Previously associated with AIDS patients, neurologists should have a clinical suspicion in patients showing WML non-typical of known demyelinating diseases. A transient clinical and radiological improvement after corticosteroids is typical.

Disclosure: The author has no conflict of interest.

EPO-666 | MPNST as a very late complication of radiotherapy: Red flags, diagnostic considerations and role of nerve biopsy

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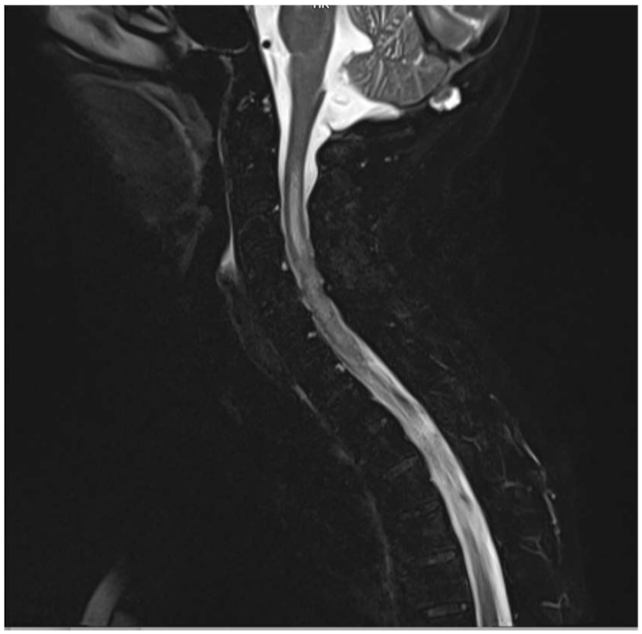
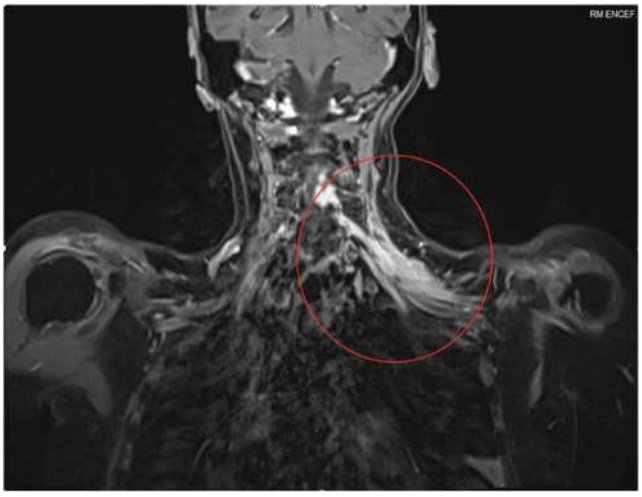
Background and Aims: MPNST is a rare, aggressive sarcoma that may arise up to many years following radiotherapy. We report a case of a fatal MPNST mimicking at onset an inflammatory brachial plexopathy and we propose diagnostic recommendations based on evidence from a systematic review.

Methods: case report of MPNST and systematic literature review.

Results: A 60-year-old female presented with progressive left upper limb proximal weakness. She was known for neck radiotherapy 36 years prior for Hodgkin lymphoma. Cervical MRI, CSF and FDG-PET were normal. Remarkably, brachial plexus MRI showed nerve roots modest thickening. IvIg and steroids treatment were not effective. Progression of symptoms occurred in the following year, when a new MRI revealed multiple cerebral and cervical T2-hyperintensities. An intradural biopsy allowed histological diagnosis of MPNST. The patients died 18 months after onset. Our literature review highlighted as major risk factors for post-radiation MPNST head and neck irradiation (77% of cases), occurred before the age of 35 years (62%). Mean time from radiation was 13.7 years. Importantly, 21/22 (95.5%) of cases presented with focal tumor-like enlargement, one case had brachial plexopathy without enlargement with hypermetabolism at PET-FDG. Mean survival from diagnosis in patients that underwent surgery is 14.3 months with 29.4% still alive at the moment of publication.



Cervical spine MPNST infiltration at MRI: diffuse C2-C7 intramedullary hyperintensity on T2-weighted sequences.



Brachial plexus MRI: T2 hyperintensity, thickening and enhancement of brachial plexus, especially first and second trunk.

	Irradiation site	Age at irradiation (years)	Mean time from radiation (years)	Radiological findings	Surgery	Survival from diagnosis (m= months)
John I, 2017	pelvis	49	7	mass	y	still alive 3 m FU
Lau D, 2014	pelvis	33	10	mass	y	60 m
Amin A, 2004	para-aortic	28	10	mass	n	died N/A
Maegawa T, 2016	head	13	17	mass	y	2 m
Adamson DC, 2004	neck	31	6	mass	y	N/A
Adamson DC, 2004	neck	25	5	mass	y	N/A
Paolini S, 2006	neck	38	12	mass	y	9 m
Siveke JT, 2003	neck	46	13	mass	n	3 m
Ilgner J, 2001	neck	32	7	mass	y	still alive N/A m FU
Stark AM, 2013	neck	41	15	mass	y	24 m
Owosho AA, 2018	neck	20	6	mass	y	7 m
Owosho AA, 2018	neck	7	38	mass	n	10 m
Owosho AA, 2018	neck	23	43	mass	y	13 m
Dawes B, 2014	head	27	17	mass	y	2 m
Guo F, 2014	head	49	19	mass	y	still alive 4 m FU
Okoshi A, 2008	neck	30	10	mass	y	12 m
Fenzi F, 1995	neck	35	10	mass	y	18 m
Lekovic GP, 2020	neck	24	4	mass	y	6 m
Yi Sun, 2016	neck	46	20	mass	y	still alive 12 m FU
Eryilmaz MA, 2014	head	47	10	mass	y	12 m
West DA, 1997	pelvis	32	8	mass	y	7 m
Chen M, 2023	breast	N/A	N/A	thickening and edema of brachial plexus	y	still alive 2 m FU
Salvucci G, unpublished	neck	24	36	thickening and edema of brachial plexus	n	2 weeks

Clinical and radiological characteristics of all malignant peripheral nerve sheath tumors reported in the literature.

Conclusion: post-radiation MPNST can occur up to 40 years after radiotherapy and it can present as an isolate brachial plexopathy without focal hypermetabolism. Since surgery may be beneficial, close radiological monitoring and early diagnostic biopsy in high-risk patients with brachial plexopathy is strongly recommended.
Disclosure: Nothing to disclose.

EPO-667 | Extending the spectrum of paraneoplastic syndromes mediated by anti-Yo antibody

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Background and Aims: Stiff-person syndrome (SPS) is characterized by fluctuating hypertonia and painful muscular spasms increasing with external stimuli being frequently mediated by anti-GAD antibodies, or amphiphysin antibodies in paraneoplastic variants. We report a case of SPS, preceded by cerebellar ataxia, with positive titles of anti-Yo antibody.
Methods:
Results: A female patient, 69 years old – with previous history of peritoneal carcinomatosis secondary to Fallopian tube carcinoma, which underwent chemotherapy with carboplatin and paclitaxel and cytoreductive surgery – developed subacute dizziness, axial and appendicular ataxia and memory disturbances during the chemotherapy cycles. While brain-CT and MRI were normal, EMG documented an axonal sensory-motor polyneuropathy. Anti-Yo antibody was positive both in serum and LCR. Assuming a cerebellar degeneration associated with anti-Yo syndrome, intravenous immunoglobulin and high dose methylprednisolone were started. Due to absence of benefit regarding the ataxia and falls with osteoporotic fractures, treatment was suspended. During the following two months, she developed painful inferior limbs spasms, aggravated by external stimuli, with an ascending pattern of truncal and cervical involuntary muscular contractions, with hypertonia and gait impairment. While maintaining exclusively anti-Yo antibody positivity, a second EMG registered abundant continuous motor unit potentials detected on the inferior limb muscles, independent of voluntary muscular activity. Neuraxis-MRI, anti-GAD and amphiphysin were negative. Gradual recovery of autonomous gait occurred with 9 cycles of monthly IVIG.
Conclusion: We underline the diversity of clinical presentations of SPS while highlighting a possible association with Anti-Yo antibody, not yet described, and emphasizing the positive therapeutical response.
Disclosure: Nothing to disclose.

EPO-668 | Extranodal NK/T cell lymphoma with primary CNS manifestation – A case report

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Background and Aims: Rare extranodal NK/T cell lymphoma (ENKTCL) occurs predominantly in Asian and Latin American countries and preferentially arises in the nasopharynx. Although EBV is normally restricted to B lymphocytes, it has been associated with tumor cells of NK/T cell origin in malignant NK and T cell tumors. EBV increases gene instability, incidence of ENKTCL and enhances escape mechanisms from T cell-mediated immune responses. We report here a rare case of EBV associated ENKTCL with a primary CNS manifestation and haemophagocytic lymphohistiocytosis (HLH).
Methods: This retrospective case report fulfills the CARE criteria.
Results: The patient initially presented herself for nuclear facial palsy. MRI of the brain showed brain stem lesions and elevated EBV copies were detected in the cerebrospinal fluid. An initial CT scan of the lungs and a sonography of the abdomen revealed no lesions. Over the course of two months, the patient developed progressive clinical symptoms and multilocular CNS lesions. Due to the high EBV copies, a rituximab infusion was performed to deplete the B cells, but did not improve clinical symptoms. The patient successively

developed a secondary HLH. A liver biopsy was performed due to the HLH-associated hepatomegaly, revealed an ENKTCL. An additional brain biopsy detected lymphocytic infiltration consistent with ENKTCL, mainly of NK cells and localized EBV type 1 in the tumor cells.

Conclusion: ENKTCL may initially manifest in the CNS. Unclear CNS lesions with massively increased intrathecal EBV copies may indicate a lymphoma in which malignant cells derived from NK/T cells can be infected with EBV.

Disclosure: Nothing to disclose.

EPO-669 | Successful identification and management of a SMART syndrome occurring 36 years after cranial radiotherapy

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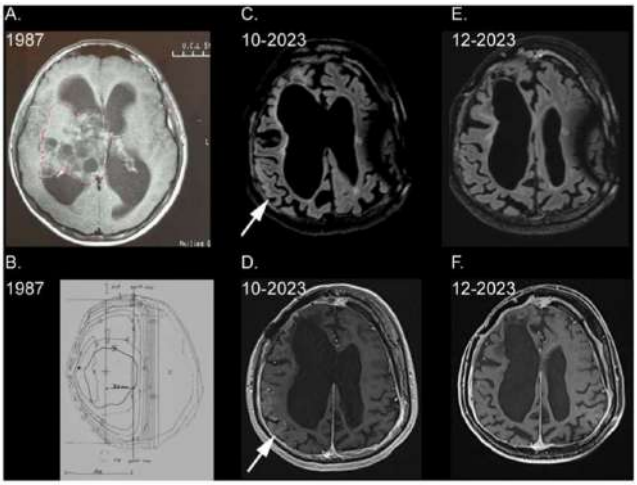
Background and Aims: Radiation therapy (RT) is a cornerstone in the management of brain tumors, either alone or combined with surgery and/or systemic therapy. SMART syndrome (stroke-like migraine attacks after RT) is a rare neurological disease believed to be a late-onset side effect of cranial RT and consists in stroke-like symptoms, epilepsy and migraine (Dossin et al., 2023; Shuper et al., 1995). This syndrome has been observed within a timeframe of 1 to 37 years after RT. Pathophysiology is believed to be multifactorial, involving white matter necrosis, vascular endothelial damage, demyelination and gliosis (Ota et al., 2023; Turnquist et al., 2020). We report a case of SMART syndrome presented with severe left hemiparesis and left facial palsy which was successfully managed with steroid pulse therapy (1000 mg/day, 5 days) (Jia et al., 2018; Ota et al., 2023).

Methods: We reviewed literature.

Results: On 4th day of treatment, he was able to walk again with a return to his basis state. Six weeks later, the patient condition was stable without any relapse. Strength on the left side was back to its initial level (i.e., slight paresis without any facial asymmetry).



A. T1 MRI sequence showing the tumour at the time of diagnosis (1987). B. Radiation dose distribution for the 24-Gy sequential boost (1987). C. T2 FLAIR MRI sequence showing hyperintensity of right parieto-occipital cortex (10-2023). D. T1 post-gadoliniu.

Conclusion: In conclusion, we report here a case of successful treatment of SMART syndrome occurring 36 years after RT, which is one of the latest occurrences of this syndrome ever described (Ota et al., 2023). We believe that recognizing SMART syndrome in patients with a history of cranial RT, even after a prolonged period, is crucial to avoid misdiagnosis and subsequent improper treatment.

Disclosure: Nothing to disclose.

EPO-670 | Autoimmune encephalitis in the era of immune-checkpoint inhibitors: Descriptive study in a tertiary hospital

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[1]Department of Neurology and Centre d'Esclerosi Múltiple de Catalunya (Cemcat); Vall d'Hebron University Hospital, Barcelona, Spain; [2]Immunology Department, Vall d'Hebron University Hospital, Barcelona, Spain

Background and Aims: This study aims to characterize patients with autoimmune encephalitis (AE) in a tertiary hospital and explore its association with cancer and immune checkpoint-inhibitors (ICI) treatment, providing valuable insights for effective treatment strategies.

Methods: Retrospective single-centre study from 2017 to 2023 including patients with antineuronal antibody (ANA) (2 techniques) or with definite immune-related encephalitis secondary to ICI. We analyzed clinical differences between subgroups with or without cancer and with or without ICI exposure.

Results: Thirty-one patients were included [64.5% female, median age 59.7 (range 37.9–69.1)] with a median follow-up of 34.6 months (range 10.5–69.6). Patients had various ANA including GAD65 ($n=6$), Hu ($n=4$), NMDAR ($n=3$), Yo ($n=3$), other ANA ($n=13$) and two seronegative treated with ICIs. Median PNS-Care score was 7 (range

4–9.5). 19/31 (61.3%) were cancer-associated, 8 had neurological symptoms before cancer diagnosis, 7 after ICI and 4 after cancer diagnosis without ICI. Among patients with cancer, 14 were advanced (lymph nodes or distant metastasis) at neurological onset. 5/31 (16.1%) patients deceased, 4 due to tumor progression. Patients with concomitant cancer were older (median 62.0 years [range 49.8–71.0] vs 38.8 [range 21.2–61.6] $p < 0.05$) and had a shorter time to treatment from disease onset (median 1.2 months [range 0.5–5.0] vs 20.4 [range 3.4–33.3] $p < 0.05$), without differences in prognosis or ICI treatment in alive patients.

Conclusion: Our study suggests that patients diagnosed with AE in recent years are frequently associated with advanced cancer which is already under treatment. Future studies are needed to optimize the management of this prevalent subpopulation.

Disclosure: Nothing to disclose.

EPO-671 | Outcomes of patients with neoplastic meningitis undergoing ventriculoperitoneal shunting and intrathecal chemotherapy

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Background and Aims: To present the outcomes of a retrospective cohort of patients with leptomeningeal disease (LMD) who received placement of ventriculoperitoneal shunt (VPS) and Ommaya reservoir for intrathecal chemotherapy.

Methods: We performed an in-depth chart review using electronic medical records of patients with LMD who had undergone placement of VPS and Ommaya in a single institution over a three-year period.

Results: Eighteen patients with LMD underwent VPS placement and Ommaya reservoir for intrathecal chemotherapy. Eleven patients had breast cancer, four had lung cancer, and the remaining three patients had thyroid, esophageal and uterine cancer respectively. Seventeen patients are deceased, and one patient was lost to follow up, and not included in our analysis. Sixteen (94%) patients had brain metastases. Eleven patients (61.1%) received radiotherapy prior to VPS placement. Karnofsky scores ranged from 60 to 90. Seven (41%) patients did not receive intrathecal chemotherapy due to rapid LMD progression. Ten (59%) patients received intrathecal Topotecan, and one received Cytarabine at the time of disease progression. The overall survival of these patients from time of VPS placement was 15.15 weeks (range 4.1–203.2), of which seven (41%) survived less than eight weeks. Six (60%) patients died from LMD progression, three (30%) from systemic disease progression, and one (10%) died of medical complications.

Conclusion: Our retrospective analysis suggests urgency for early diagnosis of LMD with increased intracranial pressure, along with spinal fluid diversion procedures for intrathecal chemotherapy administration. These interventions may allow for prolongation and improvement in quality of life.

Disclosure: Amulya Gottiparthy, Lauren Orda, Emily Morrow, and Monica LoghinDr. Gottiparthy has nothing to disclose. Mrs. Orda-Nguyen has nothing to disclose. Mrs. Morrow has nothing to disclose. Dr. Loghin has nothing to disclose.

EPO-672 | Prevalence of systemic neoplasms in a cohort of adult neurofibromatosis 1 patients: A single-center retrospective study

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Background and Aims: Neurofibromatosis type 1 (NF1), the most frequent hereditary cancer predisposition syndrome, is characterised by occurrence of tumours in both central and peripheral nervous systems (CNS and SNP), with a 5–15% higher risk of developing a neoplasm outside CNS and SNP, compared to general population. Our study aims to assess systemic cancer prevalence in a patient's cohort.

Methods: Demographic and clinical data of NF1 patients, diagnosed according to established international criteria, were analysed.

Results: In a cohort of 127 individuals [54.2% women, median age 44.6 years (SD 17.5)], participating in NF1 surveillance programme for median duration of about 10 years, 13.38% (17/127) had systemic cancer. Patients' mean age at cancer diagnosis was 43.4 years (range 6.84–76.6). Breast cancer (23.8%) was the most frequently encountered malignancy, followed by prostate cancer (17.6%), gastrointestinal (11.8%), gynaecological (11.8%), bone (11.8%), pheochromocytoma (5.9%), melanoma (5.9%) and haematological cancers (5.9%). Except for sex-unrelated tumours, no difference was found between sexes. However, 2 out of 3 patients with a previous diagnosis of malignant peripheral nerve sheath tumour (MPSNT) developed bladder cancer and pheochromocytoma at a median follow-up of 3 years, with a significant correlation ($p = 0.041$).

Conclusion: NF1 patients develop systemic neoplasms more frequently than the general population. Co-presence of a MPSNT tumour seems to be correlated with an increased risk of developing systemic tumours later in life. Adequate cancer screening in NF1 patients therefore requires a lifelong care model to prevent aggressive cancer development and to improve patients' life expectancy and quality of life.

Disclosure: Nothing to disclose.

EPO-673 | Atypical debut of systemic lymphoma with CNS involvement

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Hospital Central de la Defensa "Gómez Ulla"

Background and Aims: CNS involvement in patients with systemic lymphoma is an uncommon complication affecting ≤5% of patients, being even more atypical to debut with neurological manifestations. We present a case debuting with CNS symptoms with final diagnosis of lymphoma.

Methods: A 68-year-old male with 5 days of dysarthria, gait disturbance, bradypsychia and incoherent speech after tooth extraction 15 days before with uncertain infection, without fever or other systemic data.

Results: Brain CT was normal, laboratory tests showed hypercalcemia, EEG displayed moderate diffuse encephalopathy and LP showed 10 mononuclear leukocytes/mm^3 and hyperproteinorrachia 85 mg/dl without glucose consumption, suspecting possible encephalopathy due to hypercalcemia. The patient's level of consciousness worsened and he was admitted to the ICU requiring OIT. Suspicion of infectious encephalitis led to initiate antibiotic, which was suspended after negative microbiology. LP was repeated with 12 leukocytes/mm^3 and hyperproteinuria 53 mg/dl. Given the persistence of non-infectious inflammatory LP, a complete blood test performed showed pancytopenia, elevated beta2-microglobulin and LDH, a brain MRI without findings and another EEG with moderate-severe encephalopathy, so high-dose corticotherapy was started with excellent response and complete resolution of the symptoms. BM biopsy was normal. In the complementary etiological study, a PET-CT scan showed a hypermetabolic lesion in the left adrenal gland which was biopsied and demonstrated an intravascular lymphoma. Intrathecal+R-CHOP systemic chemotherapy was started with poor response.

Conclusion: Intravascular lymphoma is a rare subtype of diffuse large cell B-cell lymphoma that presents CNS involvement in 30–40% of cases and can be associated with adrenal gland involvement in up to 50–75%. This entity represents an important diagnostic challenge that requires a high clinical suspicion given the wide variability in its presentation and its low incidence.

Disclosure: Nothing to disclose.

EPO-674 | Peri-ictal Pseudoprogression: A rare entity to bear in mind in patients with brain tumors treated with radiotherapy

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[2]*Neuroradiology Department, Hospital de la Santa Creu i Sant Pau*

Background and Aims: The differential diagnosis in patients with brain tumors treated with radiotherapy who present with epileptic seizures might be challenging. Apart from tumoral progression, one entity to consider is peri-ictal pseudoprogression (PIPG). Clinical features include recurrent epileptic seizures or status epilepticus and progressive focal deficits.

Methods: We present the case of a 63-year-old woman who presented in the emergency room due to progressive weakness in the left upper limb and recurrent focal motor seizures involving the left face with impaired awareness. She had a history of a grade II oligodendroglioma treated with surgery and adjuvant chemoradiotherapy seven years before. She was on remission accordingly to the brain MRI performed one month earlier.

Results: The electroencephalogram (EEG) showed electrographical seizures involving the right centrotemporal region (Figure A, B). Levetiracetam 1.5 g/12 h was initiated. Due to the persistence of clinical and electrographical seizures in the follow-up EEGs, lacosamide 150 mg/12 h was added with clinical improvement. However, the brachial paresis persisted. Brain MRI showed a cortical hyperintensity with meningeal enhancement in the right frontotemporal-parietal region, suggestive of PIPG. Patient was discharged. In the outpatient clinic, there was evidence of motor improvement and a gradual reduction of antiseizure drugs was performed without seizure recurrence.

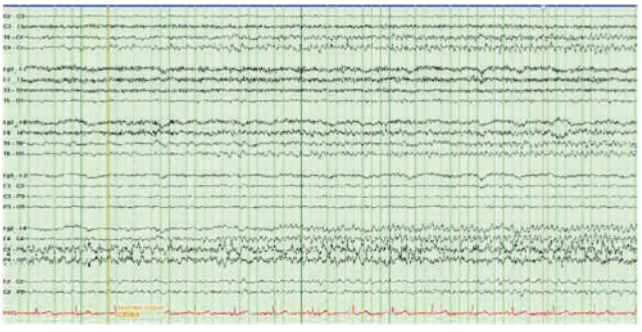

FIGURE A EEG part 1.

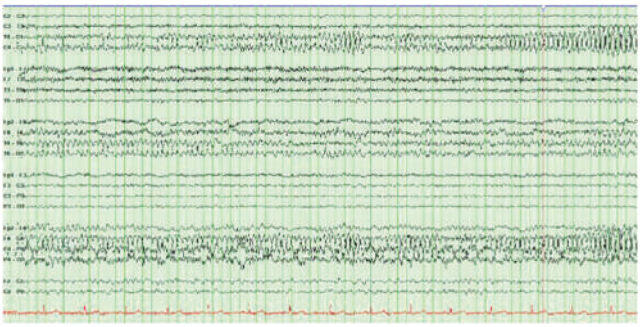

FIGURE B EEG part 2.

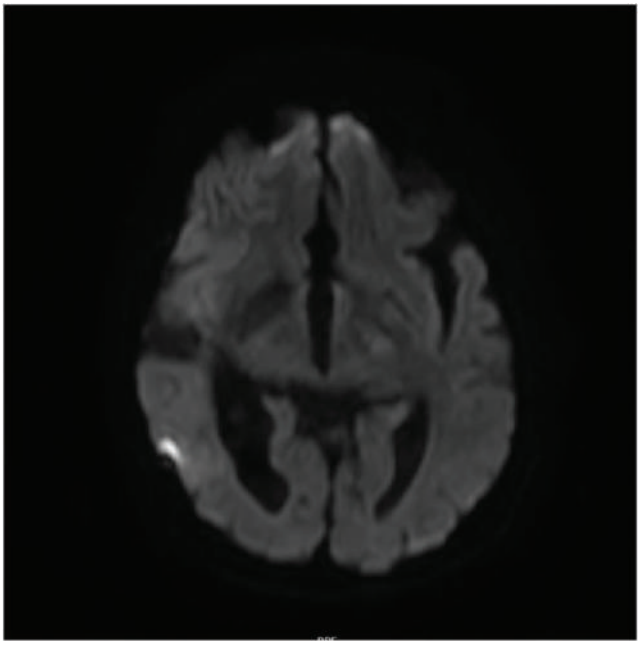

FIGURE C MRI.

Conclusion: PIPG is a rare entity that should be considered in patients treated with radiotherapy who present with typical clinical and neuroimaging features. In the coming years, the incidence is likely to increase due to the recent indication of radiotherapy in low-grade gliomas, a treatment that was previously reserved for high-grade gliomas.
Disclosure: Nothing to disclose.

Neurological manifestation of systemic diseases

EPO-675 | Acute intermittent porphyria as a rare cause of pontine and extrapontine myelinolysis: A case report

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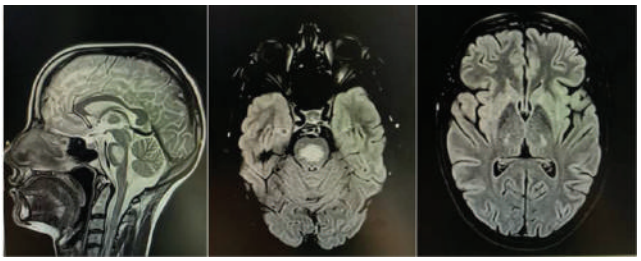
Background and Aims: Developing of severe hyponatremia attributed to inappropriate antidiuretic hormone secretion during a crisis of acute porphyria can be complicated by central pontine (CPM) and extrapontine myelinolysis (EPM). Usually acute intermittent porphyria (AIP) attacks manifest as a combination of abdominal pain, neuropsychiatric symptoms, and autonomic dysfunction.
Methods: A single case presentation.
Results: A 24-year-old female was admitted with a clinical and MRI signs of EPM and CPM. During 3 weeks before admission she was staying at the local clinic with intense abdominal pain, nausea with episodes of repeated vomiting, episodes of hyperthermia, hallucinations, confusion and electrolyte imbalance: Na – 117, K – 2.7, Cl – 78 mmol/L. Despite of electrolyte normalization, neurological examination revealed cognitive and behavioral changes, bulbar disorders, paresis of the right arm, head and hand tremors, cerebellar ataxia, and unable to walk independently. MRI showed symmetrical lesions of the basal nuclei, thalamus, central parts of the Varolii pons and cortex of both frontal lobes. After transferring to our clinic patient was successfully treated with intravenous immunoglobulin with resolving neurological symptoms of EPM and CPM. After accidental raspberry color of urine detection the assumption of possible intermittent porphyria was made. Urine analyses revealed increased concentration of porphyrin precursors porphobilinogen, delta-aminolevulinic acid, uroporphyrin, coproporphyrin.



Brain MRI shows hyperintensive pontine lesion (14 × 18 × 24 mm) and bilateral thalamic lesions (6 × 9 mm).

Conclusion: We report this case to emphasize the clinical manifestations of AIP, including combination of gastrointestinal syndrome and electrolyte imbalance, especially hyponatremia due to possible antidiuretic hormone deficiency that may threaten of CPM/EPM development.
Disclosure: Nothing to disclose.

EPO-676 | Cerebellopontine abscess due to Listeria monocytogenes

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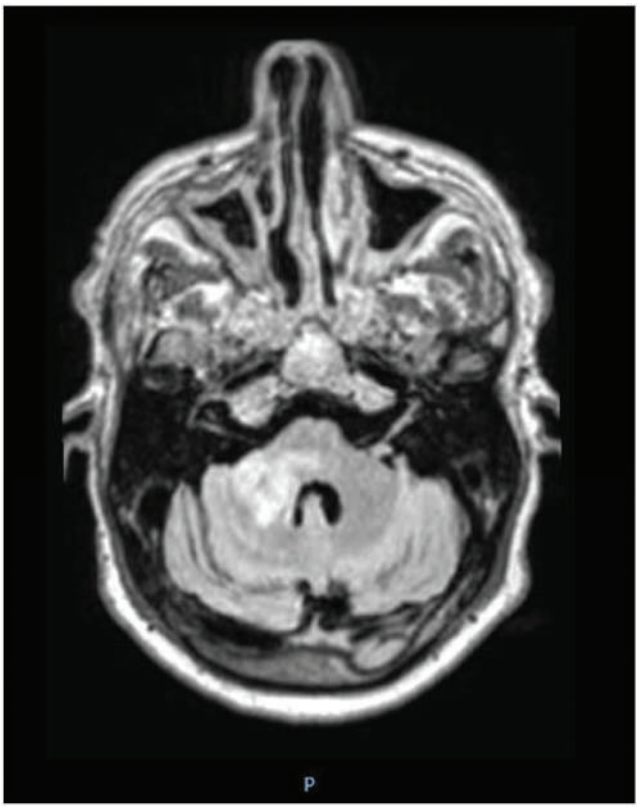
Background and Aims: Listeria monocytogenes is a gram-positive anaerobic bacillus with special tropism for the central nervous

system. The main form of neurological involvement in adults is meningitis, with rhombencephalitis and brain abscess being rarer, but with a worse prognosis.

Methods: Clinical case.

Results: A 62-year-old man with type 2 diabetes came to the emergency department with fever, headache and hypoesthesia in the left hemibody of three days of evolution. Baseline CT, CT angiography and complete blood tests were performed in the emergency room without alterations. Brain MRI showed a heterogeneous lesion in the cerebellopontine angle and raised the possibility of infectious vs. tumor pathology. CSF study was performed with normal cell count and biochemical composition and negative multiparametric PCR. Given the persistence of fever and clinical progression with the appearance of dysphagia and dysmetria in the left extremities, neurosurgery was contacted to propose a stereotactic biopsy of the lesion. Multiplex PCR was performed on the extracted material and was positive for Lysteria Monocytogenes. In view of these findings, ampicillin was started at high doses.



Conclusion: We present the case of a patient with cerebellopontine abscess due to Listeria monocytogenes, an atypical presentation with high morbidity and mortality rates. In our patient, support with diagnostic tools such as stereotactic biopsy was key to lead to the etiologic diagnosis and guide targeted antibiotic treatment.

Disclosure: Nothing to disclose.

EPO-677 | Papilledema in hypocalcaemia: A condition not to overlook

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Background and Aims: Papilledema associated with hypocalcaemia is rare, and its precise pathophysiology remains unclear. The proposed causal mechanisms include vasoconstriction and disturbances in cerebrospinal fluid (CSF) dynamics. The prognosis depends on the underlying cause of hypocalcaemia, as well as the promptness of the diagnosis and treatment.

Methods: Review of the patient's clinical records and of the relevant available literature on the topic.

Results: A 48-year-old female patient experienced a two-week progression of bilateral decreased visual acuity, more pronounced on the left eye. She also reported occasional generalized cramps and hand paresthesias over the prior year. Her past medical history included iatrogenic hypothyroidism (9 years before, due to multinodular goitre), gastric bypass surgery (3 years before), and obesity. Neurological examination revealed bilateral papilledema and reduced visual acuity (left: 0.3; right: 0.8). Optical coherence tomography confirmed asymmetric bilateral papilledema. Brain and orbital MRI were unremarkable. Blood work revealed severe hypocalcaemia (5.2 mg/dL [8.7–10.4 mg/dL]) and low parathormone. Extensive autoimmune and infectious serological testing was all negative. Calcium replacement was initiated. Lumbar puncture, performed already under treatment, showed normal opening pressure. The remaining CSF tests were normal/negative. Hypocalcaemia was attributed to the surgical hypoparathyroidism and the bariatric surgery. Three months later visual acuity had improved (0.8 bilaterally) and the papilledema had resolved.

Conclusion: Hypocalcaemia-associated papilledema is a rare, yet manageable condition. When faced with cases of papilledema, assessing calcium metabolism may prove essential, especially in people with a past history of thyroid/parathyroid surgery or other risk factors for hypocalcaemia. Awareness and prompt treatment, as in our case, is crucial for improving the prognosis in this clinical setting.

Disclosure: Nothing to disclose.

EPO-678 | CSF and blood signatures aid in distinguishing subtypes of limbic encephalitis

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Background and Aims: Limbic encephalitis (LE) represents a heterogeneous disease with antibodies targeting extracellular (LEextra) epitopes, intracellular (LEintra) epitopes, and anti-glutamic acid decarboxylase 65 LE (LE-GAD65). Moreover, LE can be diagnosed without evidence of antibodies (LEabneg). We aimed to determine immune profiles of these distinct forms of LE.
Methods: We apply computational biology to flow cytometry data of CSF/blood of LE patients comparing them to non-inflammatory controls (Ctrl) or patients suffering from relapsing remitting MS (RRMS).
Results: We identified discrete immune signatures in LE with antibody producing plasma cells and B cells as a specific feature of LEextra. In contrast, LE-GAD65 lacked inflammatory changes in CSF/blood immune profiles with LEintra falling in-between the two (LE-GAD65 and LEextra). Interestingly, similar to LE_GAD65 LEabneg showed no prominent inflammatory immune-signature.
Conclusion: Profiles identified may explain different treatment response to immunotherapy in subtypes of LE.
Disclosure: The authors have no relevant financial or non-financial interests to disclose.

EPO-679 | Risk factors, treatment and clinical outcomes of decompression sickness with neurological symptoms: A case-series study

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Background and Aims: The decompression sickness (DCS) is related to diving practice and could affect multiple organs, including the central nervous system. The incidence of DCS with neurological symptoms is estimated in 2.7/10,000 dives and may cause both brain and spinal cord symptoms. Given the little knowledge about the DCS, the potential severity of its neurological symptoms and the difficult acute diagnosis and treatment, here we report a case-series.
Methods: This is a retrospective single centre case-series study evaluating the risk factors and treatment of consecutive patients diagnosed with DCS at the Santa Lucía University Hospital, Cartagena; Spain, between 2003–2023. All patients received hyperbaric oxygen therapy.
Results: 15 patients were included in this study. All were Caucasian male, the median age was 47.3 (range: 22–66). The time of symptoms onset was 37.8 minutes after diving. 6 (40%) patients were diagnosed with brain hemispheric syndromes, 1 (6%) with posterior reversible encephalopathy syndrome (PRES), 3 (20%) with brainstem syndromes and 5 (33%) with spinal cord syndromes. MRI scans demonstrated multiple territory stroke lesions and spinal cord lesions in 12 (80%) and 5 (33%) patients, respectively. The main risk factor for DCS was an inadequate diving profile while patent foramen ovale was demonstrated in 4 patients (27%). The mean of the Modified Rankin Scale (mRS) after 3 months was 1.9.
Conclusion: An unsecure diving profile is the main risk factor. Both, a correct diagnosis and emergent treatment are the cornerstones in the management of the DCS by neurologists.
Disclosure: The authors declare no conflict of interest.

EPO-680 | Post-cytomegalovirus Guillain-Barre syndrome with anti-GM2 antibodies and acute transverse myelitis overlap syndrome

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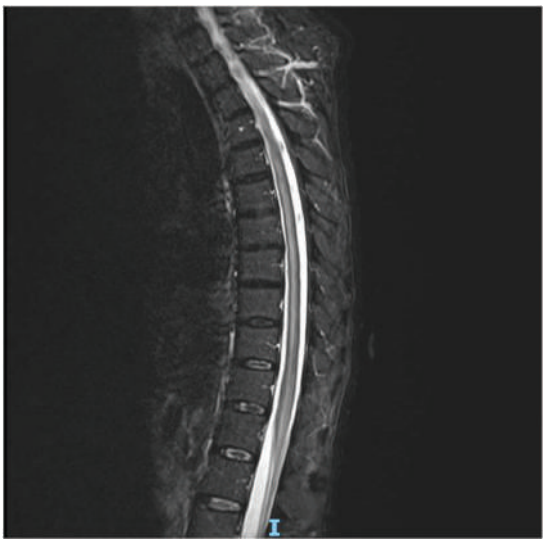
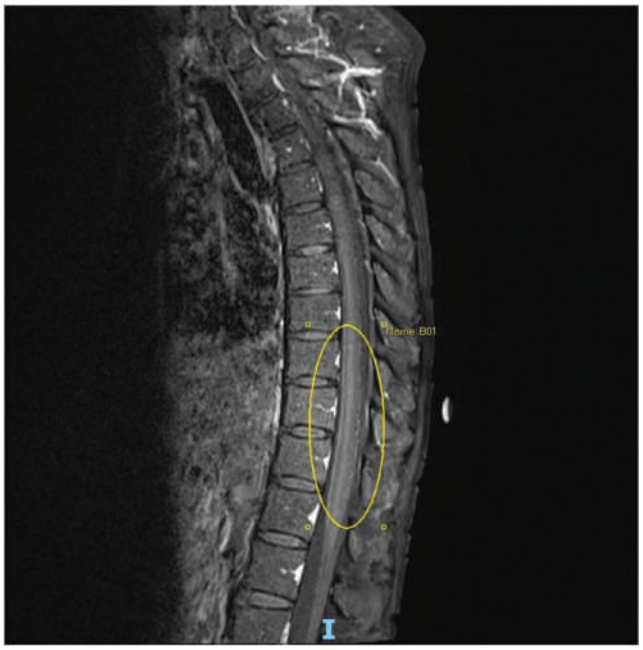
Background and Aims: A 55-year-old male presented with a three-week history of progressive lower limb weakness, distal limb paresthesia, resulting in gait instability and multiple falls. With a medical history of Angioimmunoblastic T Lymphoma and autologous stem cell transplant, he was immunosuppressed with tacrolimus. A recent hospitalization for CMV viremia infection, resolved with antiviral therapy, was noted. Clinical examination revealed flaccid lower limb weakness, impaired distal proprioception sense, and diminished deep tendon reflexes.
Methods: Nerve conduction studies demonstrated demyelinating sensorimotor polyradiculoneuropathy predominantly lower limbs. MRI of the lumbosacral spine exhibited mild enhancement along the cauda equina nerve roots. Cerebrospinal fluid (CSF) analysis revealed characteristic albuminocytologic dissociation. Anti-GM2 IgG was strongly positive. The patient was initiated on intravenous immunoglobulin (IVIG) infusion.
Results: He subsequently developed worsening of weakness with new sensory deficit up to T10 and urinary retention. MRI of the cervical and thoracic spine revealed longitudinally extensive transverse myelitis. Infective workup, autoimmune screen, paraneoplastic panel, anti-NMO Antibody, and anti-MOG Antibody, yielded unremarkable results. Treatment involved intravenous methylprednisolone with concurrent plasmapheresis, resulting in neurology recovery.



T2 sequence of the MRI cervical and thoracic spine.



T1 sequence with contrast of the MRI cervical and thoracic spine.

Conclusion: Previous cases of GBS and ATM overlap syndrome were associated with various infections, including campylobacter jejuni, Zika virus, Mycoplasma pneumonia, Legionella pneumophila, Bartonella henselae, influenza virus, paramyxovirus, mumps virus, and varicella infection. Our patient represents the first reported case of GBS and TM overlap syndrome associated with CMV infection. First-line therapy for GBS and ATM overlap are not well defined. Our case responded well to treatment with intravenous methylprednisolone and plasmapheresis, resulting in a favorable neurological recovery.

Disclosure: Nothing to disclose.

EPO-681 | Clinical manifestation and treatment efficacy of visual pathway involved neurosarcoidosis: A multicentre cohort

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[1]*Oxford University Hospitals NHS Trust;* [2]*University Hospitals Birmingham NHS Trust;* [3]*University Hospitals Coventry and Warwickshire*

Background and Aims: Sarcoidosis affecting the anterior visual pathway (AVP) presents distinctly compared to other optic neuropathies, with delayed diagnosis leading to impaired visual outcomes. The objective of this study is to evaluate visual outcomes in neurosarcoidosis patients with AVP involvement, focusing on the impact of different manifestations and treatment initiation times.

Methods: Retrospective multi-centre cohort study.

Results: Forty-six neurosarcoidosis patients with AVP involvement from four UK tertiary centers were analyzed over a median follow-up of 1.90 years. Patients were categorized into optic neuritis (ON, $n=25$) and non-optic neuritis (NON, $n=21$) groups, and further into early treatment (ET, $n=13$) and delayed treatment (DT, $n=10$) groups. The ON group exhibited a more significant visual decline compared to the NON group ($p=0.015$), with similar baseline vision ($p=0.828$) and a slightly worse nadir vision (median 0.96LogMAR vs 0.3LogMar, $p=0.078$). Additional findings in the ON group included sudden visual loss ($p=0.072$), disc swelling ($p=0.086$), RAPD ($p=0.017$), T2 hyperintensity in AVP ($p=0.033$), and uninvolved chiasma ($p=0.064$). Visual acuity improvement, stability, and deterioration rates did not significantly differ between ON and NON groups ($p=0.765$). 22.2% of patients had final visual acuity worse than LogMAR 1.0 (29.1% in ON, 14.3% in NON). No significant difference was observed in overall visual improvement between ET and DT groups (61.5% vs 50%, $p=0.685$), with 30.8% in ET and 20% in DT having final visual acuity worse than LogMAR 1.0.

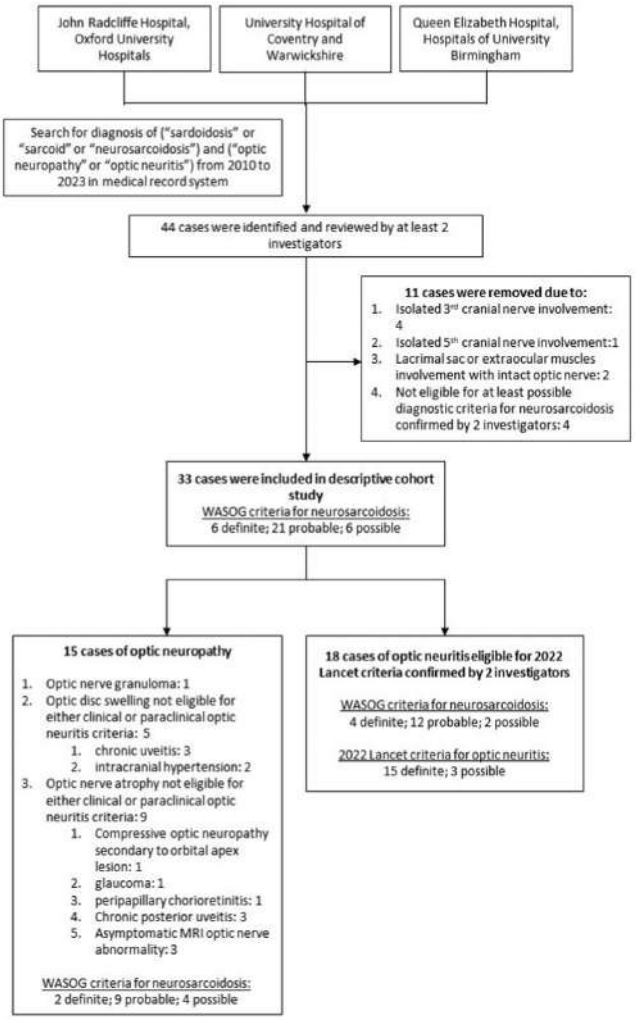

FIGURE 1 Retrospective Screening Flowchart.

Conclusion: AVP involvement in neurosarcoidosis shows varied clinical presentations. Delayed treatment yields a 50% non-responsiveness rate, not significantly differing from early treatment outcomes.

Disclosure: Nothing to disclose.

EPO-682 | Sensory involvement in patients with Sjogren's disease electrophysiological investigation

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Background and Aims: Sjogren's syndrome (SS) is a chronic, progressive, systemic inflammatory disease characterized by lymphocytic infiltration of exocrine glands. The main objectives of the study were to determine phenotypical patterns of peripheral nervous system involvement and the frequency of peripheral and central sensory involvement. We have also aimed to show the topography and extent of peripheral and central involvement by electrophysiological methods, and to examine the correlation of clinical and electrophysiological findings in patients with primary Sjogren's syndrome.
Methods: Thirty patients with Sjogren's disease were examined clinically with sensory symptoms, neurologic examination, modified Toronto Clinical Neuropathy Score and electrophysiologically with nerve conduction studies and somatosensory evoked potentials (SEP). The control group consisted of 30 healthy volunteers matched with the study group in terms of age and gender.
Results: A statistically significant difference was found in the mean median motor latency, mean tibial motor latency and mean tibial minimum F latency in the nerve conduction study parameters compared between the patient and control groups. Polyneuropathy was detected in three patients and all of them had pure sensory neuropathy. There was a significant correlation between the modified Toronto Clinical Neuropathy Score and the presence of polyneuropathy. In SEP examination no difference was detected in P37 latency, P37-N45 amplitude and P37-TP latency between the two groups.
Conclusion: In conclusion, this finding may indicate; 1. Sensory involvement was found to be present in Sjogren's syndrome. The sensory involvement was localized to peripheral nerves. 2. The sensory fibers in the dorsal column of the spinal cord were preserved.
Disclosure: there is nothing to explain.

EPO-683 | Combined subacute degeneration of spinal cord due to b12 deficiency: Pernicious anemia with hemolysis

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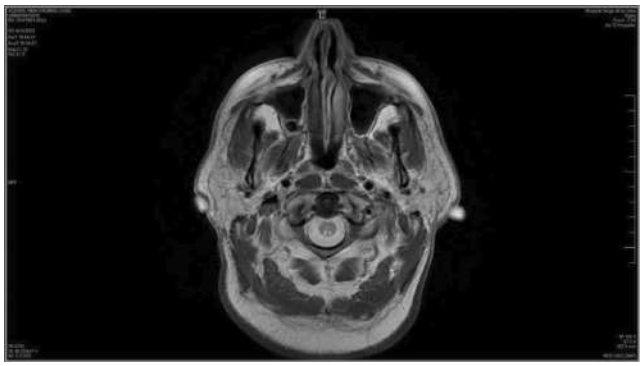
Background and Aims: Combined subacute degeneration is a neurological complication of B12 deficiency. Most common cause in adults is anemia perniciosa, due to autoimmune destruction of gastric parietal cells. It is associated to megaloblastic anemia with macrocytosis. Hemolysis is very rare and seen in only 10% of cases. It produces intramedullary ineffective erythropoiesis. B12 deficiency related hemolysis, presents as a pseudo-thrombotic microangiopathy (pseudo-TMA). Key features are low reticulocyte count and normal or mildly decreased platelets.
Methods: A 62 year-old male, with distal paresthesia, gait disturbance, fatigue and macrocytic anemia. His lab results showed low Hb 10 g/dl, elevated VCM 123 fL, elevated LDH 440 U/L, low haptoglobin 7.75 mg/dl, and schistocytes, with low absolute reticulocyte count (44.2 × 9, 1.72%). B12 levels were normal, but near to the normal low range 255 pg/ml. Hematology evaluation, ruled out autoimmune causes and TTP.
Results: He was admitted with suspicion of myelopathy. Initially, since B12 levels were normal and he had hemolytic anemia, cobalamin deficiency was not suspected. However, homocysteine levels were elevated 115 μmol/L. B12 deficiency was then suspected and intramuscular cobalamin was initiated. MRI showed typical signs of combined subacute degeneration. Pernicious anemia with elevated titers of anti-intrinsic factor antibodies (253.3 U/ml) was confirmed.



MRI. T2 axial. Inverted V sign: hyperintensity of dorsal horns, associated with combined subacute degeneration.

Conclusion: B12 deficiency can induce pseudo-microangiopathic hemolytic anemia in 10% of cases. Often, once hemolysis is seen, cobalamin deficiency is not investigated, leading to unnecessary tests. A normal lab result, must not rule out B12 deficiency when there is high clinical suspicion.
Disclosure: Nothing to disclose.

EPO-684 | A unique presentation of IgG4 disease with ocular, neurologic, and mastoid involvement

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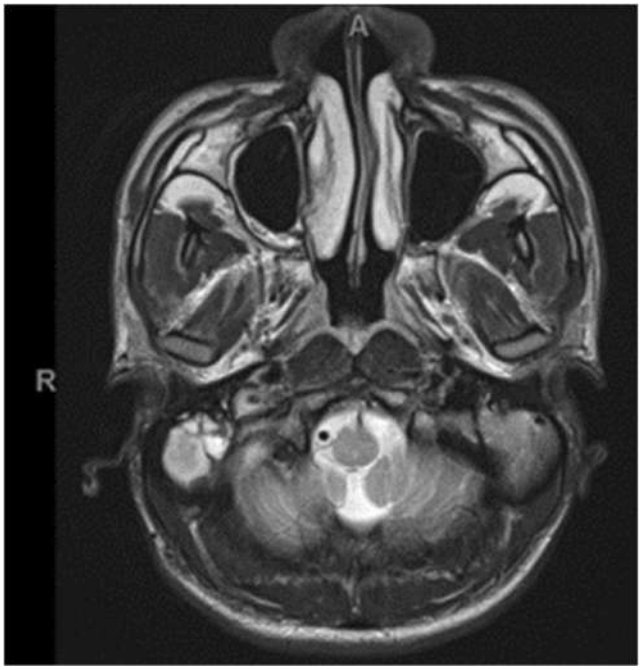
[1]Division of Neurology, Tygerberg Hospital and Stellenbosch University, Cape Town, South Africa; [2]NHLS, Tygerberg Hospital and Stellenbosch University, Cape Town, South Africa; [3]Division of Otorhinolaryngology, Tygerberg Hospital and Stellenbosch University, Cape Town, South Africa; [4]Division of Ophthalmology, Tygerberg Hospital and Stellenbosch University, Cape Town, South Africa

Background and Aims: Immunoglobulin G4 (IgG4) disease typically presents as pancreatitis, retroperitoneal fibrosis, sclerosing cholangitis or interstitial lung disease. Central nervous system (CNS) manifestations are rare. This is the first description of IgG4 disease presenting as panuveitis with associated mastoiditis and raised intracranial pressure. Case presentation: 27 year old male with sudden onset unilateral headache. After a few days, acute bilateral loss

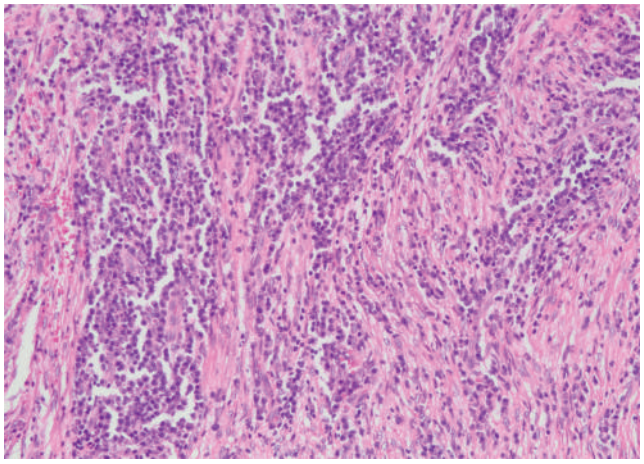
of vision, associated with tinnitus. He was found to have a non-granulomatous panuveitis and papilloedema.

Methods: CT brain demonstrated thickened optic nerves bilaterally and hyperostosis of the right mastoid. Right mastoid effusion in keeping with chronic mastoiditis was found on MRI. Lumbar puncture (LP) showed initial opening pressure exceeding 50 cm water, with normal chemistry and cell count. Serum ACE was raised, but CT chest and skin biopsy did not reveal any features of sarcoidosis. Mycobacterium tuberculosis, syphilis, mycoplasma pneumonia, HIV, and lymphoma test results were all negative. Sjogren, rheumatoid arthritis, and ANCA-vasculitis tests were also negative. There was no evidence of localised CNS infiltration and sinus thrombosis on imaging. Whole body FDG-PET confirmed mastoiditis.

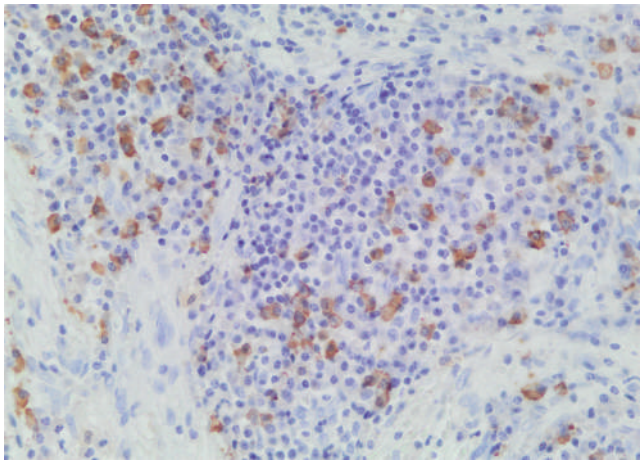
Results: Mastoid biopsy demonstrated a dense lymphoplasmacytic infiltrate with increased plasma cells and a storiform pattern of fibrosis.



T2 sequence MRI brain showing the hyperintense signal in the right mastoid.



200× microscopic examination revealing storiform fibrosis with an abundance of plasma cells.



400× immunohistochemistry showing more than 10 IgG4 positive cells per high power field.

Conclusion: The constellation of panuveitis, papilloedema (in the absence of inflammatory pseudotumour or secondary obstructive hydrocephalus following pachymeningitis), has not been previously described. There are only a limited number of reports of IgG4 chronic mastoiditis. The combination of FDG-PET/CT, along with biopsy may be prudent in atypical presentations. The patient was treated with high dose steroids, followed by long-term immunosuppressive therapy.

Disclosure: Nothing to disclose.

EPO-685 | The multisystem involvement of MERRF syndrome

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Background and Aims: Myoclonic epilepsy with ragged-red fibers syndrome (MERRF) is a mitochondrial multisystem disorder whose canonical clinical features are myoclonus, generalized seizures, ataxia, and ragged-red fiber myopathy. Approximately 80% of MERRF cases have the m.8344A>G mutation in the MTTK gene. Other clinical features include peripheral neuropathy, hearing loss, dementia, and multiple lipomas. The diagnosis is made in the presence of suggestive clinical findings and a genetic pathogenic variant.

Methods: A 63 year old man reports progressive proximal tetraparesia, exercise intolerance and involuntary movements of the right hand and foot. Additionally he has hearing loss and cervical lipomas. His mother also had cervical lipomas and died during his childhood. He has no siblings or children. Neurological examination showed proximal tetraparesis with muscular atrophy, right hand and foot dystonia with occasional focal myoclonia, ataxia, binasal hemianopsia, and hipoacusia.

Results: Cranial and cervical MRI were normal. EMG described axonal sensorimotor polyneuropathy. Blood analysis was unremarkable except for elevated CK. Ophthalmology evaluation revealed bitemporal optic atrophy. Cardiac evaluation revealed frequent supra ventricular extrasystole. The patient refused muscular biopsy.

A mitochondrial disease genetic panel revealed m.8344A>G mutation in the MTTK gene.

Conclusion: This case shows a defying diagnosis of a rare disease. Despite not all MERRF canonical features are present and the late age of onset, the patient has multiple suggestive clinical findings. The typical pathological genetic mutation found supports a MERRF diagnosis. The clinical and genetic heterogeneity of this disease renders this diagnosis a challenge, highlighting the need for future investigation.

Disclosure: Nothing to disclose.

EPO-686 | CAR T-cell-associated neurotoxicity: Single-center experience in a tertiary center

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Background and Aims: Chimeric antigen receptor T cells therapy (CAR-T) have revolutionized the treatment of patients with relapsed and refractory B- cell malignancies. CART therapy is associated with significant toxicities including cytokine release syndrome (CRS) and immune cell associated neurological syndrome (ICANS). The objective of this study is to describe the outcomes and treatments of CRS and ICANS in our hospital.

Methods: Retrospective descriptive study following five patients diagnosed of refractory diffuse large B cell lymphoma (DLBCL) treated with CAR-T therapy by the Department of Hematology. We registered age, sex, type of CAR-T used, MRI, EEG, acute phase reactant, CRS grade, ICANS, and treatment either with Tocilizumab or steroid.

Results: All five patients treated in our center developed CRS. About 60% developed CRS grade 1 and 40% CRS grade 3. Acute phase reactant (Interleukin-6, C-reactive protein and ferritin) increased in all CRS presenting patients. ICANS incidence was 80% from whom 75% were treated with steroids. Neurological related symptoms improved in all patients after steroid therapy.

Conclusion: Early recognition and treatment of ICANS associated with CAR-T is determinant for successful outcomes in patient receiving this therapy. A multidisciplinary approach is crucial to improve patient outcomes.

Disclosure: The authors have nothing to disclose.

EPO-687 | Myositis, axonal polyneuropathy and stroke in acute toxoplasmosis infection

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Background and Aims: Toxoplasma gondii is the most common cause of protozoan infection in humans. Toxoplasmosis has been associated with myositis and, in rare instances, with other neurological illnesses like polyneuropathies.

Methods: Description of a clinical case of a patient with systemic toxoplasmosis presenting several neurological affections such as myositis and sensory-motor axonal polyneuropathy.

Results: We present the case of a 56-year-old man from Gambia with heterozygous sickle cell disease. Following a recent trip to his native country, he was admitted to the hospital with a 20-day history of persistent fever, muscle pain, proximal debility, with an increase in CK levels. Serological tests showed positive IgM for T. gondii with a positive polymerase chain reaction. Antiprotozoal treatment and corticosteroids improved weakness and CK levels. Two weeks after admission, the patient experienced a progressive worsening of gait, autonomic dysfunction, and neuropathic pain. Examination revealed tetraparesis, bilateral facial paralysis, sensory ataxia, and generalized areflexia. Lumbar puncture indicated albumin-cytological dissociation, with no evidence of Toxoplasma in the cerebrospinal fluid. Electromyogram showed decreased sensory-motor amplitudes, with myopathic muscle recruitment. Plasma exchange was initiated suspecting Guillain-Barré syndrome, resulting in slight improvement. Brain MRI showed subacute thalamic ischemic lesion. Other autoimmune and infectious studies were rule out. Muscle biopsy indicated lymphocyte-predominant inflammation, MHC I overexpression and toxoplasma cysts, and peripheral nerve biopsy revealed mild axonal neuropathy.

Conclusion: In conclusion, we present a case of a patient with multiple systemic complications following toxoplasmosis infection. While neuromuscular complications have been documented, simultaneous involvement with polyneuropathy and myopathy has not been previously reported.

Disclosure: No disclosure.

EPO-688 | Acute neurological complications in liver transplanted patients: A retrospective single centre study

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Background and Aims: Neurological complications (NCs) occur in about 30 % of patients after orthotopic liver transplant (OLT). This study aimed to investigate early post-operative (PO) NCs after OLT

in our cohort of adult cirrhotic patients and to identify risk factors associated with the neurological outcomes.

Methods: We performed a retrospective single centre study; all patients who underwent deceased- and living-donor liver transplant between June 2014 and October 2021 were included. A PO acute NC was confirmed when symptoms and/or signs of central or peripheral central nervous system (NS) impairment occurred from the transplant but within the hospital stay.

Results: 275 men (73.14%) and 101 women (26.86%) were included; median age was 58 (range 22–70) years. NC occurred in 25% of patients. Encephalopathy was the most common NC (15.2%), followed by neurotoxicity (5.9%), seizures (3.7%) and central pontine myelinolysis (CPM) (3.2%). Patients with NCs had history of pre-transplant hepatic encephalopathy ($p<0.0001$), pre-surgical critical condition ($p=0.015$), higher Mayo End stage Liver Disease score ($p=0.0002$), history of pre-transplant renal insufficiency ($p=0.0124$) and a higher PO sodium shift ($p=0.01$).

Conclusion: Pre-operative neurological comorbidities, psychoactive drugs and age were not risk factors for PO NCs. NCs were correlated with PO adverse outcomes as infections, graft rejection, Intensive Care Unit (ICU) re-admission, in-hospital death, need of rehabilitation, in-hospital and ICU length of stay, post-surgical acute renal insufficiency. Our data confirm that the occurrence of NCs mostly depends on the severity of the pre-operative hepatic disease and/or systemic factors and do not depend on pre-operative neurological diseases other than HE.

Disclosure: The authors have nothing to disclose.

Sleep-wake disorders 2

EPO-689 | Clinical practice and actigraphic findings of daridorexant in chronic insomnia

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Background and Aims: Chronic insomnia, a prevalent sleep disorder, adversely affects daytime function and quality of life. This real-world study assesses the efficacy of daridorexant, a novel dual orexin receptor antagonist, in treating chronic insomnia using actigraphy over 1 and ongoing 3-month follow-ups.

Methods: Twenty-three adults (M 43.5%, F 56.5%, mean age: 56.5 ± 11.0 years) with chronic insomnia, according to the ICSD-3 criteria, were included in the study. Baseline and subsequent assessments at one month (23 patients) and three months (6 patients) involved the collection of subjective sleep parameters, including total sleep time (TST), wake after sleep onset (WASO), and latency to persistent sleep (LPS). Additionally, participants completed the Insomnia Severity Index (ISI) and the Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ). Ten patients underwent actigraphy at both baseline and one month.

Results: After one month of treatment, there was a statistically significant reduction in subjective LPS by 28 minutes (p 0.050) and WASO by 57 minutes (p 0.007), accompanied by a 32-minutes increase in TST (p 0.046). Questionnaire scores indicated a clinically meaningful reduction: ISI by 6 points ($p<0.001$), IDSIQ-total score by 22 (cut-off >17, p 0.012), and IDSIQ-cognitive domain by 10 (cut-off >4, p 0.004). Actigraphic data revealed a noteworthy 52-minutes increase in TST (p 0.042).

Conclusion: Our data confirmed Daridorexant efficacy after 1 month of treatment. Not only all sleep subjective parameters improved, but actigraphy showed an objective TST increase of almost one hour. It positively impacted quality of life, enhancing daytime cognitive functions, and significantly reducing insomnia severity.

Disclosure: Nothing to disclose.

EPO-690 | Compulsive gambling associated with modafinil: A case report

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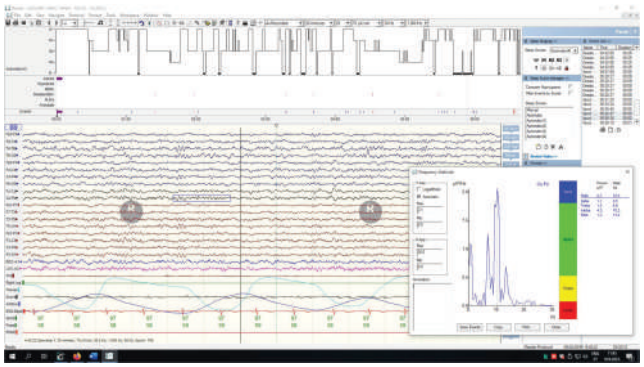
Department of neurology, University Clinical Center Republic of Srpska, Banja Luka, Bosnia and Herzegovina

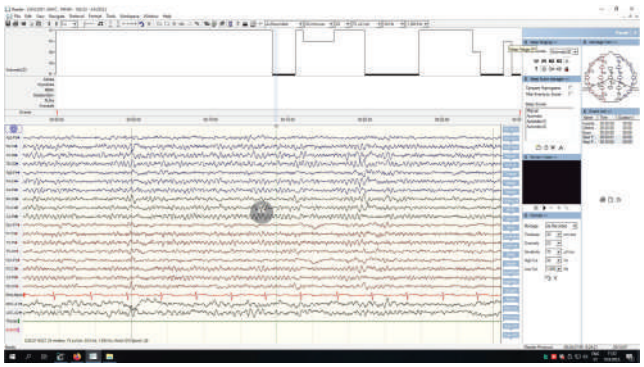
Background and Aims: We describe a case of new-onset compulsive gambling associated with the use of modafinil in a patient with type 1 narcolepsy (NT1).

Methods: Case report:

Results: A 21-year-old white woman presented to our clinic in 2023. She had history of excessive daytime sleepiness (EDS), cataplexy and sleep paralysis dating back for one year. She underwent diagnostic polysomnography (PSG) showed 7 REM sleep-onset periods, multiple sleep latency test (MSLT) with five naps showed an average sleep latency of 8 minutes and 2 sleep-onset REM periods, brain magnetic resonance (MR) imaging was normal. She was diagnosed with NT1 and commenced modafinil therapy started at a dose of 100 mg daily together with clomipramine 25 mg daily. She had no longer episodes of cataplexy but EDS symptoms only moderate controlled. One month later modafinil was increased at a dose of 200 mg daily. The patient's symptoms remained stable for the 8 months when she began gambling activities together with excessive alcohol abuse. On a follow-up visit she was refereed to psychotherapy together with lowering modafinil dose to 100 mg daily. Three months later, she reported improvement in the compulsive gambling and stopped drinking alcohol.



Polysomnography.



Multiple sleep latency test.

Conclusion: We described new-onset impairment of impulse control after taking modafinil which has been more commonly described in patients receiving dopamine agonist therapy.
Disclosure: Nothing to disclose.

EPO-691 | Pain in isolated REM sleep behavior disorder (iRBD): Study of association

G. Malomo[1]; E. Capriglia[1]; M. Solbiati[1]; L. Spelta[2]; A. Rubino[2]; C. Totaro[2]; D. Arnaldi[3]; P. Mattioli[3]; M. Pardini[4]; B. Orso[5]; F. Casoni[6]; L. Ferini Strambi[7]; A. Castelnuovo[7]; S. Natoli[8]; A. Pisani[9]; M. Terzaghi[1]

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Background and Aims: Non-motor symptoms in Parkinson's disease (PD) include chronic pain, which may occur in 20–80% of PD patients during the course of the disease. iRBD represents a prodromal phase for alpha-synucleinopathies including PD. Therefore, we aimed to identify the occurrence of pain and its characterization in an iRBD cohort.
Methods: 88 iRBD patients and 75 age- and sex-matched healthy controls were included; iRBD diagnosis was made according to ICSD-3rd criteria. Clinical evaluation included pain typology (PainDetect questionnaire) and pain perception (Brief Pain Inventory) together with motor evaluation (MDS-UPDRS), sleepiness (Epworth Sleepiness Scale), insomnia symptoms (Sleep Condition Indicator) and quality of sleep (Pittsburgh Sleep Quality Index), anxiety and depression (HADS-A, HADS-D) global cognition (MOCA), RBD scale (RBD questionnaire HK) and dopaminergic transmission (DAT-scan), measurements derived from PSG.
Results: Analysis of pain occurrence, typology and perception showed no statistically significant differences between patients and controls. In the iRBD group, statistically significant associations were detected between pain typology and perception and insomnia symptoms ($p=0.01$ and $p=0.15$ respectively) and sleep quality ($p<0.001$ and $p=0.03$ respectively). No association was found with other variables.
Conclusion: Chronic pain was not significantly increased in patients with iRBD. Mechanisms behind pain perception in iRBD may differ from those of PD-related neurodegeneration. We found a bidirectional correlation between pain and poor sleep quality in iRBD. Longitudinal data should be considered to evaluate a possible role as a marker of neurodegeneration.
Disclosure: Nothing to disclose.

EPO-692 | The levels of anxiety and depression in epilepsy based on insomnia phenotypes

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[1]Department of Neurology and Neurosurgery, National Institute of Health, Yerevan, Armenia; [2]Center for Sleep and Movement Disorders, Somnus Neurology Clinic, Yerevan, Armenia

Background and Aims: Insomnia is the commonest sleep disorder and is one of the most frequent of all mental health challenges. Insomnia phenotypes, namely sleep-onset (SOI), sleep-maintenance (SMI) and mixed insomnia (MI) are frequently encountered in adults with epilepsy (AWE). Our aim was to discover links between particular insomnia phenotypes with levels of depression and anxiety in AWE.
Methods: AWE were diagnosed according to international diagnostic criteria and enrolled from a specialized sleep and epilepsy clinic. According to insomnia clinical presentation we distinguished patients with no insomnia, SOI, SMI, and MI phenotypes based on interviews. Anxiety and depression were assessed using Hamilton Anxiety and Depression Rating Scales (HAMA and HAMD respectively). The ANOVA test was utilized for statistical analysis.
Results: A total of 170 AWE were interviewed for this study, with mean age 34.9 ± 13.4 (18–71), females – 46.5%. Seventy-eight

patients had insomnia (54.1%), divided into 29 (17.06%) with SOI, 11 (6.47%) with SMI, and 52 (30.59%) had MI. The mean values for HAMA and HAMD scales were 9.17 and 7.96 for no insomnia, 12.86 and 11.07 for SOI, 21.91 and 16.18 for SMI, 22.12 and 19.38 for MI, respectively ($p < 0.01$ for both scales). Box plots are presented in Figure 1 for HAMA and Figure 2 for HAMD.

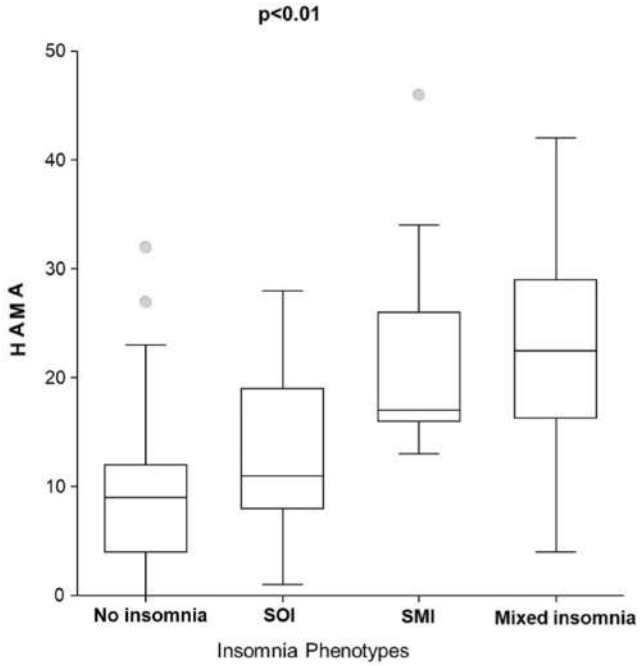

FIGURE 1 Box plot for Hamilton Anxiety Rating Scale (HAMA) according to insomnia phenotypes (SOI – sleep-onset insomnia, SMI – sleep-maintenance insomnia).

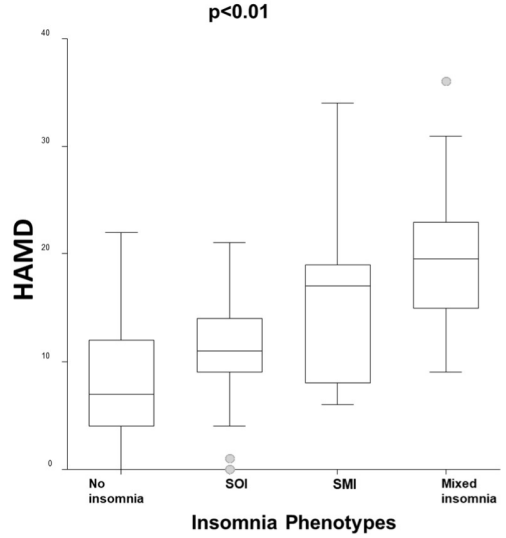

FIGURE 2 Box plot for Hamilton Depression Rating Scale (HAMD) according to insomnia phenotypes (SOI – sleep-onset insomnia, SMI – sleep-maintenance insomnia).

Conclusion: Our study highlighted a statistically significant difference in prevalence of anxiety and depression among AWE with different insomnia phenotypes. Specifically, AWE with no insomnia had the best profile, with gradually increasing severity in SOI, SMI, and MI respectively. Further research is needed to corroborate our findings.
Disclosure: Nothing to disclose.

EPO-693 | Case series of Prader-Willi syndrome and narcolepsy

I. Čelpačenko[1]; D. Burkojus[2]; G. Liakaitė-Obolevičienė[3]; E. Pajėdienė[1]
[1]Neurology Department, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Department of Pediatric Neurology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Department of Pediatric Pulmonology, Lithuanian University of Health Sciences, Kaunas, Lithuania

Background and Aims: Prader-Willi syndrome (PWS) is a rare genetic neuroendocrine disorder, which frequently presents with excessive daytime sleepiness (EDS) that may contribute to many clinical features of PWS. Sleep apnoea is a widely recognized cause of EDS in PWS, whereas other sleep disorders (SD), such as narcolepsy and cataplexy are only gaining recognition. PWS patients routinely undergo a polysomnography (PSG), however, more detailed differential diagnostics should be considered in patients exhibiting disproportionate EDS, as an effective treatment for narcolepsy is readily available and could substantially enhance patients' health, cognition, and behavioral problems.
Methods: Summarized patient's information included case history, Ullanlinna narcolepsy and Epworth Sleepiness scale scores, hypocretin-1 levels in cerebrospinal fluid (CSF), polysomnography (PSG) and Multiple Sleep Latency test (MSLT) results.
Results: Case series presents 1 male and 3 female patients with PWS, whose age ranged from 1 to 16 y/o. Based on clinical presentation, sleep studies and hypocretin-1 levels, all patients have been diagnosed with concomitant narcolepsy 1 type and sleep apnoea (Table 1)

Patient	No.1	No.2	No.3	No.4
Age	16 y/o	11 y/o	7 y/o	1 y/o
Sex	M	F	F	F
Ullanlinna scale (before treatment)	6 pts	22 pts	14 pts	-
Ullanlinna scale (after treatment)	24 pts	-	3 pts	-
Epworth Sleepiness scale (before treatment)	11 pts	15 pts	27 pts	-
Epworth Sleepiness scale (after treatment)	-	-	12 pts	-
PSG	AHI 6.7/h	-	AHI 6.5/h	AHI 1.2/h
MSLT	MSL 15 min	MSL 3 min 37 s	MSL 6 min 38 s	-
	-	2 SOREMP	1 SOREMP + epileptiform activity	-
Hypocretin-1 levels	94.3 ng/l	-	407 ng/l	131.8 ng/l

TABLE 1 Summary of patients' characteristics.

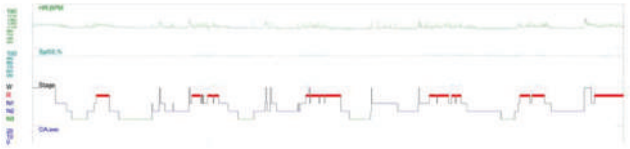

FIGURE 2 Hypnogram (patient No. 4).

Lights OUT (hh:mm:ss)	Sleep Onset (hh:mm:ss)	Sleep Latency (hh:mm:ss)	REM Latency (hh:mm:ss)
10:17:47	10:19:23	00:01:36	00:03:30
12:35:07	12:37:49	00:02:42	/
14:56:24	15:00:00	00:03:36	/
17:16:11	17:21:47	00:05:36	00:05:30

FIGURE 1 Multiple Sleep Latency test (patient No. 2).

Conclusion: This case series demonstrates that excessive daytime sleepiness in PWS may be attributable not only to sleep apnoea, but also to coexisting narcolepsy. Similarities in clinical presentation pose a challenge for the clinicians, therefore narcolepsy tends to be underdiagnosed. Multidisciplinary care is crucial for timely narcolepsy diagnosis and treatment.

Disclosure: Evelina Pajėdienė is a Co-chair of the EAN Scientific Panel for Sleep-wake disorders.

EPO-694 | iSPHYNCS: A multi-omics approach towards novel biomarkers for narcolepsy and its borderland

J. D. Warncke[1]; K. Zub[1]; E. Wenz[1]; L. G. Fregolente[1]; J. van der Meer[1]; O. Gnarra[1]; R. Morrand[1]; A. Helmy[1]; Z. Zhang[2]; R. Khatami[2]; S. von Manitius[3]; S. Miano[4]; J. Acker[5]; M. Tafti[6]; A. Datta[7]; R. Rezaei[8]; U. Kallweit[8]; D. Bijlenga[9]; J. de Boer[9]; G. Lammers[9]; B. Yilmaz[10]; S. Mougiakakou[11]; A. Tzovara[12]; M. H. Schmidt[1]; C. L. A. Bassetti[1]

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Background and Aims: The international Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (iSPHYNCS) aims at providing new data to improve the management of primary central disorders of hypersomnolence (CDH). The main aims of iSPHYNCS are: (1) discovery of new biomarkers, and assessment of (2) treatment adherence, and (3) outcomes related to patients. This abstract presents initial data related to the first objective.

Methods: The study is ongoing at 11 study sites in Switzerland, Germany and The Netherlands and plans to prospectively include 500 CDH patients and 60 healthy controls by the end of 2026. Initial evaluations comprise questionnaires, video-polysomnography, the Multiple Sleep Latency Test (MSLT), the Sustained Attention Response Task (SART), and actigraphy. Further analyses include a wearable Fitbit device, the microbiome, peptidomics/proteomics, and genetics. This comprehensive approach includes the collection of bio-samples: plasma, serum, DNA, stool samples, and cerebrospinal fluid. AI-driven analyses, including unsupervised clustering, will be used for data-driven patient phenotyping, followed by a multimodal approach that combines various data types after domain-specific analyses.

Results: 194 participants have been recruited, including 7 children. This group comprises 37 individuals with narcolepsy with cataplexy (NT1), 134 with other primary CDH, such as narcolepsy borderland (NBL), and 23 HC. Initial analyses reveal notable differences among

NT1, NBL, and HC groups across various domains, including questionnaire responses, neuropsychiatric profiles, microbiome, and Fitbit data.

Conclusion: Following an initial three-year phase in Switzerland, the internationalization of iSPHYNCS in 2023 was successful. Preliminary results suggest novel and promising clinical, biological and digital markers of CDH.

Disclosure: The authors declare no conflict of interest and the study is supported by the Swiss National Science Foundation (320030_185362 and 32003B_215721).

EPO-695 | Comparative characteristics of patients with obstructive sleep apnea and COMISA syndrome and their adherence to therapy

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Background and Aims: Insomnia and obstructive sleep apnea (OSA) are the two most common sleep disorders that are often comorbid to each other (comorbid insomnia and sleep apnea, COMISA).

Methods: Pittsburgh Questionnaire to determine sleep quality, the Epworth Sleepiness Scale. The study included 33 patients divided into 2 groups: 22 people with moderate and severe OSA and 11 people with moderate and severe COMISA syndrome. The diagnosis of OSA was verified according to respiratory sleep monitoring data. Average age of patients in group 1 was 53.5 years, the second group was 54.5 years. CPAP therapy was initiated for everyone, an automatic mode for 21 days. Follow-up visits were conducted after 1 and 2 weeks to monitor the effectiveness, technical characteristics and compliance of the treatment.

Results: Interpretation of the therapy data showed that in 11 patients of the first group, IAG averaged 6.9/h during the period of use, 5 patients were unable to use the device and refused therapy, in 7 patients of the 2nd group IAG was 14.9 /h, 6 patients were unable to use therapy and refused the study.

Conclusion: The data obtained indicate better adherence and better results of constant positive pressure therapy in patients with OSA without concomitant insomnia. It is advisable to offer treatment for both sleep disorders to patients with COMISA.

Disclosure: Nothing to disclose.

EPO-696 | Sex differences in isolated REM sleep behavior disorder: Insights from the FARPRESTO cohort

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Background and Aims: Inconsistent literature data hinders a comprehensive understanding of sex predominance and other sex-related distinctions in RBD. This investigation within the FARPRESTO multicentric, Italian, longitudinal cohort, aims to investigate variances between sexes in terms of the age of onset, diagnosis, and phenoconversion and to explore differences in cognitive and non-motor variables.

Methods: 558 iRBD patients were enrolled in the FARPRESTO study from 13 Italian centers, Age at RBD diagnosis, diagnostic delay, motor and non-motor symptoms, cognitive deficits, conversion rate to neurodegenerative disorders, and RBD-related injuries were analyzed according to sex. Statistical analysis utilized Mann-Whitney *U* and Pearson's chi-squared tests with significance set at $p < 0.05$.

Results: Mean age at the diagnosis was higher in females (males 62.0, females 65.0), whereas no significant sex differences in cognitive test scores were detected. Orthostatic hypotension and depression

were more prevalent in females (38.1 % vs 20.4 and 27.4 % vs 43.3 %, respectively). No difference in conversion rate has been reported. In addition, in women, injuries affecting patients at the first visit were significantly more frequent (71.0% vs 53.5%) than injuries affecting the partner or both.

Conclusion: Studies investigating sex differences in this field are still limited. However, as diagnostic and therapeutic possibilities advance, a nuanced understanding of sex-specific characteristics becomes increasingly essential for tailored clinical approach.

Disclosure: Nothing to disclose.

EPO-697 | The burden of insomnia and excessive daytime sleepiness: Switzerland's pilot study preliminary results

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Background and Aims: At present, the specific needs of individuals affected by excessive daytime sleepiness (EDS) and/or insomnia (IN) complaints, in conjunction with its overall socio-economic burden remains unexplored. To address this gap, a pilot trial for a multi-stage, European-wide, multi-center research study is being conducted in Switzerland since mid-2023.

Methods: prospective, national, cohort observational study for the systematic evaluation of the burden of EDS and IN and its evolution 12 months after the first assessment. Patient recruitment is facilitated through nine primary care providers, concluding in June 2024. Primary outcomes include the feasibility of the study, while secondary outcomes focus on the prevalence of EDS/IN in primary care settings and the association between EDS/IN and health-related quality of life (QOL), assessed using validated instruments. Patients are screened for EDS/IN, and those with positive indications are invited to participate in the online portion of the study comprised standardized and socio-economic/health status questionnaires.

Results: To date, 632 subjects have been screened, with 238 (44%) presenting EDS and/or IN. Of these, 111 expressed interest in participation, with 43 enrolled in an online segment. Among those with symptoms, 58% of individuals expressed concern for their symptomatology. A significant positive correlation was found between the presence of concern and medication usage ($p < 0.01$).

Conclusion: This research will provide long-due information and report on important aspects of the QOL most associated with EDS/IN. First data indicate a high frequency of these disorders as well as significant links between patients 'concerns and pharmacotherapy use.

Disclosure: Nothing to disclose.

EPO-698 | "Wet, wobbly, wacky and woke?"

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Background and Aims: Normal pressure hydrocephalus (NPH) is defined by a clinical triad of urinary incontinence, gait apraxia and cognitive impairment. Recent research has identified a high prevalence of sleep disordered breathing (SDB) in these patients. This audit investigates the diagnosis and management of patients with NPH and the prevalence of SDB in clinical practice.

Methods: Retrospective audit of clinical records from January 2014 to January 2024 ($n = 26$). Audit standards for diagnosis, investigation and management were defined from regional NPH guidelines. Prevalence of SDB in clinical practice was defined by Epworth Sleepiness Scale of 10–15 or diagnostic polysomnography.

Results: 26 (100%) patients had supportive neuroimaging and 23 (88.5%) patients had the full symptom triad. 22 patients (84.6%) had documented high volume CSF lumbar punctures and underwent gait assessment pre- and post-procedure. 13 patients (50%) progressed to ventriculoperitoneal shunt insertion, with all demonstrating symptomatic improvement. Only 2 patients (7.7%) were diagnosed with SDB, managed with non-invasive ventilation.

Conclusion: Documentation of diagnostic symptom triad, investigation, and management was completed to a high standard. However, the documented prevalence of SDB was significantly lower than in previous studies. These results suggest that SDB in NPH patients may be underdiagnosed, prompting inclusion of SDB to local

protocols. Future studies could investigate whether diagnosis and treatment of SDB improves outcomes for these patients.
Disclosure: Nothing to disclose.

EPO-699 | Importance of sleep quality and the effects of deprivation on doctors amidst conflict in Sudan

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Background and Aims: Healthcare professionals working in demanding environments and leading busy lives are more prone to burnout, disruptions in their sleep schedules, and sleep deprivation. These factors can affect their productivity and performance, potentially compromising patient care and medical outcomes. The main objective of this study was to evaluate the effects of sleep quality and deprivation on healthcare professionals in Sudan.
Methods: To achieve this objective, we conducted a cross-sectional study using a structured questionnaire after thoroughly reviewing the existing literature on Sudanese healthcare professionals. The study aimed to assess sleep quality, stress, anxiety, and depression and evaluate their impact on performance. Additionally, we explored the associations between personal backgrounds, susceptibility to burnout, and sleep disturbance.
Results: Our results revealed that the majority of participants experienced poor sleep quality and daytime sleepiness. We also found a significant prevalence of stress, anxiety, and depression among Sudanese healthcare professionals. Furthermore, we identified associations between demographic factors such as sex, marital status, profession, and sleep quality.
Conclusion: This study underscores a critical issue for physicians' health programs in Sudan, highlighting the importance for hospitals to implement measures that enable healthcare professionals to take more days off, obtain adequate sleep, and reduce on-call service days. It is imperative for healthcare professionals themselves to acknowledge the significance of these factors in preserving their own health and delivering sustainable healthcare services.
Disclosure: Nothing to disclose.

EPO-700 | Insomnia and excessive daytime sleepiness in patients with breast cancer

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Background and Aims: Sleep disturbances in women with breast cancer are poorly detected and managed in routine clinical practice. Our study aim was to evaluate sleep patterns and excessive daytime sleepiness (EDS) in patients during breast cancer treatment.
Methods: Fifty-nine women were recruited. Demographic data, sleep, neuropathic pain, anxiety, and depression were evaluated with the Epworth scale (ES), Insomnia Severity Index (ISI), PainDetect, DN4, Beck Anxiety Inventory (BAI), and Hamilton Depression Rating Scale (HDRS). We calculated descriptive statistics. Mean values for demographic data and scale scores were calculated using an unpaired *T*-test or Chi-square test between patients with EDS (ES >10) and clinically moderate to severe insomnia (ISI >15). At the end, we calculated Spearman´s correlations.
Results: Mean age was 60.6 ± 14.4 years, mean disease duration was 15.4 ± 20.9 months, mean ES was 7.6 ± 5.6 and mean ISI was 10.4 ± 7.7. Twenty-two percent of patients had EDS, and 27% had clinically moderate to severe insomnia. There were no statistically significant differences between groups in age, disease duration, BMI, metastases, hormone receptor status, therapy, presence of neuropathic pain, polyneuropathy symptoms, and severity of depression and anxiety. We found a positive correlation between ES and ISI (rho = 0.397; $p < 0.01$). Clinically moderate to severe insomnia and EDS correlated with depression (rho = 0.572; $p < 0.01$ and rho = 0.355; $p < 0.01$, respectively), anxiety (rho = 0.613; $p < 0.01$ and rho = 0.290; $p < 0.05$, respectively), and neuropathic pain (rho = 0.272, $p < 0.05$, both conditions). Additionally, EDS correlated with BMI (rho = 0.271; $p < 0.05$).
Conclusion: Our results indicate that insomnia is more prevalent than EDS in patients with breast cancer. We should be vigilant for patients with neuropathic pain and neuropsychiatric symptoms.
Disclosure: I disclose no conflict of interest.

EPO-701 | Sleep-wake cycle disturbance as the first symptom in an anti-CV2/CRMP-5 encephalitis

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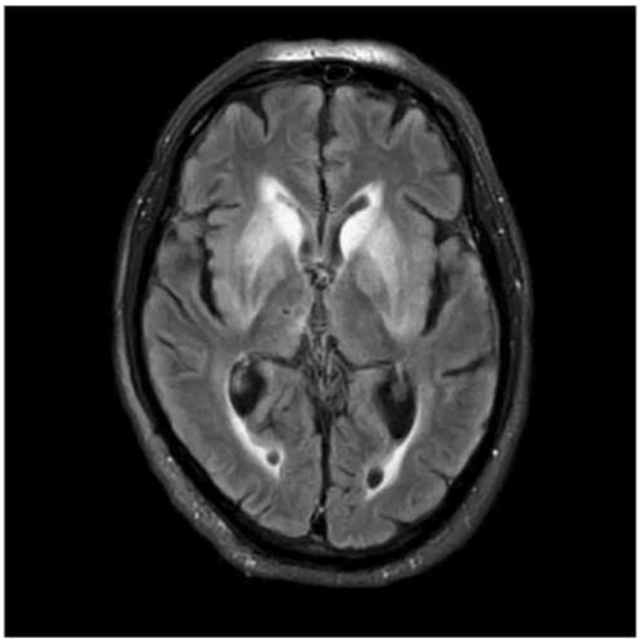
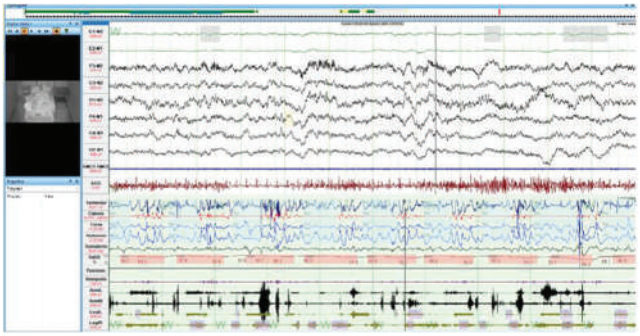
Background and Aims: We present the case of a patient with an anti-CV2/CRMP5 autoimmune encephalitis, whose initial and predominant symptoms were sleep disturbances. To our knowledge, no reported cases have highlighted sleep disturbances as the predominant clinical symptom, which tend to be overshadowed.
Methods: A 67-year-old male with a history of smoking, hypertension, and diabetes presented with a four-month course of symptoms that abruptly began with a severe alteration of the circadian sleep-wake pattern with night-time insomnia and excessive daytime sleepiness, and involuntary movements during sleep. Three months later he developed generalized weakness, gait disturbances, a toxic syndrome, dysarthria, and dysphagia. Neurological examination

showed bradypsychia, dysarthria, dysphagia, apraxia, bradykinesia, appendicular rigidity, and truncal ataxia.

Results: Video-polysomnography recorded undifferentiated periods of sleep and wakefulness, non-specific NREM sleep, with increased limb movements, and vocalizations during sleep. Positive anti-CRMP5/CV2 antibodies were detected in serum. Brain MRI revealed hyperintensities in the brainstem, both medial temporal lobes, and basal ganglia, consistent with striatal and limbic encephalitis. PET-CT scanning detected a thoracic hypermetabolic later confirmed as metastatic small cell lung carcinoma. Corticosteroid treatment as well as chemotherapy were started, with neurological improvement observed in a few days, and resolution of the sleep-wake cycle disturbance.



Brain MRI. Symmetrical hyperintensities in bilateral striatal regions as well as bilateral mesial temporal regions, compatible with a striatal and limbic encephalitis.



V-Polisomnography. Undifferentiated sleep and wakefulness periods, with undifferentiated N-REM (no graphoelements) and no registered periods of REM. OSA with significant desaturation.

Conclusion: This case underscores the importance of considering autoimmune encephalitis in the differential diagnosis of patients presenting with sleep disturbances and nonspecific neurological symptoms. These symptoms tend to be elusive and nonspecific and can lead to diagnostic delays. A multidisciplinary approach engaging both neurologists and sleep specialists can facilitate in an accurate and earlier diagnosis.

Disclosure: Nothing to disclose.

EPO-702 | Sleep architecture of patients with idiopathic hypersomnia and identification of neurophysiological markers for subtypes

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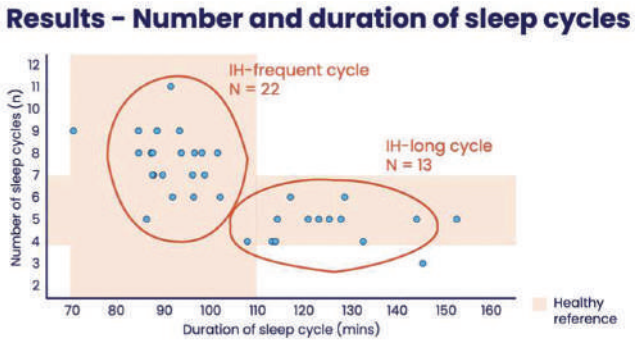
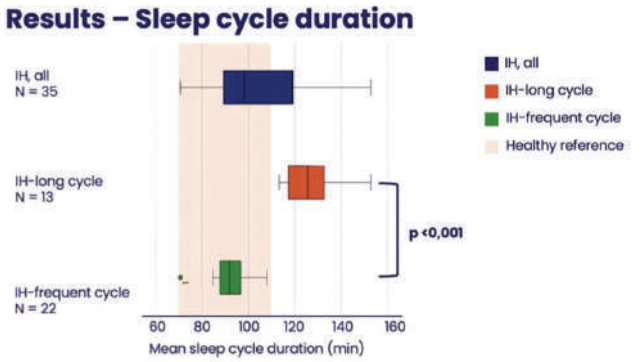
Background and Aims: Idiopathic hypersomnia (IH) is a rare neurologic disease characterised by excessive need of sleep including prolonged nocturnal sleep and excessive daytime sleepiness. Clinical observations have indicated at least two subtypes of IH, one associated with long sleep cycles. The aim of the study is to systematically examine differences in sleep architecture of patients with IH in order to identify particular neurophysiological parameters for subtypes.

Methods: In this retrospective pilot study polysomnography of 35 consecutive IH patients between 2017 and 2023 from two major sleep centres are analysed. Only patients without any psychopharmacological medication and without moderate or severe depression were included.

Results: 35 patients were included (27 female, 8 male). Mean age was 24.4 years. Mean total sleep duration was 605 ± 122 mins. Mean number of sleep cycles (MNSC) was 6.5 ± 1.9. Mean sleep efficiency was 93.8 %. Mean sleep cycle duration (MSCD) was 105 ± 20 mins. The MSCD of 22 patients was 92 ± 8 mins, their MNSC was 7.5 ± 1.5. The MSCD of the other 13 patients was 128 ± 13 mins, with a MNSC of 4.8 ± 0.8. With $p < 0.001$ for these two groups the difference in sleep cycle length is statistically highly significant.



Number (*n*) and duration of sleep cycles (mins).



Mean sleep cycle duration (mins).

Conclusion: Data indicates two subtypes of IH: IH-long cycle is associated with long sleep cycles and a normal number of sleep cycles. IH-frequent cycle shows an increased number of sleep cycles and normal length of sleep cycles. Subtyping will contribute to the understanding of the etiopathogenesis and possibly to individualized therapy.
Disclosure: Nothing to disclose.

Neuroimaging 2

EPO-703 | MERS (Mild encephalitis with a reversible splenial lesion); a case report

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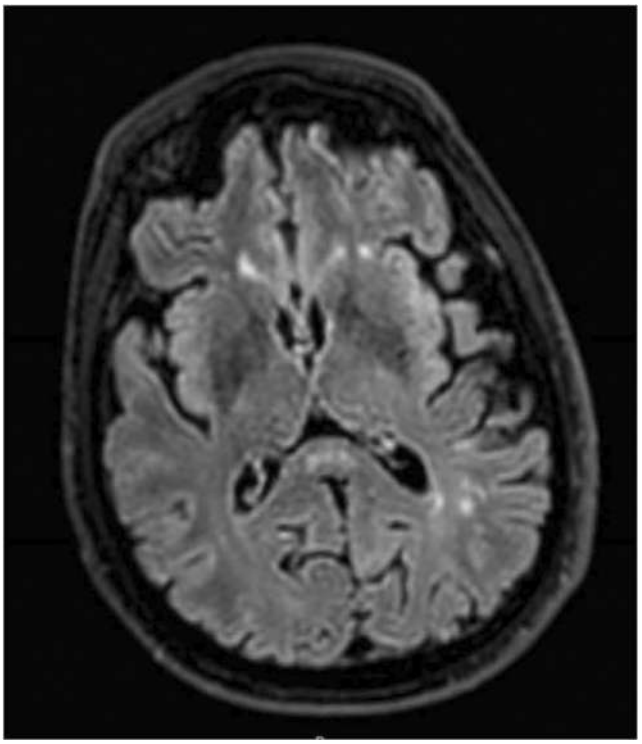
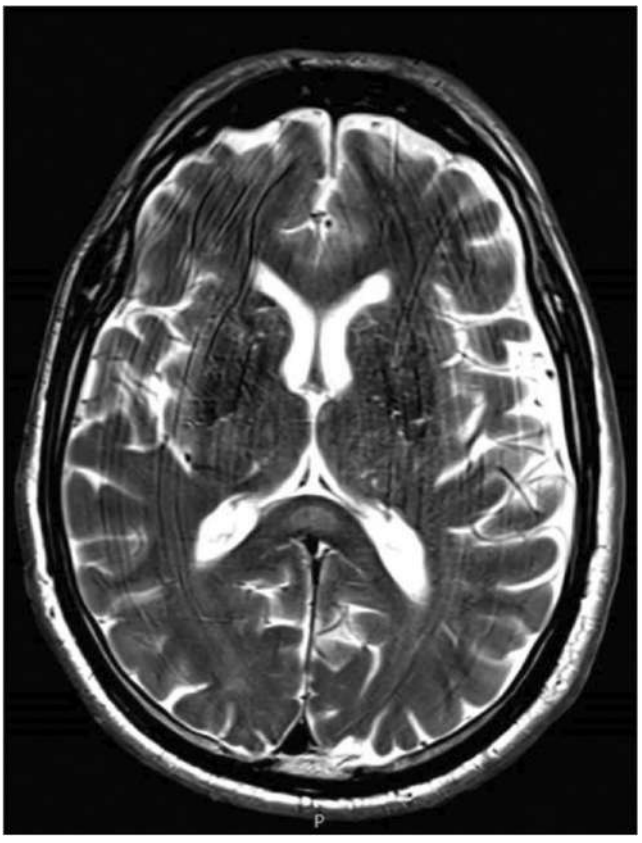
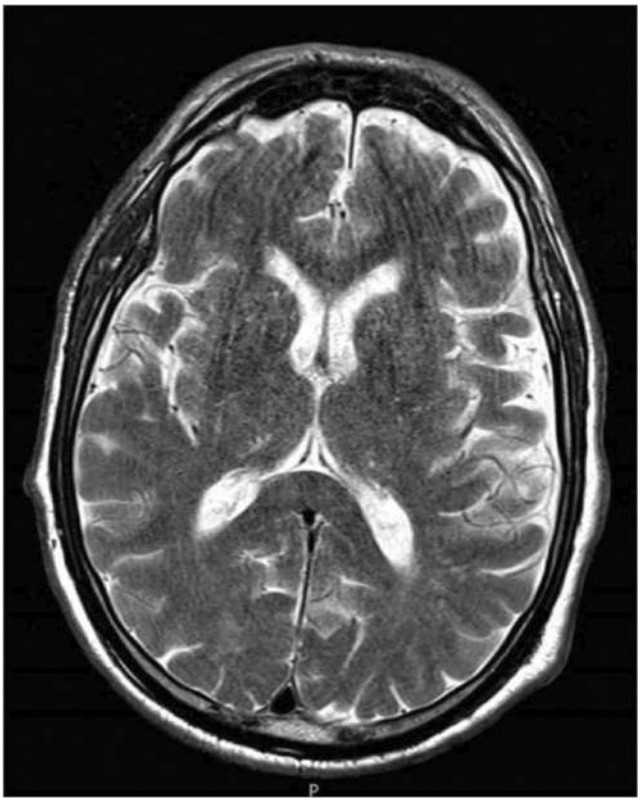
Background and Aims: Case of MERS (Mild encephalitis with a reversible splenial lesion) due to psychotropic drugs VS metabolic disorder.
Methods: In our hospital, we report the case of a 69-year-old man with a previous Bipolar Disorder, who develops abruptly a behavioral alteration and disorientation. Due to this, he is transferred to Neurology where he is diagnosed of MERS in possible relation to psychiatric medication and acute diarrhea.
Results: After the adjustment of the psychotropic drugs and the resolution of the diarrhea, the patient improved from the symptomatology and the hyperintense lesions disappeared in the Magnetic Resonance.



Initial cranial MRI of the patient shows an hyperintense lesion in the middle of SCC in FLAIR.



Initial cranial MRI of the patient shows an hyperintense lesion in the middle of SCC in T2.



Last cranial MRI shows a resolution of the lesion.

Conclusion: MERS is a reversible encephalopathy that affects the corpus callosum and can produce both neurological and psychiatric symptoms in relation to different etiologies, finding a hyperintense lesion in T2 and FLAIR sequences that are located in the splenium of the corpus callosum.

Disclosure: Nothing to disclose.

EPO-704 | Large scale white matter disruption and longitudinal degeneration in stroke

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Background and Aims: Stroke result in both local and distal brain connectivity alterations. While functional connectivity changes have been widely established, alterations in the structural connectivity patterns are still unclear. Here we assessed longitudinal changes of white matter organization in stroke and the relationship with behavior.

Methods: We prospectively enrolled first-time stroke patients, assessed at two-week and three-month intervals. Patients underwent behavioral and diffusion weighted-imaging (DWI) assessments. A latent factorial analysis was applied to behavioral data. Structural gradients were assessed for both intra- and inter-hemispheric tractography and averaged across networks. Statistical analyses included analysis of variance and longitudinal assessments through linear mixed model. Finally, we explored the relationships between structural gradients and behavior.

Results: Fifty patients (age 59 ± 11) and 29 controls (age 57 ± 11) were enrolled. Factorial analysis identified five cognitive factors, explaining 50% of variances. We reported three gradients for both intra- and inter-hemispheric connections (50% of variance). Network-wise analysis unveiled widespread acute stage alterations, impacting multiple networks for both intra- and inter-connectivity. Longitudinal assessment suggested significant degradation of this gradient structural organization. There was also an association between structural connectivity patterns and visuospatial-memory performance more strongly at the acute stage.

Conclusion: Stroke-induced structural connectivity damage extends beyond the lesion and worsens over time. The weak relationship between longitudinal changes in the structural organization and behavioral performance might implying that white matter modifications are independent with the recovery or disability status of stroke patients.

Disclosure: Nothing to disclose.

EPO-705 | High resolution intracranial vessel wall imaging in small vessel vasculitis of the central nervous system

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Background and Aims: Diagnosis of small vessels primary angiitis of CNS (SV-PACNS) is based on meninge/brain biopsy, but criteria for exposing to this invasive procedure high-risk cases only are lacking. In this study, accuracy of high resolution vessel wall MR imaging HR-VWI, a non-invasive method for visualizing SVs inflammation, for detecting patients at high risk of SV-PACNS was explored.

Methods: Patients with relapsing or chronic neurological symptoms/syndromes suggesting SV-PACNS ($n = 11$) or with secondary SV vasculitis of the CNS (SV-SACNS; $n = 4$) and patients with non-vasculitic brain hyperintensities (NVBH; $n = 34$; – multiple sclerosis, $n = 18$; – small vessel disease, $n = 12$; – migraine, $n = 4$) were enrolled. The patients received one MRI scan including HR-VWI sequences (3D PD weighted black blood with gadolinium) on a 3T scanner. SVs inflammation was considered present if linear HR-VWI enhancements corresponding to SVs and/or >3 punctiform enhancements noticeable in HR-VWI but not in other sequences were observed. HR-VWI enhancements corresponding to leptomeningeal enhancement, restricted diffusion areas or to microbleeds were excluded.

Results: HR-VWI positive SVs were observed in 7/15 SV-PACNS/SACNS (47%) and in 0/34 NVBH (0%), corresponding to 47%

sensitivity and 100% specificity. Stratifying the SV- PACNS/SACNS according to disease duration, 7/8 of the <1 year duration cases (87%) showed SV inflammation, thus in this setting increasing HR-VWI sensitivity to 87%.

Conclusion: In patients with short disease duration HR-VWI could represent an accurate tool for selecting patients at high risk of SV-PANCS eligible for cerebral/meninge biopsy. This probably because over time therapies mask the disease-related pathogenic inflammation.

Disclosure: Nothing to disclose.

EPO-706 | DAI changes of head injury patients in CT imaging: The HEAD Helsinki study

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Background and Aims: Diagnostic value of computed tomography (CT) imaging for diffuse axonal injury (DAI) changes is considered limited. We determined how many patients with magnetic resonance imaging (MRI) positive DAI changes had them visible in head CT after diagnosed traumatic brain injury (TBI).

Methods: Our retrospective register-based study cohort of patients with head injury treated at emergency hospitals in Helsinki between 01 January and 31 December in years 2010 and 2018. Confirmed DAI patients' initial and follow up head CTs were analyzed. Based on MRI findings, definitive corresponding CT findings were accepted according to Gentry's classification: Hemorrhagic and/or edematous strands at grey-white matter junctions in grade 1 and edematous and/or petechial contusions in grade 2 and 3. Small single petechial contusions located in the subcortical or white matter regions were excluded in grade 1.

Results: Of the 1963 screened patients, 64 had MRI positive DAI changes. A total of 24/64 (37.5%) MRI-DAI patients had visible DAI changes in CT, of which 9/24 (37.5%) were grade I, 6/24 (25.0%) grade II and 9/24 (37.5%) grade III. However, 7/24 (29.0%) did not show any visible changes during the primary CT obtained within 24 hours after the accident, and they only became evident in follow-up CTs taken 1–4 days after the initial scan.

Conclusion: Detection of DAI-changes in CT compared with MRI was low despite of increased sensitivity in follow-up CT scans. MRI-imaging combined with clinical history remain the primary source of tool for assessing DAI-changes in TBI-patients.

Disclosure: Nothing to disclose.

EPO-707 | Stroke echo scan from a neurologist perspective

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Background and Aims: More than 20% of ischaemic strokes occur due to a cardioembolic cause The point of care echocardiography (PoCUS) protocol comprises eleven aspects with binary responses focussing on specific target structures: functions of left ventricle, left atrium, right ventricle, valvular abnormalities, large intracardiac thrombi, aortic plaque thrombi, aortic plaque, pericardium and signs of hypovolaemia.

Methods: We applied this screening to identify stroke patients associated with an increased cardioembolic risk in order to find treatable cardioembolic causes and to find an interrater reliability between neurologist and cardiologist, whose diagnosis was chosen as the gold standard.

Results: According to the defined protocol, 50 patients (female, $n=24$; mean age = 62 a, SD 17 a) underwent the PoCUS echocardiography test. It displayed a global sensitivity of 77.8% and global specificity of 94.1% ($k=0.73$). This high sensitivity and specificity were achieved particularly with regard to the assessment of pumping function and enlargement of the cardiac cavities, but less for other items such as heart valve abnormalities (SEN 30%; SPE 97.4%), large intracardiac thrombi (SEN not available, SPE 100%).

Conclusion: A good interobsever reliability was found between neurologist and cardiologist. Future prospective studies are warranted to improve the interrater reliability.

Disclosure: Nothing to disclosure.

EPO-708 | Supra and infratentorial atrophy in cerebellar ataxias: Unveiling distinctions across different etiologies

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Background and Aims: This study investigates structural changes in patients with cerebellar ataxias (CA) due to different causes.

Methods: 28 Autosomal dominant (AD) CA patients, 17 autosomal recessive (AR) CA patients, 29 sporadic cases of CA, 8 multiple system atrophy patients (MSAc) and 20 controls were included. MRI

was performed; whole-brain Voxel-Based Morphometry (VBM) and cerebellar-optimized VBM (SUIT toolbox) were used to assess gray matter (GM) atrophy. Brainstem and superior cerebellar peduncles (SCP) volumes were estimated and compared.

Results: Compared to controls, all CA groups showed widespread GM cerebellar atrophy; additionally, AD and AR groups showed distinct clusters of supratentorial atrophy, mainly involving temporal and parietal regions. No supratentorial GM differences were found among CA groups. SUIT-VBM revealed more severe atrophy in the medial Crus-I and II in MSAc compared to AD, and in AR compared to AD. AD, AR, and MSAc groups exhibited reduced whole-brainstem, midbrain, and pons volumes compared to controls; AD and MSAc groups also exhibited reduced whole-brainstem and pons volumes compared to sporadic cases. AD and AR showed reduced medulla volumes compared to controls and sporadic cases. SCP volume reduction was evident in all CA groups compared to controls, with AD showing also decreased SCP volume compared to sporadic cases.

Conclusion: AD and AR groups showed supratentorial patterns of atrophy. Conversely, the sporadic group showed less involvement of brainstem structures. The evidence of distinct patterns of structural alterations in different CA etiologies might contribute to an improved differential diagnosis.

Disclosure: S Pisano, O Stojiljković, S Mesaros, and N Dragasevic have nothing to disclose. S Basaia received research supports from the Italian Ministry of Health. VS Kostic has received speaker honoraria from Actavis and Solveo. F Agosta received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and has received research supports from IMH, Italian Ministry of University and Research, ARiSLA, ERC, EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease. M Filippi consulting or speaking activities or advisory boards for Alexion, Almirall, Biogen, Bayer, Bristol-Myers Squibb, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research, and FISM.

EPO-709 | Chronic active lesions contribute to depression in multiple sclerosis

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Background and Aims: Chronic neuroinflammatory processes may contribute to depression in multiple sclerosis (MS). Paramagnetic rim lesions (PRLs) and choroid plexus (CP) enlargement represent novel magnetic resonance imaging (MRI) markers of chronic inflammation in MS that are associated with more severe clinical disability. Currently, their interplay with the presence of depression remains unexplored. Here, we examined whether the number and volume of PRLs and CP enlargement may contribute to depression in MS patients.

Methods: Brain 3T MRI and clinical evaluation with the assessment of depression using Montgomery–Asberg Depression Rating Scale (MADRS) were obtained from 126 MS patients and 72 age- and sex-matched healthy controls (HC). Patients with MADRS score >9 were classified as depressed. PRLs were identified on phase images of susceptibility-weighted imaging, whereas CP volume was quantified using a fully-automatic method on 3D T1-weighted and FLAIR MRI sequences. Predictors of depression were identified using LASSO logistic regression.

Results: Forty-six out of 126 (36.5%) MS patients were depressed. Fifty-nine (46.8%) MS patients had ≥1 PRLs (median = 0, interquartile range = 0; 2). Compared to HC, MS patients showed significantly higher T2-hyperintense white matter lesion (WM) and normalized CP volume volumes, as well as lower normalized brain, thalamic, hippocampal and WM volumes (p from <0.001 to 0.023). PRL number (standardized-β = 0.078) and volume (standardized-β = 0.029) were independent predictors of depression (area under the curve = 0.60).

Conclusion: Higher number and volume of PRLs may contribute to the pathophysiology of depression in MS patients, emphasizing the role of chronic neuroinflammatory processes in determining depression independently from disease severity.

Disclosure: M Rubin, A Meani, N Tedone have nothing to disclose. P Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He has received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). M Margoni reports grants and personal fees from Sanofi Genzyme, Merck Serono, Novartis and Almiral. M Filippi received compensation for consulting

or speaking activities from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPO-710 | Loss of serotonergic function in carriers of Parkin mutations: A [11C]DASB PET study

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Background and Aims: Idiopathic Parkinson's disease (iPD) features loss of presynaptic serotonergic function. Serotonergic loss has also been detected in autosomal dominant forms of monogenic Parkinsonism. In this study we present preliminary in vivo data of serotonergic terminal integrity in the striatum of symptomatic PRKN mutation carriers (PRKN-PD), an autosomal recessive form of monogenic Parkinsonism.

Methods: Eight individuals with PRKN-PD (mean age 49.32 ± 8.74, disease duration 9.51 ± 5.59 years, Hoehn & Yahr 1.81 ± 0.53), eight iPD patients (mean age 65.38 ± 7.58, disease duration 4.82 ± 4.17 years, Hoehn & Yahr 1.88 ± 0.99) and eight healthy controls (HC, mean age 46.25 ± 6.02) underwent clinical assessments, Magnetic Resonance Imaging (MRI) scans, and single [11C]DASB PET scan. Regions of Interest (ROIs) were delineated on each subject's T1 space MRI, using Multi-Atlas Propagation with Enhanced Registration (MAPER), with grey matter masking. The Logan reference model, with the posterior cerebellar grey matter excluding the vermis as the reference region, was utilised to generate parametric [11C]DASB distribution volume ratio (DVR) images with DVR-1 equal to non displaceable binding potential (BPND).

Results: PRKN-PD patients exhibited significant reduction in [11C]DASB BPND compared to HC in Putamen (−33.8%, $p < 0.001$), and Caudate (−37.2%, $p = 0.005$). iPD patients showed significant decrease of [11C]DASB BPND in putamen (−36.1%; $p < 0.001$) and caudate (−43.9%; $p < 0.001$) compared to HC. No significant difference in [11C]DASB BPND was observed between iPD and PRKN-PD patients in these regions.

Conclusion: These findings offer preliminary evidence of a noteworthy striatal loss in presynaptic serotonergic integrity among symptomatic PRKN mutation carriers. Ongoing data collection for additional PRKN carriers will further illuminate these findings.

Disclosure: Nothing to disclose.

EPO-711 | BOLD fMRI functional connectivity informed by IEDs in high-risk and low-risk SUDEP epilepsy patients

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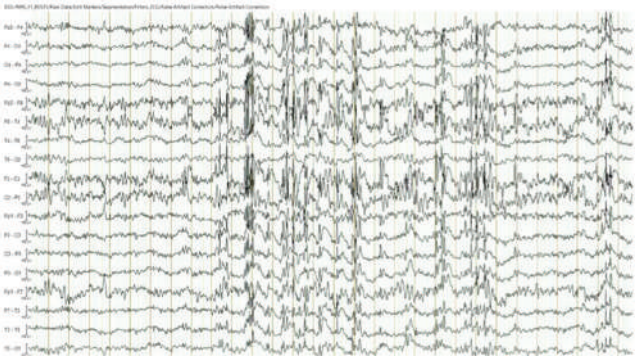
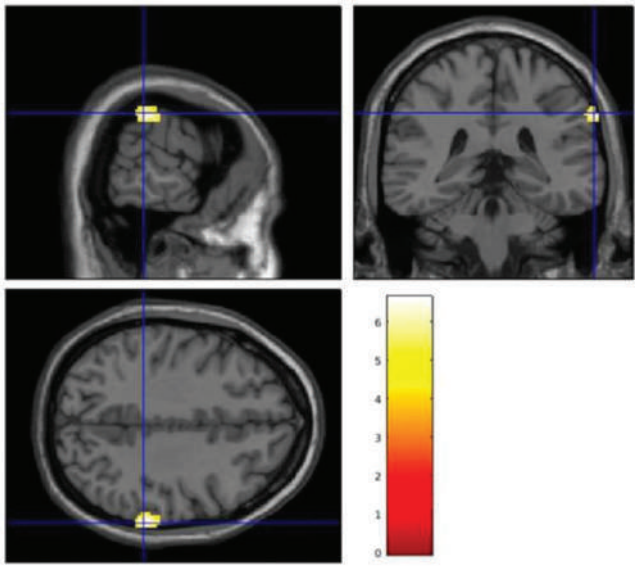
Background and Aims: According to recent literature, interictal epileptiform discharges (IEDs) might provide a facilitating environment for Sudden Unexpected Death in Epilepsy (SUDEP) to happen. Here, we explore the effects of IEDs on the functional connectivity between regions of interest (ROIs) known to be involved in the SUDEP pathogenesis and the rest of the brain in a population of high-risk (HR) and low-risk (LR) SUDEP epilepsy patients.

Methods: A cohort of 39 adult epilepsy patients was investigated with EEG-coregistered to fMRI and then stratified in HR and LR according to SUDEP-3 and SUDEP-7 inventories. Additional stratification was performed based on the occurrence of tonic-clonic seizures (GTC criteria). Seven ROIs were considered: Anterior Cingulate Cortex, Insula, Brainstem, Thalamus, Amygdala, Putamen. The IED-related functional connectivity between the ROIs and the rest of the brain was investigated through a Psychophysiological Interaction (PPI) analysis.

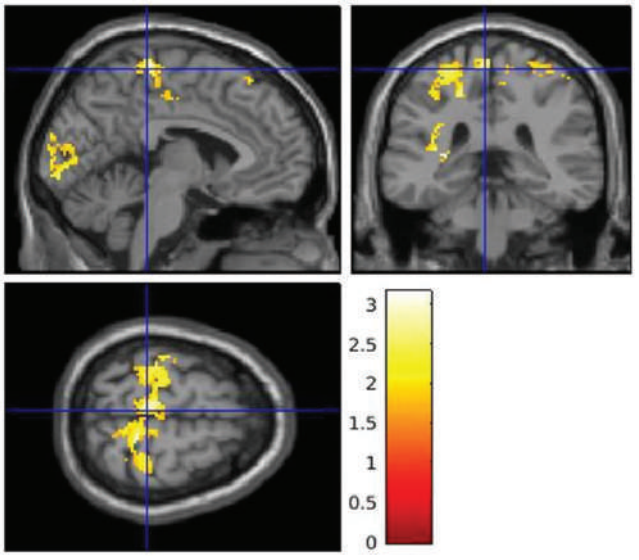
Results: In the SUDEP-7 and GTC stratified groups, PPI analyses show in HR versus LR an increased IEA-informed functional connectivity between amygdala, thalamus and putamen seeds and supramarginal gyrus and a decreased functional connectivity between the same ROIs and motor and premotor cortex. These patterns are consistent with the PPI results obtained with the same approach in a single "Probable SUDEP" case.



"Probable SUDEP" case interictal EEG trace acquired during fMRI.



Increased spike-related FC in the GTC HR group compared with LR patients between bilateral putamen and left supramaginal Gyrus.



Reduced spike-related FC in the SUDEP-7 HR groups compared with LR patients between bilateral thalamus and premotor cortex.

Conclusion: Our findings suggest that in SUDEP and HR patients compared to LR, IEA modulate the functional connectivity between specific subcortical ROIs and brain networks involved in response to stimuli and surroundings (SMG) and in the regulation of the cardiovascular system (premotor cortex) thus providing new insights in the pathogenesis of SUDEP.

Disclosure: Nothing to disclose.

EPO-712 | Availability and integration of neuroimaging research database in Nigeria

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Background and Aims: Brain injuries and brain diseases in Nigeria are particularly prevalent, with an annual incidence of 2170 per 100,000 individuals. Approximately 78% of Nigeria's neuroimaging institutes use low-field-strength systems that are inefficient for generating conventional neuroimaging database.

Methods: DATA COLLECTION. The central repository data would be established in accordance with the highest ethical standards approved by the ethical committee of the diagnostic centers or its equivalent. Data would be collected from consented individuals presenting to the diagnostic centers for neuroimaging services. DATA PROCESSING. This neuroimaging data would be de-identified, with personal information removed for research accessibility by the help of African Brain Data Network.

Results: The prospective result of integrating neuroimaging research data would increase the availability of neuroimaging data, which would allow for more robust research. It would contribute to the advancement of neuroimaging and healthcare research in Nigeria.

Conclusion: Our research underscores the pressing need for an integrated neuroimaging data platform in Nigeria, a nation grappling with limitations in neuroimaging capabilities.

Disclosure: Nothing to disclose.

EPO-713 | Clinical use of tau PET in Aβ PET positive individuals: A case series – The HEAD study

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Background and Aims: Clinical phenotypes combined with structure imaging biomarkers, as levels of tau PET pathology, allow a sensitive and specific diagnosis of Alzheimer's disease (AD). We present here the cases of four patients who visited the memory clinic at the University of Pittsburgh Medical Center between June and December 2023 and underwent both Aβ and tau-PET scans.

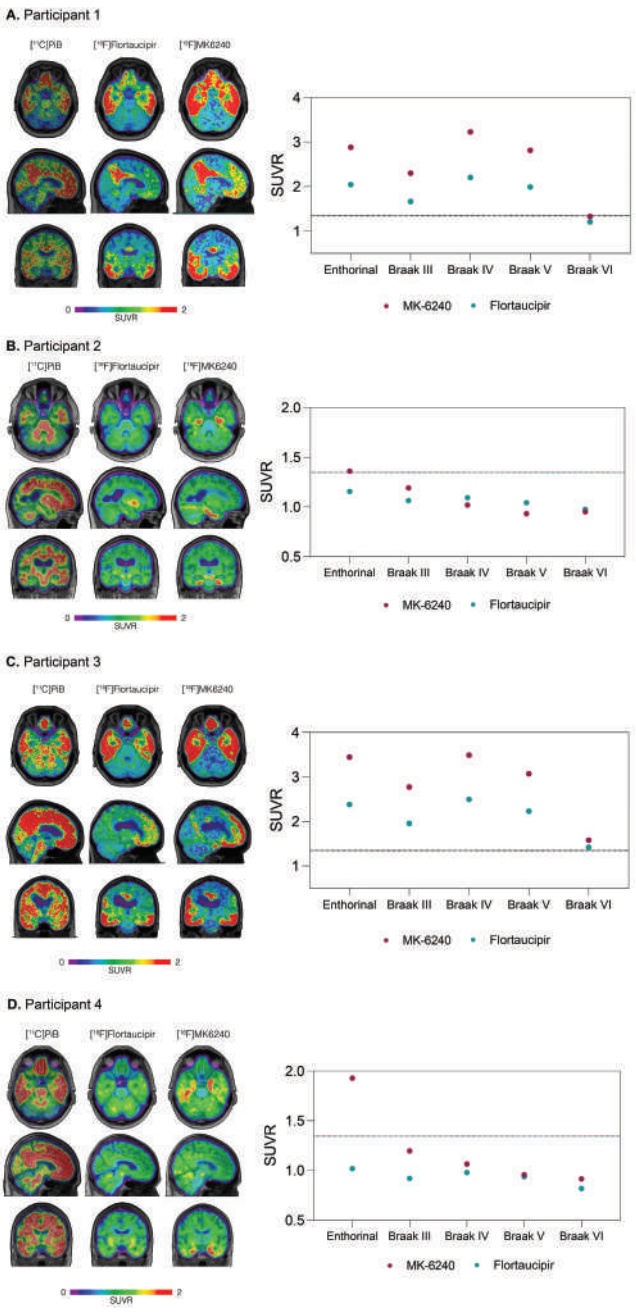
Methods: These individuals had standard clinical and cognitive outcomes, typical blood tests ordered in patients with memory impairment, MRI, PET PIB Aβ and two tau PET tracers (MK6240 and Flortaucipir).

Results: All patients had their blood tests normal. Patients 2–4 exhibited mild ischemic changes (Table 1). All patients tested positive for amyloid PET, with varied tau PET results. Patients 1 (MOCA = 6) and 3 (MOCA = 19), who were demented with impaired Instrumental Activities of Daily Living (IADL), had Braak stages V-VI using both tau PET tracers. Conversely, the mild cognitive impairment (MCI) Patients 2 (MOCA = 19) and 4 (MOCA = 9, neuropsych evaluation indicating MCI) tested positive for MK6240 but negative for FTP.

TAB 1 – Demographic and results

Patient	Age, y	Sex	MOCA	MRI	IADL	Aβ	AV1451 BRAAK	MK6240 BRAAK
1	71	M	6	Normal	YES	+	5	5
2	73	M	19	Ischemic changes	NO	+	0	1
3	74	F	14	Ischemic changes	YES	+	5	6
4	81	M	29	small PCA infarction	NO	+	0	2

Figure 1 - Amyloid and tau-PET in the participants



Tau PET-scans and the difference between the tracers.

Conclusion: The symptoms of typical amnestic AD presentation were confirmed with similar pattern of Aβ PET. Tau PET demonstrated greater variability, with lower levels observed in less cognitively impaired patients (Figure 1). This small series did not exclude that a low MOCA score combined with Aβ PET could be useful in identifying individuals in the earliest stages candidates to Aβ- lowering therapies. Larger samples are necessary in regarding these discrepancies between tau PET uptake and cognitive tests, reinforcing the need for tau PET markers as complementary tests.

Disclosure: Nothing to disclose.

EPO-714 | Exploring atypical forms of Alzheimer's disease through connectomics in early and late-phase amyloid PET and FDG PET

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Background and Aims: Alzheimer's disease (AD) is the most common form of dementia, characterized by prominent amnestic impairment of insidious onset. However, atypical presentations such as logopenic variant of primary progressive aphasia, posterior cortical atrophy, corticobasal syndrome and frontal AD, pose diagnostic challenges. This study presents retrospective analysis investigating brain functional differences between typical and atypical AD. Specifically, a structural connectome, a comprehensive map of anatomical white matter connections, was employed alongside late-phase amyloid-PET, which resembles regional amyloid uptake. Additionally, this research aims to examine whether early-phase amyloid-PET can serve as a surrogate for synaptic dysfunction, similar to [18F]FDG-PET.
Methods: Thirty patients were selected: 13 with atypical AD and 17 with typical amnestic phenotype. Neuropsychological tests, MRI, [18F]FDG-PET, and [18F]FBB-PET were performed for each subject. Structural and functional images underwent spatial registration, segmentation, and intensity normalization, using a custom Python pipeline based on FreeSurfer and ANTs tools. Structural connectomes derived from probabilistic tractography on DWI images of 30 healthy subjects were employed.
Results: Results revealed a significant preservation of the hippocampus in atypical AD ($p < 0.05$). The connectome analysis demonstrated variations in interconnections among late-phase amyloid-PET uptake regions between atypical and typical AD. Furthermore, our findings support the hypothesis that early-phase amyloid-PET serves as a reliable marker for synaptic dysfunction.
Conclusion: These findings suggest that structural connectomes in PET imaging can reveil unique neurodegenerative pathways in atypical AD. Moreover, this study supports that early amyloid-PET phases provides similar information to [18F]FDG-PET on neurodegeneration among atypical AD patients.
Disclosure: Nothing to disclose.

EPO-715 | Integrated diagnosis and treatment of acute ischemic stroke by nanoparticles based on MRI/NIR dual-modality imaging

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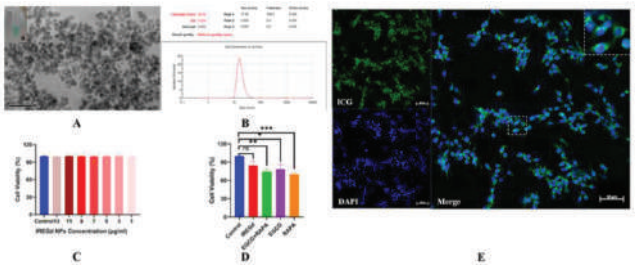
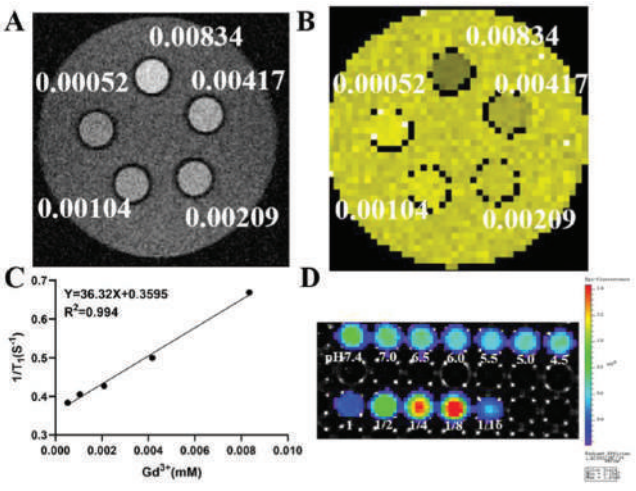
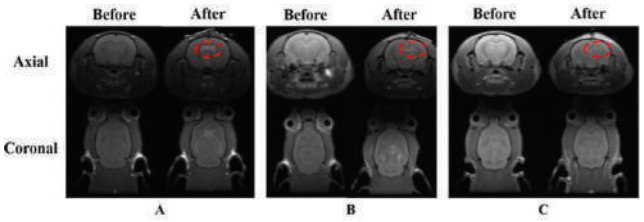
Background and Aims: Rapamycin (RAPA) is an effective autophagy modulator that can promote neuronal survival under ischemic conditions through rational autophagy regulation and is receiving increasing attention. However, its low solubility and poor stability seriously hinder its further application.
Methods: In this study, RAPA, indocyanine green (ICG), epigallocatechin gallate (EGCG), and Gd3+ serving as neuroprotective drugs, near-infrared fluorescence (NIRF) imaging agents, biomimetic coatings, and magnetic resonance imaging agents, respectively, were co-assembled into carrier-free, highly biocompatible ICG-RAPA-EGCG-Gd nanoparticles (IREGd NPs) for synergistic diagnosis and treatment of acute ischemic stroke.
Results: The results showed that the IREGd NPs had good stability and could load RAPA efficiently. IREGd NPs were efficiently uptaken by PC-12 cells and had a superior neuroprotective effect on oxygen-glucose deprivation and reoxygenation (OGD/R)-treated PC-12 cells than RAPA or EGCG. In addition, IREGd NPs showed good signal characteristics for MRI and NIRF imaging. Finally, in vivo, experiments confirmed that IREGd NPs preferentially aggregated in the ischemic hemisphere and were neuroprotective in transient middle cerebral artery occlusion (tMCAO) rats.



TEM (A) and DLS (B) display the characteristics of IREGd NPs. (C) Cell viability of PC12 cells after incubation with different concentrations of IREGd NPs for 24 h and (D) after incubation with EGCG+RAPA, EGCG, and RAPA for 24 h. (E) CLSM images of cell.



MR and NIF imaging properties of IREGd NPs. (A, B) T1-WI and T1-mapping images of different Gd3+ concentrations (mM) at pH = 7.4; (C) functions made with the Gd3+ concentration as the horizontal coordinate and 1/T1 (T1 represents the longitudinal relaxation.



T1-WI images of in vivo lateral ventricles (A) and brain parenchyma (B) injected with IREGd NPs or PBS (C). Signal altered (A, B)/ unaltered (C) areas are within the red ovals.

Conclusion: Overall, carrier-free IREGd NPs provided a simple alternative approach to achieve bimodal imaging and therapeutic integration in acute ischemic stroke.
Disclosure: Nothing to disclose.

EPO-716 | Contribution of spinal cord magnetic résonance imaging (MRI) as a prognostic biomarker in multiple sclerosis

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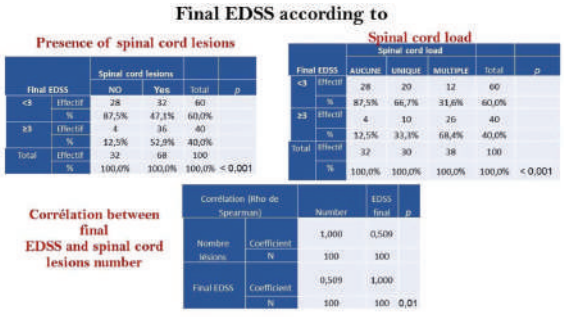
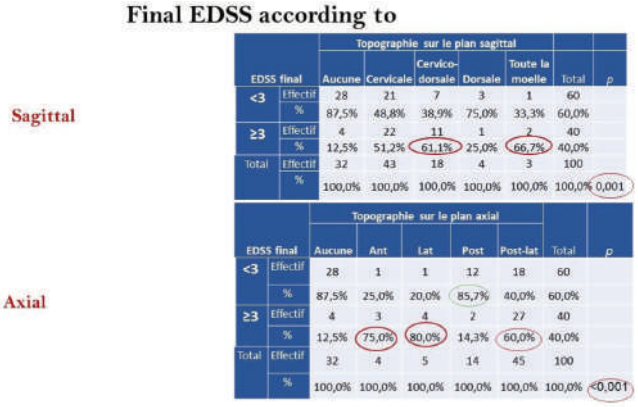
Background and Aims: Multiple sclerosis (MS) is the leading cause of acquired motor disability in young adults. The aim of this study was to determine the prognostic value of spinal cord lesions on the occurrence of relapses and the progression of short-term disability in MS patients.
Methods: A descriptive, monocentric, prognostic study of a cohort of 100 remittent MS patients, followed for 3 years, all with baseline MRI and follow-up MRI at 12 months and 30 months. Clinical evaluation was based on the Expanded Disability status scale (EDSS).
Results: Mean age at onset was 28.06 years, mean duration of the disease was 41 months. 68% of patients had spinal cord lesions at the initial stage; initial spinal cord involvement was predictive of relapse onset and worsening of disability over the course of the disease ($p < 0.001$), and an impact on ambulation in 19% of cases. Multiple spinal cord lesions were significantly associated with a high initial and final EDSS score (≥3) ($p = 0.001$; $p < 0.001$). Cervical and cervicodorsal sites were predictive of disability aggravation in more than half the cases. In axial terms, >60% of lateral lesions were associated with disability. Posterior lesions were associated with a final EDSS score <3 ($p < 0.001$). The absence of spinal cord lesions (32%) was associated with an initial and final EDSS score <3 ($p = 0.04$; $p < 0.001$)



Final EDSS according to spinal cord load lesions.



EDSS final		Topographie sur le plan sagittal: Aucune	Cervicale	Cervico-dorsale	Dorsale	Toute la moelle	Total	p
<3	Effectif	28	21	7	3	1	60	
	%	87,5%	48,8%	38,9%	75,0%	33,3%	60,0%	
≥3	Effectif	4	22	11	1	2	40	
	%	12,5%	51,2%	61,1%	25,0%	66,7%	40,0%	
Total	Effectif	32	43	18	4	3	100	
	%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	0,001

EDSS final		Topographie sur le plan axial: Aucune	Ant	Lat	Post	Post-lat	Total	p
<3	Effectif	28	1	1	12	18	60	
	%	87,5%	25,0%	20,0%	85,7%	40,0%	60,0%	
≥3	Effectif	4	3	4	2	27	40	
	%	12,5%	75,0%	80,0%	14,3%	60,0%	40,0%	
Total	Effectif	32	4	5	14	45	100	
	%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	<0,001

Final EDSS according to sagittal and axial topography of spinal cord lesions.

Multivariate analysis

Variables	B	E.S	Wald	ddl	Exp(B)	Intervalle de confiance 95% pour EXP(B): Inférieur	Supérieur	P value
Antérolatérale	4,898	1,863	6,912	1	133,967	3,478	5160,505	0,009
Latérale	4,470	2,023	4,881	1	87,326	1,656	4605,542	0,027
Postérolatérale	2,122	,907	5,476	1	8,351	1,412	49,408	0,019
Age 30-39 ans	5,608	2,099	7,140	1	272,665	4,457	16679,521	0,008
initial EDSS ≥3	4,843	1,304	13,803	1	126,863	9,856	1632,899	<0,001
Relapse under traitement	3,535	1,176	9,034	1	34,304	3,421	343,972	0,003

Multivariate analysis; risk factors to reach EDSS 3.

Conclusion: The presence of spinal cord lesions at the start of the disease has a major prognostic role in the development of ambulatory disability, but must be taken into account with other known prognostic factors.
Disclosure: Nothing to disclose.

Peripheral nerve disorders

EPO-717 | Guillain Barre syndrome; clinical features and outcome in three referral hospitals in Cameroon

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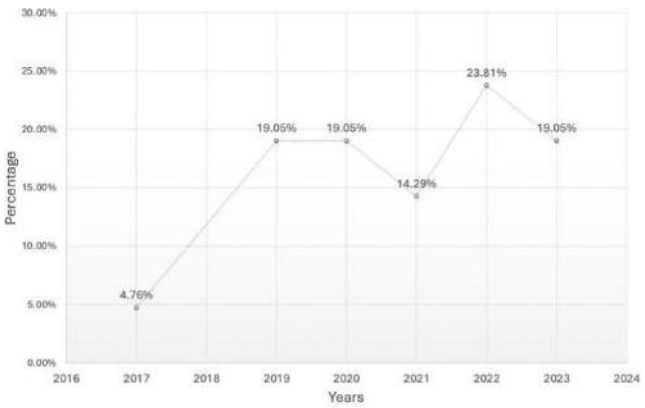
Background and Aims: Guillain Barré Syndrome (GBS) is an inflammatory pathology of the peripheral nervous which is characterized by bilateral and progressive sensory-motor impairment of the

peripheral limbs, sometimes extending to the respiratory muscles and cranial nerves. We aimed to determine the clinical features and outcome of Guillain Barré Syndrome cases in Cameroon.

Methods: We reviewed all cases of GBS admitted from January 2017 to March 2023, in General and Laquintinie hospitals of Douala and in Yaoundé General hospital. We excluded patient aged under 16 and incomplete files based on the Brighton diagnostic criteria. Data on sociodemographic characteristic, clinical features, workup, treatments and outcome data were collected and analyzed using SPSS 23.0.

Results: A total of 21 cases of GBS were included, and patients aged < 40 years represented 52.4% of cases. Men represented 61.9% of patients. The average admission rate was 3.5 cases/year. Mean age was 40.8 ± 17.6 years. Most frequent triggering factors were respiratory tract infection (38.1%), and immunization (14.3%). The most common signs were tetraparésis (85.7%), deep tendon areflexia (71.42%) and hyperesthesia (52.38%). Albumino-cytology dissociation was observed in 6 cases out of 11 CSF sampled. ENMG was performed in 11 patients and classified axonal type ($n = 7$) and the demyelinating type ($n = 4$). IV immunoglobulins were administered in 28.6% of patients. Pressure sores (57.9%) and autonomic disorders (14.3%) were the most frequent intra-hospital complications. We recorded 2 cases of in-hospital death.



Trend of admission of patients with GBS in Douala General and Laquintinie hospitals and Yaoundé General hospital.

Conclusion: Guillain Barré syndrome is an uncommon condition with sometimes dramatic complication which need more attention.

Disclosure: Nothing to disclose.

EPO-718 | Charcot-Marie-tooth type 2CC misdiagnosed as chronic inflammatory demyelinating polyneuropathy

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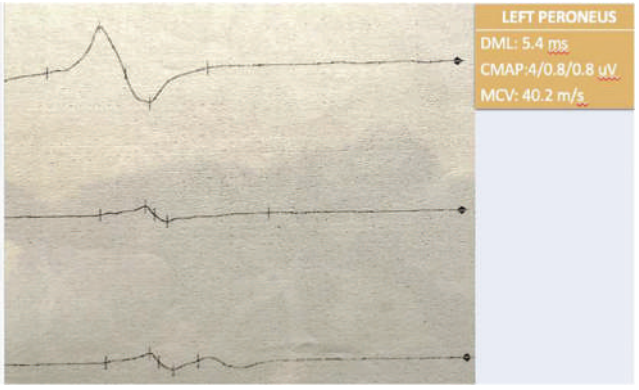
Background and Aims: Charcot-Marie-Tooth (CMT) is a group of genetic neuropathies typically characterized by distal muscle wasting and sensory loss, pes cavus and areflexia. Herein we describe a case of Charcot-Marie-Tooth with equivocal features misdiagnosed as chronic inflammatory demyelinating polyneuropathy.

Methods: A 30-year-old woman was referred to our neuromuscular unit at 28 years old with proximal muscle weakness. Neurological examination showed weakness in lower limb (LL) muscles, marked proximally and mild distally, and absence of ankle deep tendon reflexes. Familial history was negative for neuromuscular diseases. Electromyography showed chronic neurogenic changes in proximal and distal muscles of LL. Nerve conduction study (NCS) showed both normal NCV and slowing with conduction blocks, so a diagnosis of CIDP was advanced and she was treated with intravenous immunoglobulins that were ineffective. At electrophysiological revaluation (after two months) CB in peroneal nerve was not more detectable as also distal CMAP had decreased.

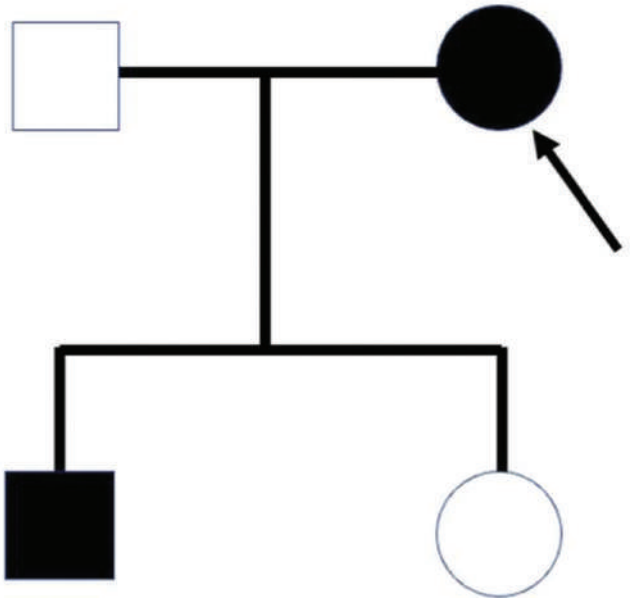
Results: The hypothesis of genetic neuropathy was considered, and her 8-year-old son was evaluated. Neurological examination revealed mild weakness of distal and proximal muscles at lower limbs and mild pes cavus. Neurophysiological investigation showed an intermediate-axonal pattern. A targeted-NGS showed heterozygous frameshift mutation (c.3057dupG; p.K1020fs*43) in the NEFH gene, coding for the neurofilament heavy chain and causing CMT2CC, a rare form of axonal CMT with proximal weakness.



Conduction block in the proband peroneal nerve.

	Left	Right
MEDIAN		
SAP	7.7 uV	3.6 uV
SCV	36.6 m/s	35.4 m/s
DML	4 ms	4.7 ms
CMAP	16.6/15.7 mV	9.7/9.5 mV
MCV	44.6 m/s	35.5 m/s
TIBIAL		
DML	6.4 ms	6.6 ms
CMAP	11.1/1.7 mV	6.1/0.6 mV
MCV	40.7 m/s	36.9 m/s
SURAL		
SAP	NO	NO
SCV	NA	NA

Proband electrophysiological findings.



Proband family tree.

Conclusion: Diagnosis of a genetic neuropathy may be challenging when clinical features are atypical or electrophysiological findings suggest acquired demyelination.
Disclosure: Nothing to disclose.

EPO-719 | **Abstract withdrawn**

EPO-720 | **Redundant nerve roots on MRI can predict ongoing denervations in lumbar spinal stenosis patients**

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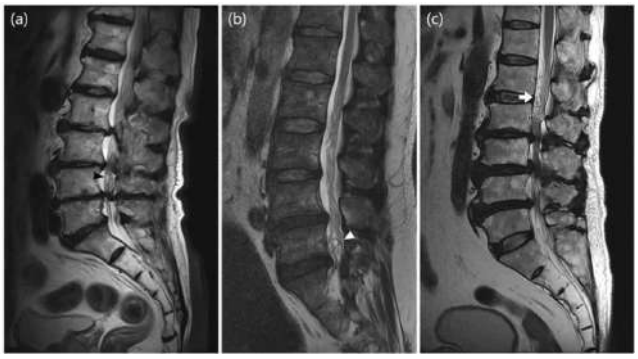
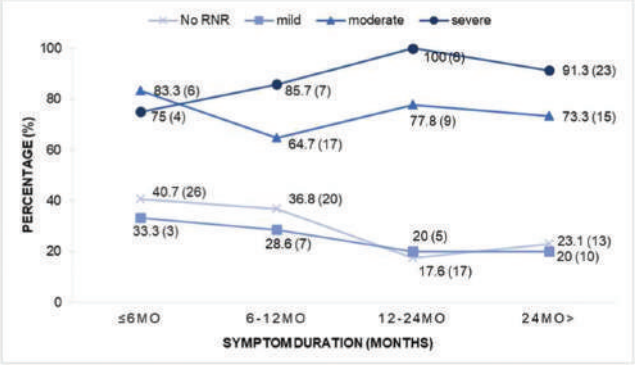
Background and Aims: Redundant nerve roots (RNRs), which are abnormally elongated and tortuous nerve roots, can be developed secondary to degenerative spinal stenosis. It has been reported that RNRs are associated with worse clinical outcome after decompressive surgery. However, there are limited studies about clinical significance of RNR. This study aims to investigate association of RNRs and denervation potentials observed in electromyographic study (EMG).
Methods: Among 2003 patients who underwent electrodiagnostic study of lower extremities from January 2020 to March 2023, 193 patients were included demonstrating lumbar spinal stenosis on their spinal MRI. Their clinical information and image findings including presence and of RNRs were investigated. In the EMG study, presence of abnormal spontaneous activity (ASA) was collected. Statistical analysis was performed to compare the difference between patients with and without RNRs. Multivariate logistic regression analysis was conducted to find out factors associated with development of ASA.
Results: RNRs were associated with advanced age ($p<0.001$), longer symptom duration ($p=0.009$), narrower CSA ($p<0.001$) and higher frequency of ASA ($p<0.001$). Higher probability of ASA was correlated to the increasing redundancy of nerve ($p<0.001$). Multiple logistic regression analysis showed that occurrence of ASA was associated with narrower CSA, multiple stenotic sites, severe RNR.



Grading of RNR. (a) mild: the angulation at the most tortuous portion of the roots (black arrowhead) is less than 120 degrees but equal to or greater than 90 degrees, (b) moderate: the angulation at the most tortuous portion of the roots (white arrowhead).



Percentage of patients with ASA at extremities as symptom durations.

Independent Variables	B	S.E.	OR [95% CI]	P-value	VIF
Intercept	0.113	1.52	1.12 [0.06-22.04]	0.941	
Age	-0.003	0.02	0.99 [0.96-1.03]	0.878	1.08
Sex					1.02
Female	Reference				
Male	0.442	0.38	1.56 [0.74-3.28]	0.246	
CSA (mm^2)	-0.024	0.01	0.98 [0.96-0.99]	**0.013**	1.11
Multiple stenosis	1.388	0.39	4.01 [1.86-8.62]	**<0.001**	1.08
Severity of RNR					1.05
No RNR	Reference				
Mild	-0.677	0.57	0.51 [0.17-1.57]	0.508	
Moderate	0.771	0.48	2.16 [0.85-5.50]	0.106	
Severe	1.774	0.64	5.90 [1.67-20.8]	**0.006**	

Multivariate logistic regression model for factors potentially associated with presence of abnormal spontaneous activity at extremity muscles.

Conclusion: Presence of RNR, especially severe RNR, is a significant risk factor for development of denervation potentials in electromyographic study. It may help physicians to predict the prognosis of spinal stenosis patients.
Disclosure: None to disclose.

EPO-721 | Neurofilament light chain correlate with small nerve fibre damage parameters in hereditary transthyretin amyloidosis

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Background and Aims: Both serum neurofilament light chain (sNfL) levels and small fibre related variables, as skin biopsy and quantitative sensory testing (QST), are valuable disease biomarkers of hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN). Our study aimed to explore the relations between sNfL and small fibre related skin biopsy and QST data in a cohort of ATTRv-PN patients and asymptomatic carriers.
Methods: We conducted a retrospective analysis of data from 34 individuals (13 ATTRv symptomatic patients and 21 pre-symptomatic carriers) who underwent sNfL dosage, skin biopsy, and QST, and analyzed correlations between sNFL, IENFD, and thermal cold (CDT) and warm detection thresholds (WDT).
Results: We found that both sNfL and small fibre related skin biopsy and QST parameters significantly differed between carriers and patients (sNfL: $p<0.0001$; IENFD: $p=0.0008$; CDT, WDT: <0.0001). sNFL levels were normal in all carriers and altered in 85% of patients; IENFD was abnormal in 41% of carriers and 77% of patients, CDT and/or WDT were impaired in 19% of carriers and 54% of patients. sNfL negatively correlated with distal IENFD ($r=-0.47$, $p=0.005$) and significantly correlated with small fibre related QST parameters impairment (CDT: $r=-0.68$, $p<0.0001$; WDT: $r=0.57$).
Conclusion: Our study showed that sNfL reliably discriminates symptomatic ATTRv-PN patients from pre-symptomatic carriers, and found significant relations between sNfL, skin biopsy, and QST small fibre related parameters, suggesting that sNfL might be a supportive criterion for symptomatic disease transition.
Disclosure: Nothing to disclose.

EPO-722 | Short-term treatment of CIDP with Efgartigimod: A single center experience in China

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Background and Aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a type of autoimmune neuropathy that presents treatment challenges due to the limitations of standard-of-care therapies. Efgartigimod, a neonatal Fc receptor antagonist, has shown potential in treating antibody-mediated disorders, but its effectiveness for CIDP treatment has not been established.
Methods: This single-center study in China evaluated the short-term efficacy and safety of Efgartigimod in five CIDP patients. Clinical effectiveness was assessed using the Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale, Inflammatory Rasch-built Overall Disability Scale (IRODS), Medical Research Council (MRC) sum score, grip strength, Neuropathy Impairment Score (NIS), and Time Up and Go Test (TUG). Safety was evaluated by monitoring adverse events and measuring white blood cell count, serum albumin concentration, and plasma IgG concentration.
Results: All five (100%) patients responded to Efgartigimod treatment, with four (80%) meeting predefined effectiveness criteria within 8 weeks. Significant improvements were observed across clinical scales, with varied responses among patients. The average reduction rate in total IgG was 43%. Adverse events were minimal, with one patient experiencing transient diarrhea, and no aggravation of pre-existing conditions was noted.
Conclusion: Efgartigimod demonstrates promising efficacy and safety for short-term treatment of CIDP, offering a potential alternative therapy. This study provides valuable evidence from real-world application of Efgartigimod in CIDP, and the results indicate further research is warranted.
Disclosure: Nothing to disclose.

EPO-723 | Effectiveness and safety of ofatumumab in autoimmune nodopathy: A single-center cohort study

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Background and Aims: Autoimmune nodopathy is a peripheral neuropathy characterized by acquired motor and sensory deficit with autoantibodies against the node of Ranvier or paranodal region in the peripheral nervous system. Ofatumumab is the first fully human anti-CD20 monoclonal antibody, and may bring benefits to patients with autoimmune nodopathy.
Methods: This prospective observational study included 7 patients with autoimmune nodopathy, receiving subcutaneous ofatumumab 20 mg every 4 weeks (q4w) (from Week 4, after initial doses on Days

1, 7, and 14). The INCAT disability score, I-RODS, grip strength, and TUG were collected at entry and every 4 weeks. Antibodies against NF155 and CNTN1 were tested every 4 weeks, using a cell-based assay at a titer of 1:100.

Results: Six patients with anti-NF155 antibodies and one patient with anti-CNTN1 antibodies were included in the studies. At the last visit, six of the seven patients showed clinical improvement on either the INCAT, centile I-RODS or grip strength. Three of the six patients did not respond well to rituximab. The median time of reaching minimal clinically important difference was 16 weeks. Six of the seven patients improved in the 3m-TUG, and the median time of the first improvement was 4 weeks. The paranodal antibodies in these patients remain positive during the follow up visit.

Conclusion: Ofatumumab 20 mg q4w subcutaneously was effective and safe in a part of patients with autoimmune nodopathy. The association between clinical improvement and anti-paranodal antibodies needs further investigation.

Disclosure: Nothing to disclose.

EPO-724 | Fatigue in chronic inflammatory demyelinating polyradiculoneuropathy

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Background and Aims: Fatigue is a common symptom in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), significantly affecting the patients' quality of life. In this study, we aimed to evaluate the severity of fatigue in CIDP patients and its correlation to other clinical and electrophysiological parameters.

Methods: This is a prospective study. We invited all patients with CIDP diagnosis according to latest criteria and performed Fatigue Severity Scale (FSS), INCAT (Inflammatory Neuropathy Cause and Treatment Disability Scale), I-RODS (Inflammatory Rasch-built Overall Disability Scale), Hamilton Depression Rating Scale (HAM-D), Pittsburgh Sleep Quality Index (PSQI) and Visual Analogue Scale (VAS) for pain, nerve conduction studies. The final score on FSS represents the average of nine items; a score above 4.0 indicates the presence of fatigue. We compared the clinical and electrophysiological findings between patients with and without fatigue.

Results: There were 27 patients with CIDP in study period (mean age: 54 ± 12.6 years; age range 19 and 73 years; %29.6 women). Among patients included, 26% had fatigue. All patients with fatigue had axonal involvement in the follow-up examination. The number of nerves with conduction block or reduced conduction velocity did not differ between groups. INCAT and I-RODS scales did not differ significantly between groups while PSQI, HAM-D and VAS scores were slightly higher in the fatigue group.

Conclusion: Fatigue can be related to various factors independent of disease progression; such as sleep, depression and pain.

Disclosure: Funding: TUSEB 2023-B-01 Group B Project.

EPO-725 | CASPR2 antibodies in CSF in Isaac's syndrome: Altering the central neuropathic pain perception?

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Background and Aims: Isaacs syndrome (IS) or acquired neuromyotonia is a rare immune-mediated neuromuscular disorder, resulting in increased excitability of the peripheral nerves. Clinically it is characterized by fasciculations, cramps, excessive sweating and often presence of CASPR2 autoantibodies. IS can occur as a paraneoplastic condition, or it can remain idiopathic.

Methods: Case report and review of the literature.

Results: A 65-year-old man with a past medical history of prostate cancer, treated with radiotherapy 4 years ago, was referred to our Department because of a 3-year history of neuropathic pain and painful cramps in the lower limbs. Neurophysiological examination revealed spontaneous duplet, triplet and multiplet potentials in all muscles examined. IS was suspected and confirmed with the presence of positive VGKC, CASPR2 and LGI1 auto-antibodies in the serum and the cerebrospinal fluid, despite the fact there was no CNS involvement clinically. Our literature review identified six more IS cases in which CASPR2 antibodies were checked in the CSF. Out of these, two showed positive CASPR2 antibodies. In one IS remained idiopathic while in the other was associated with recurrence of malignant thymoma. Including ours, all 3 cases reported neuropathic pain.

Conclusion: To our knowledge, this is the first reported case of IS in a patient with a past medical history of prostate cancer and one of a few where CASPR2 antibodies were present in the CSF despite the lack of clinical features of CNS involvement. Presence of CASPR2 antibodies in the CSF in IS patients may be associated with an increased perception of neuropathic pain.

Disclosure: Nothing to disclose.

EPO-726 | Peripheral neural correlates of isolated genital numbness with selective serotonin reuptake inhibitor exposure

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Background and Aims: Isolated genital numbness is an uncommon neurological presentation and very little guidance exists on its assessment and aetiology. Selective serotonin reuptake inhibitors are an effective treatment for depression and anxiety disorders however

in recent years, it has become apparent there are sexual side effects and genital sensory changes have been described. We aim to describe the clinico-neurophysiologic profile in non-neurological individuals with isolated genital numbness and exposure to selective serotonin reuptake inhibitor (SSRI).

Methods: Consecutive referrals with impairment of genital sensation to a tertiary referral centre from 2018 to 2023. Urogenital clinical symptoms, contributing factors and past medical history were recorded. Pelvic sensory examination (pinprick and von frey hair) was performed at the time of sacral sensory neurophysiology testing.

Results: 12 Individuals were identified with genital numbness and current or previous exposure to SSRI (female, 33.3%). The median age was 37 years. Nine individuals reported an abnormal clinical pelvic sensory examination and had normal pelvic neurophysiology. Two individuals with SSRI exposure had abnormal pelvic neurophysiology. SSRI exposure was not a significant predictor for genital numbness. Seven reported sexual dysfunction.

Conclusion: Recent diagnostic criteria for post-SSRI sexual dysfunction is defined as somatic or erogenous genital sensation after treatment stops. We found 83% of individuals with genital numbness and exposure to SSRI had a normal pelvic neurophysiology examination. The concept of erogenous sensation is relevant and we postulate that the aetiology of SSRI associated genital numbness with normal neurophysiology is due to central sensory and emotional processing dysfunction.

Disclosure: SLW reports a relationship with Roche that includes honoraria and support to attend conferences; with Merck for speaking honoraria and support to attend conferences. Jalesh Panicker reports a relationship with: Wellspect HealthCare UK that includes: speaking and lecture fees; with Idorsia Pharmaceuticals Ltd that includes: consulting or advisory; with Coloplast Ltd that includes: consulting or advisory and speaking and lecture fees; with Corporate Allergan Inc that includes: speaking and lecture fees; with Novartis that includes: speaking and lecture fees; Cambridge University Press: royalties; Continence Reports Editorial Board.

EPO-727 | Unmet need in patients with chronic inflammatory demyelinating polyneuropathy: Results from a Real-World Survey

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Background and Aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a disabling neurological condition characterised by progressive muscle weakness and impaired sensory function. The aim of this study was to identify unmet needs among patients with CIDP.

Methods: Data were drawn from the Adelphi CIDP Disease Specific Programme™, a cross-sectional survey of neurologists in France, Germany, Italy, Spain, UK (September 2022 – April 2023), treating at least two CIDP patients per typical month. Patients completed patient-reported outcome assessments, including the Inflammatory Rasch-Built Overall Disability Scale (I-RODS) and Work Productivity and Activity Impairment questionnaire (WPAI:SHP). This real-world data is limited by participating physicians' confirmation of the included patient's CIDP diagnosis.

Results: 83 physicians provided data for 542 patients with CIDP, of whom 463 were receiving maintenance treatment (1st line: 293; 2nd: 140; 3rd: 26; 4th/5th: 4 [excluded from analyses]). Physicians reported dissatisfaction, or partial satisfaction with treatment for 57.9% of patients (1st: 57.7%; 2nd: 52.1%; 3rd: 92.3%). Across all lines, the most frequent reason for lack of satisfaction was "efficacy declining over time". Patients reported a mean (SD) I-RODS centile score of 59.8 (18.5) (1st: 61.8 [19.4]; 2nd: 56.6 [16.4]; 3rd: 57.4 [21.4]), and a mean WPAI percentage activity impairment of 43.0 (25.2) (1st: 40.1 [24.4]; 2nd: 47.3 [25.5]; 3rd: 50.0 [32.2]).

Conclusion: Patients with CIDP reported substantial disability and impairment in daily activities, and in many cases their physicians were not fully satisfied with treatment. Identifying factors associated with poor initial treatment response and loss-of-efficacy, and new therapeutic developments, may lead to improved outcomes for these patients.

Disclosure: Data collection was undertaken by Adelphi Real World as part of an independent survey, entitled the Adelphi Real World CIDP Disease Specific Programme. Janssen were one of multiple subscribers to the dataset. The study described here was funded by Janssen.

EPO-728 | Nodal-/paranodal autoantibody-associated autoimmune nodopathies in Estonian population

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Background and Aims: Autoantibodies to peripheral nerve molecules seem to play role in the pathogenesis and also provide diagnostic, prognostic, and therapeutic value for autoimmune peripheral neuropathies, such as CIDP. Corticosteroids, intravenous immunoglobulin (IVIg) and plasma exchange are mainstays of treatment, yet some patients respond poorly to standard treatments. Disease-specific antibodies targeting proteins at the node and paranode of Ranvier, such as neurofascin-155 (NF155), contactin-1 (CNTN1), contactin-associated protein 1 (Caspr1), neurofascin-140/186 (NF140/186), have been described in small subsets of CIDP patients with similar clinical features, treatment response, namely poor response to IVig and more favourable to rituximab, and hence differing from typical CIDP.

Methods: This study presents an overview of autoimmune nodopathies in Estonian population based on cohort of polyneuropathy patients in West-Tallinn Central Hospital's Neurology department tested over a period form October 2022 to October 2023.

Results: 11 out of 112 patients tested positive for nodal-/paranodal autoantibodies: 7 for contactin1, 3 for NF155 IgG, 1 for NF155 IgM, 3 for NF155 IgG and IgM, 1 for contactin1 and NF155 IgG antibodies. Most frequent clinical picture among nodopathy patients was severe flaccid tetra- or paraparesis with sensory disturbances. Other clinical pictures included cerebellar findings, gait problems, but also central symptoms not reported in scientific literature as part of nodopathy syndrome.
Conclusion: Testing for nodal/paranodal antibodies can help improve diagnostic accuracy and guide treatment for polyneuropathy patients, especially those suspected of having inflammatory demyelinating polyneuropathy. Considering the varied clinical picture in our cohort, there also remains the question whether all positive results are of clinical significance.
Disclosure: Nothing to disclose.

EPO-729 | Characteristics and outcome of CIDP patients according to their electrodiagnostic certainty (2021 EAN/PNS criteria)

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Background and Aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) has heterogeneous presentation and clinical course. The aims of this study are to describe the clinical and electrophysiological characteristics of patients with CIDP or possible CIDP, according to the latest 2021 EAN/PNS criteria, and to compare the long-term outcome in both groups.
Methods: We retrospectively included 29 adult "CIDP" and 21 "possible CIDP" patients. We reviewed their clinical data, which included the neuropathy impairment scale (NIS) and modified Rankin Scale (mRS), response to treatment, cerebrospinal fluid examination, and nerve conduction studies parameters. Data were collected at first evaluation of the patient (T0), and at one (T1), two (T2) and three years (T3).
Results: At baseline, CIDP patients had a higher NIS score (median NIS score of 38 versus 20.5, $p=0.03$), and more frequently a "typical CIDP" phenotype ($p=0.02$) than possible CIDP patients. Other variables did not differ significantly. CIDP patients tended to have a better objective response to immunotherapy (66% responders) than possible CIDP patients (43% responders, $p=0.15$). Between baseline and T3, there was a median (IQR) Δ NIS of −12.8 (−32, 0) and Δ mRS of −1 (−2, 0) for CIDP patients and 2.5 (−7.8, 8.5) and 0 (−0.8, 0) for possible CIDP patients ($p=0.01$ and <0.01 respectively).
Conclusion: "CIDP" patients had a more severe neuropathy, estimated with the NIS score, and "possible CIDP" patients had a more atypical phenotype at baseline. Our data suggest that patient outcome is better in CIDP than possible CIDP.
Disclosure: Nothing to disclose.

Neurorehabilitation

EPO-730 | TDCS effects on motor and cognitive function in paediatric brain injury: Systematic review and meta-analysis

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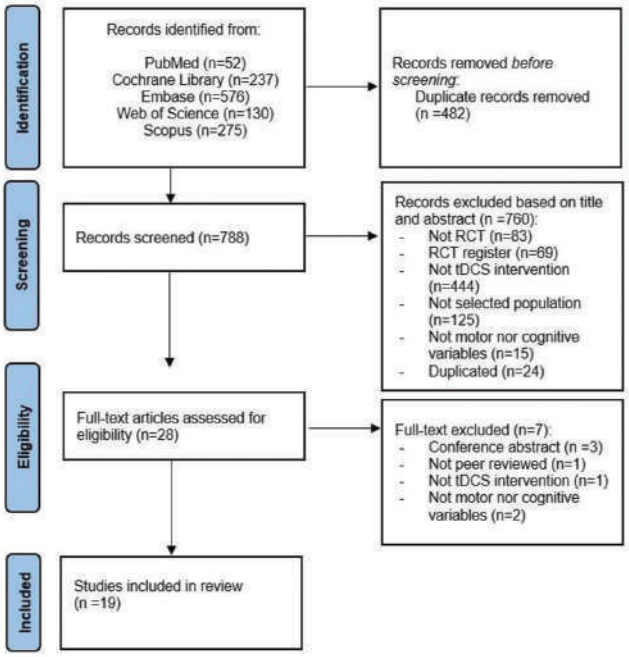
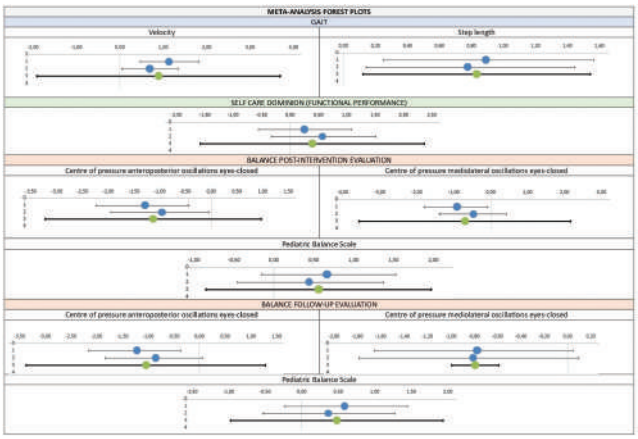
Background and Aims: Paediatric non-progressive brain injuries result in diverse impairments, including motor and cognitive issues. Transcranial direct current stimulation (tDCS), emerges as a technique to influence neuroplasticity processes as an adjunct therapy in rehabilitation. This review aims to assess tDCS effects on motor and cognitive variables in non-progressive paediatric brain injuries, correlation with intervention parameters and associations between functions.
Methods: A systematic review and meta-analysis were conducted, assessing randomized controlled trials in patients with paediatric brain damage and cognitive or motor variables with tDCS interventions. 5 databases were searched. PEDro scale, ROB-2 and GRADE assessed methodological and evidence quality.
Results: Data from 19 studies (447 participants) (fig.1) revealed positive effects on gait, balance, functional performance, and cognition. Upper limb function evidence remains inconsistent due to limited publications. Cognitive intervention influenced motor outcomes, and motor-centered interventions impacted functionality related to cognition. Meta-analysis showed statistically significant improvements in gait (SMDs: 0.83–0.90, $p<0.0001$), balance (Centre of pressure oscillations SMDs: −0.51 to −1.13, $p<0.02$; PBS SMDs: 0.48 to 0.56, $p<0.0001$) and self-care (SMD: 0.40, $p<0.01$) (Table 1). Mean PEDro scale score was 7.46. According to ROB-2, two studies presented low risk of bias, 12 studies had some concerns and 5 presented high risk. Quality of evidence is small for gait and self-care, and medium for balance.



PRISMA flow diagram.



Meta-analysis forest plots.

Conclusion: TDCS seems beneficial for cognitive and motor variables in paediatric brain damage. Both variables seem to be interconnected, so further research with homogeneous samples, standardized and combined protocols is needed.

Disclosure: Authors had no conflicts of interest. Funding by GMP foundation.

EPO-731 | Aerobic capacity moderates the association between cervical cord atrophy and disability in MS patients

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Background and Aims: Cervical cord atrophy has been associated with disability in multiple sclerosis (MS). Higher aerobic capacity (AC) has shown positive effects on several symptoms related to MS, which may also influence disability level. This study aimed to understand whether AC moderates the association between cervical cord atrophy and disability in MS.

Methods: In this cross-sectional analysis, expanded disability status scale (EDSS), peak of maximal oxygen consumption (VO_2max) and mean upper cervical cord area (MUCCA) calculated from 3D T1-weighted brain MRI images were obtained for 60 MS patients and 36 healthy controls (HC). The HC group was used to define VO_2max *z*-scores and −1 standard deviation was considered as cut-off to identify patients with low or high AC. In MS patients, an age- and sex-corrected analysis was conducted to understand if AC can moderate the association between MUCCA and EDSS.

Results: Compared to HC, MS patients showed lower MUCCA and VO_2max values ($p<0.001$). The interaction between MUCCA and AC was significant ($\beta=-0.142$, $p=0.002$), indicating that the relationship between MUCCA and EDSS was moderated by AC. Lower MUCCA was associated with higher EDSS score only in patients with low AC ($\beta=-0.115$, $p<0.001$), no association was found in patients with high AC ($\beta=0.027$, $p=0.486$).

Conclusion: This study shows that AC is a moderator of the relationship between MUCCA and EDSS, suggesting that high level of AC may represent a functional reserve able to prevent or limit clinical disability in MS patients. Funding. Partially supported by Italian Ministry of Health (GR-2019-12369599).

Disclosure: M Albergoni, C Dallari, A Meani, and P Valsasina have nothing to disclose; P Preziosa received speaker honoraria from Roche, Biogen, Novartis, Merck Serono, Bristol Myers Squibb, Genzyme, Horizon and Sanofi, and research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). M. Filippi received compensation for consulting or speaking activities services from Alexion, Almirall, Biogen, Bayer, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly,

Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, Italian Ministry of Health, Italian Ministry of University and Research, and FISM. MA Rocca received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche; speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; research support from MS Society of Canada, Italian Ministry of Health, Italian Ministry of University and Research, and FISM.

EPO-732 | A combined neuromodulation protocol to enhance cognitive and lower limb rehabilitation in corticobasal degeneration

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Background and Aims: Corticobasal Degeneration (CBD) is characterized by asymmetrical motor alterations and neuropsychological impairments. No effective therapy is known. Non-invasive neuromodulation can modulate cortical activity in other diseases, improving motor performance (1). Motor imagery and action observation are known to improve motor control and gait in several neurological disorders (2). We describe the outcome of a personalized neuromodulation protocol on a 71-year-old female, diagnosed with CBD. A PET-CT revealed right frontal hypoactivity. Although lower limb strength is normal, alien leg and apraxia rendered her wheelchair-bound. The objective was to assess the effectiveness of a non-invasive neuromodulation protocol—tDCS, Action Observation (AO), and Motor Imagery (MI)—for enhancing motor and cognitive performance.

Methods: 20 sessions of 20-minute 2 mA anodal tDCS stimulation over right M1, combined with 30-minute AO+MI (fig 1). Treatment was administered daily for 4 weeks. Training involved different movements each weekday (fig 2), with a gradual shift from AO to a more active approach as weeks progressed.

Results: Post-treatment improvements were observed in balance (16 to 23), functional strength (5TSTS 83 to 53), and partially sustained postural control enhancements (5TSTS 83 to 67 in follow-up). Persistent gains in set-shifting, inhibitory control (TMT-B), working memory (Inverse Digits), and attentional span (Direct Digits) were noted. Post-treatment improvements in emotional well-being and general health (SF-36) weren't sustained. FES-I scores remained stable post-treatment but rose during follow-up.

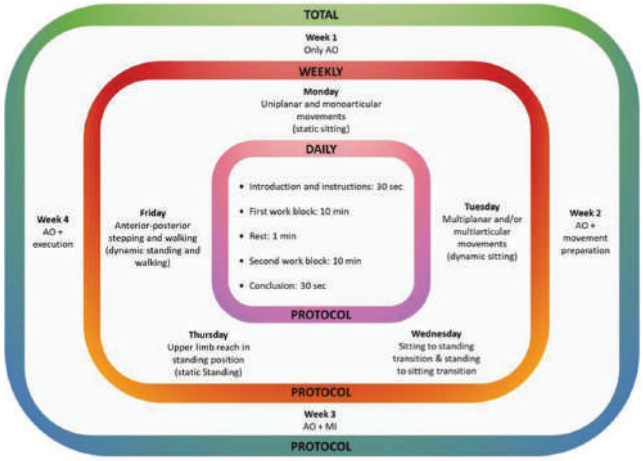

FIGURE 1 The four-week intervention protocol based on graded progression. AO: Action Observation; MI: Motor Imagery; tDCS: Transcranial Direct Current Stimulation.

FIGURE 2 The weekly intervention protocol based on graded progression.

	A	B	C
Motor domains			
Berg Balance Scale	16	23	14
5-Times Sit to Stand (in seconds)	83	52.89	67
10-Meter Walking Test (in m/s)	0.229	0.243	0.166
Cognitive domains[1]			
Wechsler Adult Intelligence Scale-IV			
Symbol search	12	12	11
Direct digits	10	8	13
Inverse digits	10	14	14
Trail Making Test			
A	12	9	13
B	10	11	12
STROOP			
Word	7	6	7
Colour	8	7	10
Word-Colour	9	10	13
Functional domains			
Cortical Basal ganglia Functional Scale			
Part A	20	19	25
Part B	3	3	5
Total	23	22	30
Short Form Health Survey-36			
Physical Functioning	0	0	0
Role Limitations due to Physical Health	0	0	0
Emotional well-being	52	60	44
Social Functioning	87.5	87.5	50
Role Limitations due to Emotional Health	100	100	0
Pain	100	100	100
General Health	40	45	35
Energy/Fatigue	50	45	50
Falls Efficacy Scale – International	57	57	62

TABLE 1 Outcome measures pertaining to each domain evaluation. Score columns A to C correspond to each of the 3 evaluations: baseline, post-intervention and follow-up.

Conclusion: The combined tDCS+AO+MI protocol maintained or improved balance, motor control, attentional, mnesic, and executive functions in a CBD patient, highlighting the potential of this technology in CBD rehabilitation and treatment.
Disclosure: Nothing to disclose.

EPO-733 | Motivation and recovery: An analysis of reward sensitivity and motor learning after ischemic stroke

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Background and Aims: Stroke is a major global cause of disability, posing challenges in neurological rehabilitation. Cerebral network reorganization and learning limitations are critical in this process. Despite the recognized importance of behavioral rehabilitation, the specific role of the brain's reward system in post-stroke learning remains unclear. Hypothesis: Building on our prior findings (Wagner et al., 2023), we posit an intrinsic link between the reward system's functionality and motor learning abilities after a stroke. We propose parallel recovery processes for both, with a gap in understanding their timelines.
Methods: A cohort study of 20 stroke patients (mean age: 67, range: 55–80 years) evaluated at t 3–4 months post-stroke. Motor learning and reward system functionality were assessed using the Monetary Incentive Delay (MID) task during MEG for connectivity analysis. A (VR) learning environment was used for five days to control fluctuations and to study motor learning consolidation.
Results: Patients displayed reduced reward sensitivity, needing greater incentives for improvement, and experienced learning deficits. These deficits correlated with altered connectivity patterns during the MID task, revealing stroke's impact on the reward system and behavior. Learning impairment closely linked to reward sensitivity, irrespective of lesion localization (Coherence Analyses ongoing).
Conclusion: By demonstrating the connection between stroke, reward sensitivity, and learning ability, this research contributes valuable knowledge to the field, suggesting why some stroke survivors continue to experience long-term challenges despite rehabilitation. The findings underscore the necessity of assessing reward sensitivity in stroke patients to optimize rehabilitation protocols, thereby maximizing their recovery potential.
Disclosure: Nothing to disclose.

EPO-734 | The role of sleep in motor memory consolidation in subacute stroke patients: A pilot study

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Background and Aims: Since sleep improves motor learning and stroke patients are frequently characterised by sleep disorders, it is essential to evaluate its contribution in memory consolidation in this context. While evidence already exists in chronic stroke, data are still scarce on the subacute phase during neurorehabilitation treatment. In order to characterise the role of sleep in subacute stroke, we evaluated: i) whether sleep promotes the consolidation of declarative and non-declarative memory; ii) possible correlations between sleep and motor and cognitive performance.
Methods: Eight subacute stroke patients, on different days, underwent two experimental conditions each including two sessions of the Memory Similarity Task (MST) and two sessions of the Finger-tapping Task (FTT). The two conditions, in randomised order, involved: (I) Day trial: patients were tested first at 8 am and, thereafter, at 8 pm, avoiding sleep during the day; II) Night trial: test times were reversed with a night's sleep between them. Moreover, sleep and biometric data were collected by means of a ©Fitbit device.

Results: Accuracy and recognition memory at MST showed a significant effect of session ($p < 0.001$). Furthermore, patients' recognition memory improved in the sleep condition rather than in wakefulness ($p = 0.041$). Similarly, FTT accuracy had a significant effect of session ($p < 0.001$). Moreover, an improvement in sleep-related accuracy was observed ($p = 0.025$). The session-by-condition effect was not statistically significant in both tasks.

Conclusion: Sleep seems crucial in the consolidation of procedural memory also in the subacute stroke timeframe. Thus, sleep quality interventions are fundamental in promoting recovery from the earliest stroke stages.

Disclosure: The authors declare no conflicts of interest. This work was supported by the project MNESYS (PE0000006) – A Multiscale integrated approach to the study of the nervous system in health and disease (DN. 1553 11.10.2022).

EPO-735 | Gait rehabilitation of patients after stroke using the C-Mill treadmill

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Background and Aims: Patients after stroke often have gait disturbances with asymmetry, slowing, discoordination of gait and increased risk of falling. Gait rehabilitation on the C-Mill walking/treadmill is one way to improve gait parameters. Aim of the study: to test whether using the C-Mill treadmill will improve walking parameters such as walking speed and gait quality.

Methods: 20 probands in subacute to chronic stage after stroke participated in the study. All patients had gait impairment but with the condition of walking without support. Patients were randomly divided into a control group (standard rehabilitation + 1 hour of C-Mill walking per week) and an experimental group (standard rehabilitation + 5 hours of C-Mill walking per week). Before starting therapy, medical history and clinical tests were taken and questionnaires were filled in for all patients. After a 3-week hospitalization with intensive rehabilitation and C-mill walking training, an exit examination was performed. Gait speed, subjective perception of gait quality, and self-sufficiency were assessed.

Results: At baseline examination, patients in the experimental group showed clinically and statistically significant ($p < 0.05$) improvement compared to the control group. This was evident in all measured domains, i.e.: gait speed, subjective perception of gait quality and self-sufficient.

Conclusion: the combination of complex rehabilitation (physiotherapy, mechanotherapy, physical therapy and gait training on the C-Mill treadmill positively affects gait in patients in the subacute and chronic stage after stroke.

Disclosure: We have no conflicts of interest.

EPO-736 | Outcome measures to assess the efficacy of physical therapy in postural orthostatic tachycardia: A systematic review

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Background and Aims: Physical therapy is recommended as first-line treatment for individuals with POTS by expert consensus. There is a need to identify the evidence base of this treatment approach. Here we evaluated how primary (p) and secondary (s) outcome has been measured to date.

Methods: We systematically screened the databases PubMED, Cochrane and Web of Science combining the keywords: "Postural orthostatic tachycardia", "physical therapy", "exercise".

Results: We selected 17 studies and two study protocols. Change after exercising was measured by active standing test (primary np = 3, secondary ns = 10) or head-up tilt test (np = 5, ns = 3), cardiopulmonary exercise tests (np = 3, ns = 8), pulse-oximetry (np = 0, ns = 1), walking test (np = 0, ns = 1) or questionnaires (np = 1, ns = 13). Mean or highest heart rate response to exercise measured at different timepoints was a common outcome (np = 6, ns = 12). Further primary outcome measures were: time spend upright and steps per day ($n = 1$), number of individuals who fulfilled the POTS-criteria ($n = 2$) or peak oxygen uptake (VO_2max, VO_2peak) ($n = 3$). Symptom severity improvement as secondary outcome was assessed with the Short Form Health Survey in three studies, Composite Autonomic Symptom Score −31 items ($n = 2$), Vanderbilt Orthostatic Symptom Score ($n = 3$), Malmö-POTS-questionnaire and Boston Autonomic Symptom Questionnaire (one study each). Health related quality of life was assessed with the EQ-5D-5L in two studies and with the SF-36 in one.

Conclusion: Recent studies and ongoing trials adopt detailed outcome assessments, taking into account POTS clinical heterogeneity and focusing on meaningful changes of functional ability.

Disclosure: Nothing to disclose.

EPO-737 | Abstract withdrawn

EPO-738 | Role of supination, extension and abduction posture in upper limb spasticity prevention in acute stroke

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Background and Aims: Post-stroke spasticity is a common complication of stroke. The study evaluated the efficacy of a posture opposite to the typical spastic posture i.e. Supinated forearm, Extended

fingers and elbow and Abducted and externally rotated shoulder (SEA) with wrist in neutral position (Figure 1) in acute stroke patients with flaccid weakness in prevention of development of spasticity.

Methods: Hemodynamically stable acute stroke patients between 18–80 years of age with flaccid upper limb weakness presenting within 72 hours were included. It was a prospective, single-center, randomized, open-label trial with blinded endpoint assessment.

Results: Of 170 acute stroke patients, 76 met the inclusion criteria. 38 patients randomized in each splint (Group 1) and control arm (Group 2). Ten patients lost to follow up. Of remaining 66 patients (34 in splint and 32 in control), the median age of patients was 55 years. Forty-two (64%) patients were male. There was no significant difference in baseline demographic, clinical, radiological, and biochemical parameters between the two groups (Table 1). At 3 and 6 months, there was significant difference (p value < 0.05) in Modified Ashworth upper limb spasticity score at elbow, forearm (pronation and supination), wrist and fingers between the two groups. Barthel Index for Activities of Daily Living was also significantly better in group 1 at 3 and 6 months (Table 2). However, there was no difference in mRS score during follow up.

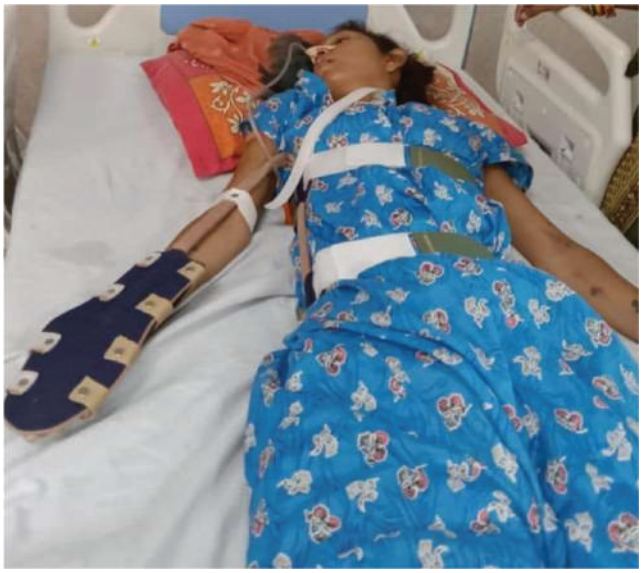

Figure depicting the application of a splint keeping the flaccid upper limb of a patient in a SEA posture i.e. Supinated forearm, Extended fingers and elbow and Abducted and externally rotated shoulder (SEA) with wrist in neutral position.

Baseline variables	Group 1 (N=34), Number (%)	Group 2 (N=32), Number (%)	P-value
Age (years), mean±SD	56.44±10.96	57.47±13.14	0.73
Male	21	21	0.74
ICH	18	24	0.06
Ischemic stroke	16	8	
NIHSS, mean±SD	14±3.91	15.50±4.78	0.42
ICH score, mean±SD	1.16±0.76	1.33±1.12	0.56
mRS, median (IQR)	5 (4-5)	5 (5,5)	0.28
Barthel index, median (IQR)	0 (0)	0 (0)	0.48
Seizure	1	1	1.00
Altered sensorium	15	12	0.58
Risk Factors			
Addiction	17	15	0.80
Diabetes mellitus	7	6	0.90
Hypertension	28	29	0.20
Obstructive sleep apnea	0	1	0.47
Coronary artery disease	2	0	0.49
Dyslipidemia	4	8	0.14
Atrial fibrillation	1	0	1.00
Hyperhomocysteinemia	16	14	0.88
Laboratory parameters			
Hemoglobin, mean±SD	12.80±1.88	12.57±1.85	0.63
Total leucocyte count, mean±SD	10285.58±3888.28	10758.75±3580.23	0.61
Urea, mean±SD	41.82±19.44	38.66±22.03	0.54
Creatinine, mean±SD	0.96±0.23	0.95±0.37	0.88
HbA1c, mean±SD	5.89±1.08	5.89±1.57	0.99
Protein, mean±SD	7.84±1.62	7.71±0.84	0.68
Albumin, mean±SD	3.95±0.38	3.98±0.49	0.78
TC, mean±SD	180.85±43.89	190.81±39.50	0.34
TG, mean±SD	150.88±64.36	149.65±52.72	0.93
LDL, mean±SD	116.06±42.45	107.77±32.02	0.37
HDL, mean±SD	45.27±15.34	51.35±16.94	0.13
VLDL, mean±SD	32.14±19.60	32.86±23.71	0.89

Abbreviations: HbA1c- Glycosylated hemoglobin, HDL- High density lipoprotein, ICH- Intracerebral hemorrhage, LDL- Low density lipoprotein, mRS- modified Rankin Scale, NIHSS- National Institutes of Health Stroke Scale, TC- Total cholesterol, TG- Triglyceride, VLDL- Very low density lipoprotein

Comparison of baseline demographic, clinical, radiological and laboratory variables between the two groups.

Outcome parameters		Group 1, median (IQR)	Group 2, Median (IQR)	P- value
At 3 months				
mRS				0.56
	1	1	0	
	2	7	4	
	3	15	12	
	4	9	12	
	5	2	4	
Modified Ashworth spasticity score				
	S	2 (1-3)	3 (2-3)	0.055
	E	2.5 (1-3)	3 (2-4)	0.014
	PS	2 (2-3)	3 (2-4)	0.012
	W	2 (1-3)	3 (2-4)	0.008
	F	2 (2-3)	3 (2-4)	0.007
Barthel index		75 (48.75- 90)	50 (32.5- 77.5)	0.017
At 6 months				
mRS				0.25
	1	1	0	
	2	9	5	
	3	17	13	
	4	5	11	
	5	2	3	
Modified Ashworth spasticity score				
	S	2 (1-2.25)	2 (2-3)	0.537
	E	2 (1-3)	3 (2-3)	0.028
	PS	2 (1-3)	3 (2-4)	0.027
	W	2 (1-3)	3 (2-4)	0.007
	F	2 (2-3)	3 (2-4)	0.01
Barthel index		82.5 (70-95)	65 (41.25- 82.5)	0.021

Abbreviations: E- elbow, F- Fingers, mRS- modified Rankin Scale, PS- Pronation-supination, S- Shoulder, W- Wrist

Comparison of outcome measures between the two groups at 3 and 6 months.

Conclusion: SEA posture if applied early in acute stroke patients is effective in reducing the grade of upper limb spasticity.

Disclosure: Nothing to disclose.

EPO-739 | Creating interactive virtual reality applications for social deficit remediation in children with neurological disorders

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Background and Aims: The aim was to evaluate the suitability of SocialVR applications developed for pediatric neurorehabilitation with assessing anxiety levels during difficult social situations.
Methods: 33 children aged 6–15 yrs participated: 17 with neurological disorders (ND) and 16 healthy controls. Therapist observed scenarios on screen, selecting the avatar's according to child's skills. Headsets Oculus Rift or HTC Vive were used. 10 difficult social VR metaphors with 2 levels of complexity were created by authors (cafeteria, cinema, bullying, etc.). Social anxiety was assessed by heart rate (HR) changes in all children and with Spence Anxiety Questionnaire (SCAS) in 14 children.
Results: Applications of varying severity were suitable and indicated for developing social neurorehabilitation. Most challenging situations were "friend losing a phone" (average HR rise 9.1) and "ball in neighbor's garden" (HR rise 9). Therefore, metaphors requiring patients to console or apologize showed higher anxiety compared to the control group (HR 7.9 and 8.3, respectively). Examination of social attention showed lower abilities in finding details. By SCAS 8/9 ND patients reported elevated anxiety base levels in at least one domain; only 2 out of 5 controls reported some anxiety symptoms.

FIGURE 1 Child with ND participating in a cafeteria metaphor during a social rehabilitation session.

Conclusion: Artificial VR environments allow children to practice communication skills in socially and emotionally challenging but safe situations. SocialVR is a new promising pediatric neurorehabilitation tool to support prosocial learning and reduce social anxiety in children.
Disclosure: Authors declare no relevant or material financial interests that relate to research. The study was funded by Estonian Science Foundation PRG789.

EPO-740 | Effectiveness of shock wave therapy in the treatment of patients with neurological post-COVID-19 erectile dysfunction

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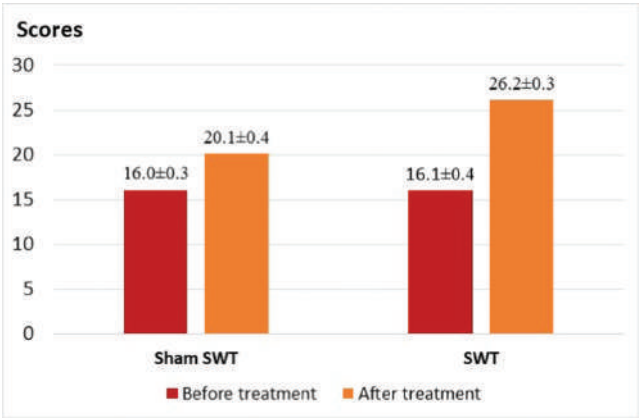
Background and Aims: To study the effectiveness of shock wave therapy (SWT) in treatment of patients with neurological post COVID-19 erectile dysfunction compared to sham SWT.
Methods: We observed 40 patients with neurological erectile dysfunction after suffering from COVID-19. The patients were divided into 2 groups. In addition to standard drug therapy 20 patients underwent sham SWT (control group) and 20 patients received effective SWT (treatment group). Impairment of the pudendal nerve has been confirmed by clinical and neurophysiological examinations.
Results: The International Index of Erectile Function (IIEF) scores after SWT were 1.54 times higher than after sham SWT ($p < 0.01$). Sexual quality of life (QoL) became 1.52 times better after SWT compared to sham SWT ($p < 0.01$). In addition, SWT increased the effectiveness of PDE-5 inhibitor drugs in improving erectile function by 2.54 times ($p < 0.01$).



Dynamics of the international index of erectile function in the treatment of patients with erectile dysfunction after COVID-19 in the control and treatment groups.

Conclusion: SWT therapy has proven effective in improving erections in patients with neurological post COVID-19 erectile dysfunction. The high effectiveness of SWT is due to the activation of regenerative processes in tissues, improved blood circulation, increased excitability of nerve fibers, stimulation of neovascularization and normalization of NO levels in cavernous endothelial cells.
Disclosure: Nothing to disclose.

EPO-741 | Efficiency of low level laser therapy in improvement of fine movement skills after carpal tunnel decompression

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Background and Aims: To compare the effectiveness of low level laser therapy of median nerve in improvement of fine movement skills after carpal tunnel decompression surgery.
Methods: We observed 50 patients with residual fine movement skills impairment after Carpal Tunnel Decompression Surgery. 25 patients underwent sham laser therapy (control group) and 25 patients received low level laser therapy (treatment group). Fine movement skills were assessed in all patients using the Jebsen-Taylor test before treatment, after treatment and after 3-months of follow-up period.
Results: After treatment: a significant improvement in Jebsen-Taylor's test scores was found in treatment group after low level laser therapy, but not in control group. The total test execution time in treatment group decreased by 12% ($t=2.14$, p-value$=0.036$). After 3 months of follow-up period additional positive therapeutic response was found in reduction of the test duration in all subtests by 10.6% ($t=4.91$, p-value$=0.01$).
Conclusion: Low-level laser therapy for the median nerve has been shown to be very effective in improving residual fine motor skills after carpal tunnel decompression surgery. This is due to decreased fiber axonopathy and effective reinnervation, which improve coordinated sensorimotor control of the fingers.
Disclosure: Nothing to disclose.

EPO-742 | Efficacy and safety of modafinil/armodafinil for post-traumatic hypersomnia: A systematic review and meta-analysis

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Background and Aims: Traumatic Brain Injury (TBI) is a global health issue frequently related to chronic debilitating symptoms such as excessive daytime sleepiness (EDS). While the optimal management of EDS is still unclear, neurostimulants are often empirically employed. Thus, we aimed to perform a systematic review and meta-analysis to assess the efficacy and safety of modafinil/armodafinil versus placebo on post-TBI patients experiencing EDS.
Methods: We searched PubMed, Cochrane, Embase, Web of Science, and ClinicalTrials.Gov databases and identified studies comparing modafinil or armodafinil to placebo in post-TBI patients experiencing EDS. A random-effects model was used in all analyses.
Results: We included three randomized controlled trials involving 188 patients. The mean age was 34.11, and 61.9% were male. In patients treated with modafinil (dose range: 100–400 mg) or armodafinil (dose range: 150–250 mg), the mean Epworth Sleepiness Scale score was decreased in comparison to placebo (mean difference −1.70; 95% confidence interval [CI] −3.32 to −0.09; $p=0.04$; Fig. 1). The risk of insomnia was higher in the modafinil/armodafinil group compared to placebo (risk ratio 3.73; 95% CI 1.11 to 12.54; $p=0.03$). There was no difference between groups in the risk of other adverse events, such as nausea ($p=0.09$), headache ($p=0.56$), dizziness ($p=0.25$), and nasopharyngitis ($p=0.67$).

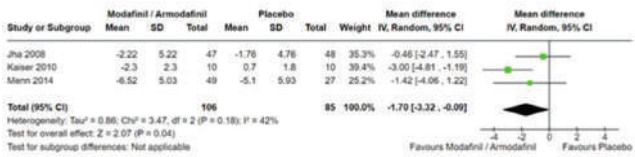

FIGURE 1 In patients with post-traumatic hypersomnia, somnolence, as measured by the Epworth Sleepiness Scale, was significantly reduced in the modafinil/armodafinil when compared to placebo.

Conclusion: Treatment with modafinil or armodafinil was associated with a significant reduction in somnolence in post-TBI patients when compared to placebo. However, this therapy also increased the risk of insomnia. Further research is warranted to optimize the risk-benefit profile of these agents in this population.
Disclosure: Nothing to disclose.

EPO-743 | EEG evaluation of the influence of rTMS in the rehabilitation of patients with ischemic stroke

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Background and Aims: Objective: To study the influence of rTMS on the state of the brain's bioelectric activity in patients with ischemic stroke in order to determine the prognostic parameters for better motor recovery and to develop an optimal therapeutic protocol.
Methods: For the period between January 2015 and September 2022, a total of 136 patients with ischemic stroke were included in the study. Patients were divided into three groups: In the first, 17 patients (12.5%) received 10 consecutive sessions of rTMS with LF stimulation in the unaffected hemisphere, in the second – 18 (13.2%) HF stimulation in the affected hemisphere, and in the third – 101 (74.3%) combined rTMS protocol in both hemispheres. EEG was performed in all patients before the start of the course and after the last session.
Results: The main trend of influence of rTMS on the brain activity is associated with a clear increase in the share of alpha rhythm, especially

pronounced in the combined stimulation group. A correlation was observed between the increase in alpha activity in the affected hemisphere, recorded on EEG, and the motor performance of the patient, demonstrated by the decrease in the motor threshold over the course of treatment.

Conclusion: rTMS appears to be a promising therapeutic method to improve functional recovery in patients with ischemic stroke. The routine use of EEG is an invaluable technique for monitoring and optimizing the individual effect of each patient during the course of treatment.

Disclosure: Nothing to disclose.

EPO-744 | Longitudinal goal attainment following treatment with abobotulinumtoxinA in adults with lower limb spasticity

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Background and Aims: This prospective, observational study (NCT04050527) assessed the longitudinal attainment (over 16 months) of function-related goals after one or more abobotulinumtoxinA injections for lower limb spasticity in the clinical setting.

Methods: Ambulatory adult patients with unilateral lower limb spasticity (able to take at least 5 steps with/without assistance) were treated with abobotulinumtoxinA in accordance with local prescribing guidelines to achieve individualized function-related goals.

Results: At the population level, goal attainment was as expected over repeated cycles; mean cumulated GAS-leg *T* score at 16 months (primary endpoint) was 48.2 [47.4, 48.9] (mean change from baseline of 9.9 [9.1, 10.7]). Patients who were injected with injection guidance at baseline were significantly more likely to attain their goals than those in whom no guidance was used (odds ratio: 2.63 [1.72, 4.0], $p < 0.0001$). Patients treated concomitantly for upper limb spasticity were also more likely to attain their goals than those only injected in the lower limb (odds ratio: 2.3 [1.3, 4.3], $p = 0.005$). Adverse events (AEs) were reported by 56 (13.5%) patients; most were mild-moderate and considered unrelated to treatment. Six patients (1.4%) had an AE possibly/probably related to treatment.

Conclusion: This large, international study provides evidence for the benefit of repeated cycles of abobotulinumtoxinA in the lower limb in helping patients achieve meaningful goals, demonstrates the importance of appropriate injection guidance techniques and points to the benefit of treating the upper limb in combination with lower limb when clinically indicated. Treatment with abobotulinumtoxinA was generally well-tolerated and safe; no new safety issues were identified.

Disclosure: Funded by Ipsen.

Movement disorders 7

EPO-745 | Movement disorders after basal ganglia ischemic lesions following mechanical thrombectomy: An emerging clinical entity

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Background and Aims: Post-stroke movement disorders (PMDs) following ischemic lesions of the basal ganglia (BG) are a known entity, but data regarding incidence are missing. Ischemic strokes secondary to proximal middle cerebral artery (MCA) occlusion treated with thrombectomy represent a model of selective damage of the BG. Aim of this study was to assess prevalence and features of movement disorders after selective BG ischemia in patients with successfully-reperfused acute ischemic stroke.

Methods: We enrolled 64 consecutive subjects with acute ischemic stroke due to proximal MCA occlusion treated with thrombectomy. Patients were clinically evaluated by a movement disorders specialist for PMDs onset at baseline, after 6 and 12 months.

Results: None of the subjects showed an identifiable movement disorder in the subacute phase of the stroke. At 6- and 12-months respectively 7/25 (28%) and 7/13 (53.8%) of evaluated patients developed PMDs. The clinical spectrum of PMDs encompassed parkinsonism, dystonia and chorea, either isolated or combined. In most patients, symptoms were contralateral to the lesion, although a subset of patients presented with bilateral involvement and prominent axial signs.

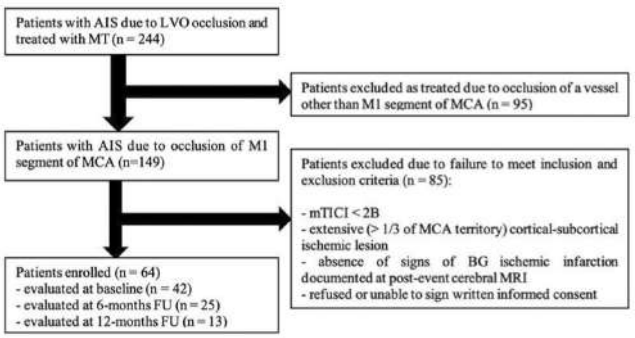

Figure 1: Flowchart of the study; Abbreviations: AIS: acute ischemic stroke; LVO: large vessel occlusion; MT: mechanical thrombectomy; MCA: middle cerebral artery; mTICI: modified treatment in cerebral ischemia score; BG: basal ganglia; MRI: magnetic resonance imaging; FU: follow-up

Flowchart of the study.

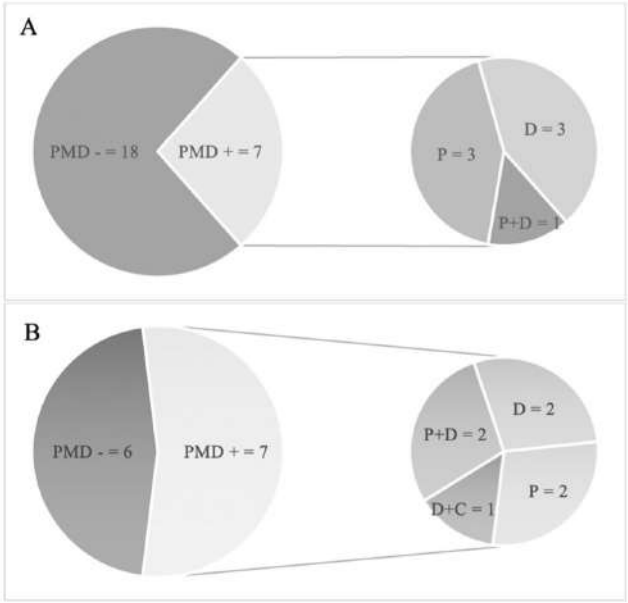

Figure 2: Prevalence and clinical subtype of post stroke movement disorders six (A) and twelve (B) months after the acute event. Abbreviations: PMD-: subjects who did not develop post-stroke movement disorders during the follow-up; PMD+: subjects who developed a post-stroke movement disorder throughout the follow-up; P: parkinsonism; D: dystonia; P+D: combined parkinsonism-dystonia; D+C: combined dystonia-chorea

Prevalence and clinical subtype of post stroke movement disorders six (A) and twelve (B) months after the acute event.

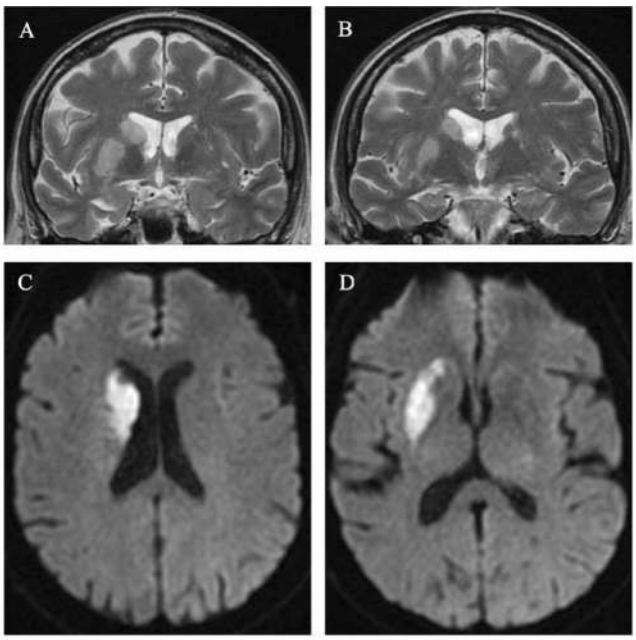

Figure 3: Selective ischemic lesion of the basal ganglia occurring after an acute proximal occlusion of the middle cerebral artery in a patient successfully treated with mechanical thrombectomy from our cohort. **A** and **B** panels: T2-weighted sequences coronal sections at the level of the basal ganglia; **C** and **D** panels: diffusion-weighted sequences axial sections at the level of the basal ganglia

Selective ischemic lesion of the basal ganglia occurring after an acute proximal occlusion of the middle cerebral artery in a patient successfully treated with mechanical thrombectomy from our cohort.

Conclusion: PMDs are not uncommon in a long-term follow-up of successfully reperfused acute ischemic strokes. A prosecution of follow-up in a multidisciplinary team is strongly advisable in patients with selective lesions of the BG after AIS, even if asymptomatic at discharge.

Disclosure: Nothing to disclose.

EPO-746 | Effect of a single session of transcranial pulse stimulation on tremor in Parkinson patients

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Background and Aims: Tremor is a common signs in movement disorders. Tremor itself is very sensitive to brain stimulation, from deep brain stimulation to Transcranial magnetic stimulation. Transcranial pulse stimulation (TPS) is a painless and non-invasive new technique which produces a magnetic field by low frequency ultrasound. Aim of the study is to investigate possible long term changes on cortical activity after Transcranial Pulse Stimulation in motor cortex in patients with Parkinson and tremor.

Methods: TPS was delivered in 14 patients affected by PD tremor dominant, which was measured at the baseline (T0) after the TPS (T1) and after 24 hours (T2). The resting tremor was present in all patients with an average of 9–10 Hz/sec. The treatment protocol was 4 Hz, 0.20 mJ/mm^2 by default. A single-session of 1500 pulses were delivered to the subjects' motor cortex (M1) of the contralateral to the most affected side of the tremor.

Results: We noted a reduction of tremore at T1 and T2 compared to baseline T0 in 13 patients, from 20% to 40% in amplitude, reaching a decrease of 57% in one case. In all the patients we noted a decrease in amplitude and duration of tremor at rest but not in frequency. No effect was note in placebo stimulation.

Conclusion: TPS as a new brain stimulation method induces a reduction of tremor for 24 hours without side effects documenting a significant physiological changes in these patients. TPS is a new techniques for brain stimulation effective on motor areas.

Disclosure: Nothing to disclose.

EPO-747 | Opicapone's real-world experience in Spanish patients with Parkinson's disease: The OPTIMO study

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Background and Aims: Opicapone (OPC), a third generation COMT inhibitor, has been shown to be generally well-tolerated and efficacious in reducing off time in two pivotal trials in patients with Parkinson's disease (PD) and motor fluctuations (MF) (BIPARK-I and -II). The OPTIMO study aims to confirm these data in the everyday

practice by evaluating the clinical performance of opicapone in Spanish movement Disorders Units.

Methods: OPTIMO was an observational, retrospective, post-authorization study in patients with PD conducted at outpatient consultations for movement disorders in 16 Spanish centers. The inclusion period lasted 12 months. Clinical data were collected before the start of treatment with OPC and between 3 and 7 months post-treatment. Adverse effects were documented, with particular focus on monitoring the development of dyskinesias.

Results: 245 patients were enrolled (mean age, 67.7 years; mean time of PD evolution, 8.3 years; mean levodopa daily dose, 620.7 mg). Treatment with OPC reduced the percentage of patients with wearing-off MF (98% vs. 61.6%), delayed-on ($p=0.010$), non-on ($p=0.027$) and non-motor fluctuations ($p=0.010$). The daily OFF-time was significantly reduced (143 vs. 67.9 minutes). 74.2% of patients described clinical improvement in MF, which did not worsen dyskinesias in 64.6%. No significant increase in ON-time with dyskinesias was observed. Only 8.6% of patients experienced OPC-related adverse events.

Conclusion: These results confirm the findings of previous clinical trials, demonstrating that, in routine clinical practice, OPC significantly reduces motor and non-motor fluctuations without a significant increase in severity of dyskinesias, along with a good tolerance profile.

Disclosure: Supported by BIAL Spain.

EPO-748 | Expanding phenotype of LRRK2 G2019S mutation: Case description of two sisters showing peculiar phenomenological traits

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Background and Aims: LRRK2 is the most common risk gene for Parkinson's disease (PD). It presents with a milder course and a less common non-motor involvement than idiopathic PD.

Methods: The aim of this report is to describe LRRK2 phenomenology. We describe two sisters, one presenting with cervical dystonia (CD) and the other one presenting with typical parkinsonian features, although showing prominent non-motor fluctuations.

Results: A 80-year old lady was referred to our outpatient clinic due a 2-year history of head tremor. She showed cervical dystonia characterized by head tremor, inclination to the left side, left shoulder elevation, head rotation to the right, antecollis, retrocaput and limitation of range of motion. She had positive family history for Parkinson's disease (two of her mother's siblings, one of her father's and 5 of her own). Her sister was a 83-year old lady, who had been diagnosed with Parkinson's disease 8 years previously. Her major complaints were related to her non-motor fluctuations: her OFF phases were characterized by severe anxiety and pain. We run genetic testing for both patients and found the CD one to be a heterozygotic carrier of G2019S mutation and the PD sister to be a homozygotic carrier of the same mutation. We added safinamide and duloxetine to the treatment of the PD sister, with a major impact on non-motor fluctuations and QoL, and decided to treat the CD sister with levodopa/carbidopa, with considerable clinical improvement.

Conclusion: Our data may contribute to expanding LRRK2 phenotype and providing insights on its clinical course and treatment.

Disclosure: Dr Cartella SM received speaking honoraria from Zambon and Bial Dr Cartella G received speaking honoraria from Abbvie.

EPO-749 | Proinflammatory IgG glycans correlate with putaminal damage in patients with parkinsonism

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Background and Aims: Objectives: To examine the correlation between dopaminergic denervation evaluated with DaTSPECT and the different types of IgG glycans distributed into mature, youth, and shields glycan groups. The glycan mature group provides proinflammatory, while glycan youth and shield groups provide antiinflammatory potential to IgG antibodies.

Methods: Study design: Cross-sectional study with historical data Participants and methods: Data used in this study is part of another study that has been approved by the local ethical committee (R2-3775/2022). Patients diagnosed and treated with Parkinson's disease or atypical parkinsonism were included. Blood samples for evaluating IgG glycan composition were analysed by Genos Glycoscience laboratory in Zagreb. Data on DaTSPECT were analysed from the computer system of the patient registry.

Results: Results: Fifteen patients (10 male, 5 female) were evaluated, 12 with Parkinson's disease and 3 with atypical parkinsonism. The median age was 60 (IQR 55–66), and the disease duration was 3 (IQR 1–4) years. A negative correlation was observed between the IgG glycan mature group, right putamen (Rho = −0.626; $p=0.013$), and right putamen/caudate ratio (Rho = −0.703; $p=0.003$). A positive correlation was seen between the IgG glycan youth group with right putamen (Rho = 0.627; $p=0.012$) and right putamen/caudate ratio (Rho = 0.699; $p=0.004$), while the IgG glycan shield group positively correlated with right putamen/caudate ratio (Rho = 0.725; $p=0.002$). No significant correlation was observed between glycans, age, or disease duration.

Conclusion: Conclusion: Higher IgG glycan mature group values correlate with increased putaminal degeneration, while higher IgG

glycan shield and youth values correlate with reduced putaminal degeneration.

Disclosure: Gordan Lauc is named as an inventor on the GlycanAge patent and serves as the founder and CEO of Genos Ltd.

EPO-750 | Sleep evaluation in functional neurological disorder – Preliminary data of a pilot study

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Background and Aims: Functional neurological disorder (FND) is a common neuropsychiatric condition with high burden on patients and where self-reports often deviate from objective measures. Despite frequent observations of patients suffering from sleep disturbances as a comorbidity, studies evaluating sleep in FND are scarce. We thus aim to describe objective sleep parameters and patients' subjective perception of sleep in FND.

Methods: In a pilot study, FND patients and age- and sex-matched healthy controls (HC) completed the Pittsburgh Sleep Quality Index (PSQI; subjective), whereas patients additionally underwent a 2-week actigraphy measurement (objective). We describe subjective sleep quality in FND compared to HC. Furthermore, we report the FND cohort's objective sleep quality in terms of clinical relevance threshold and assess between-measure accuracy.

Results: 26 FND patients (73% female, mean age = 38.4 y) and 26 HC (73% female, mean age = 36.5 y) were included. Patients reported significantly worse scores of subjective sleep including a higher PSQI total score ($p < 0.001$). Similarly, subjectively reported sleep latency ($p = 0.014$), time-in-bed ($p = 0.032$) and sleep efficiency ($p = 0.009$) significantly differed between FND and HC. Analysis of actigraphy as objective sleep quality measure revealed reduced sleep efficiency (<85%) in 73% of patients. Moreover, in the FND cohort, an incongruency between objective and subjective reports was observed regarding sleep latency ($p = 0.005$).

Conclusion: This pilot study depicts sleep disturbances in FND patients compared to a healthy cohort and in terms of clinically relevant thresholds. Furthermore, we identified inaccurate perception of one's own sleep onset among FND patients. Studies on larger sample sizes are required to disentangle the role of sleep in FND.

Disclosure: Nothing to disclose.

EPO-751 | Prevalence, pre-existing conditions, and prior treatments among european adults diagnosed with Tardive dyskinesia

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Background and Aims: Tardive dyskinesia (TD) is a hyperkinetic movement disorder mostly associated with chronic antipsychotic (AP) exposure. TD prevalence and associated risk factors in Europe are understudied. This study aimed to evaluate TD prevalence, pre-existing conditions, and pre-TD treatments in European adult populations.

Methods: A retrospective study of adults (≥18 years) from 6 European healthcare databases representing Belgium, France, Germany, Italy, Spain, and United Kingdom (UK) was conducted. The index event was first TD diagnosis within the study period (1 Jan 2016–31 Dec 2021). To adhere to regional reporting practices, patient numbers <10 for France and <5 for all others were masked.

Results: Cumulative adult TD prevalence was 1, 3, and 3 per 100,000 in France (<88 of 11,171,508), Germany (660 of 23,235,594), and UK (78 of 2,486,459), respectively. Italy ($n = 1,829,406$), Spain ($n = 1,507,900$), and Belgium ($n = 712,035$) had <5 adults with TD reported, which did not enable prevalence calculations. In ages 18–40 years in France ($n = 4,148,423$), Germany ($n = 8,022,427$), and UK ($n = 1,221,030$), TD prevalence was <0.24, 0.96, and 1.06 per 100,000. For ages ≥41 years in France ($n = 7,023,085$), Germany ($n = 15,213,167$), and UK ($n = 1,265,429$), TD prevalence was 1.14, 3.83, and 5.14 per 100,000. In Germany and UK, 22%–46% of patients with TD had diagnosed schizophrenia, 34%–48% had schizophrenia spectrum disorder, and <5%–34% had anxiety disorders; 40%–56% previously received atypical APs and 15%–42% had received typical APs.

Conclusion: TD prevalence was low and variable across European countries, suggesting limited awareness, underdiagnosis, and coding differences in European health settings.

Disclosure: This study was supported by funding from Teva Branded Pharmaceutical Products R&D, Inc. Mark J. Edwards and Christoph U. Correll have received fees and/or honoraria from Teva Pharmaceuticals. Shoshana Reshef, Mark Forrest Gordon, Nayla Chaijale, Anna Kurzeja, and Maurice T. Driessen are employees and/or stockholders of Teva Pharmaceuticals.

EPO-752 | Post hoc analysis of foot abnormalities in patients with Friedreich ataxia in the MOXIe trial

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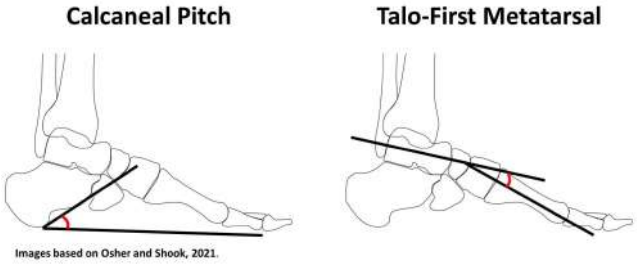
[1]*Department of Neurology, Medical University Innsbruck, Innsbruck, Austria;* [2]*Ataxia Centre, Department of Clinical and Movement Neurosciences, University College London, London, UK;* [3]*Department of Research and Development, Biogen, Cambridge, USA;* [4]*Departments of Pediatrics and Neurology, The Children's Hospital of Philadelphia, Philadelphia, USA*

Background and Aims: The MOXIe trial (NCT02255435/EudraCT2015-002762-23) evaluated omaveloxolone in patients with Friedreich ataxia (FA); 20% were considered to have severe pes cavus, determined by a flashlight test, and not included in the full analysis set (FAS). This exploratory analysis compared foot angle abnormalities in the MOXIe severe pes cavus and FAS populations.

Methods: Weight-bearing lateral foot radiographs were obtained and centrally read. Post hoc analyses assessed frequency and distribution of abnormalities in radiological angles indicative of pes cavus (calcaneal pitch >30°, talo-first metatarsal angles >5°) in the FAS and severe pes cavus populations (Figure 1).

Results: Patients with severe pes cavus ($n=20$) had similar baseline characteristics to FAS patients ($n=82$); ~90% of patients were ambulatory in each group. Overall, 11% and 45% of FAS and severe pes cavus patients, respectively, had an abnormal calcaneal pitch, and 42.7% and 50% had abnormal talo-first metatarsal angles (Table 1). Calcaneal pitch and talo-first metatarsal angles were distributed across a range of values in both populations, though the pes cavus population had more severe angle abnormalities (Figure 2). In patients with severe pes cavus, mFARS results at Week 48 directionally favored omaveloxolone versus placebo; in the all-randomized population, omaveloxolone demonstrated benefit over placebo. Safety profiles were similar between patients with versus without severe pes cavus.

Figure 1: Calcaneal Pitch and Talo-First Metatarsal X-Ray Angles Measured in MOXIe Part 2



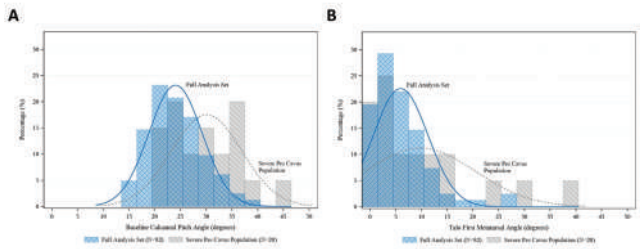
Images based on Osher and Shook, 2021.

Table 1: Baseline Foot X-Ray Results in the FAS and in Patients With Severe Pes Cavus

Parameter	Normal Range (Degrees)[a]	Direction for Deviation From Normal in Pes Cavus	N (%) Patients in FAS With Abnormal Angle N=82	N (%) Patients in Severe Pes Cavus Population With Abnormal Angle N=20
Calcaneal Pitch	20-30	Increased	9 (11.0)	9 (45.0)
Talo-First Metatarsal	0-5	Increased	35 (42.7)	10 (50.0)

Abbreviation: FAS=full analysis set.
[a] Osher L, Shook JE. *Clin Podiatr Med Surg.* 2021;38(3):303-321.

Figure 2: Distribution of Calcaneal Pitch (A) and Talo-First Metatarsal (B) Angles for Full Analysis Set and Severe Pes Cavus Population



Conclusion: Patients with severe pes cavus were not phenotypically or clinically distinct from the FAS. Pes cavus appears as a continuum in patients with FA. Omaveloxolone was safe and demonstrated benefit over placebo across a full spectrum of foot deformities.

Disclosure: This study was funded by Reata Pharmaceuticals. Reata was acquired by Biogen in 2023. S Boesch has received fees for consultancy, advisory boards, and/or honoraria from AbbVie, Ipsen, Reata Pharmaceuticals, Merz Pharma, Stada Arzneimittel, and VICO Therapeutics. P Giunti has received grants and fees for advisory boards from Reata Pharmaceuticals, and fees for consultancy from VICO Therapeutics, Triplet Therapeutics, and PTC Therapeutics. S Chimalapati, W Costello, A Goldsberry, S Rich, and C Ruhl are employees of Biogen. D Lynch reports grants from FARA, the Muscular Dystrophy Association (MDA), the National Institutes of Health (NIH), Reata Pharmaceuticals, and Retrotope.

EPO-753 | Path to prevention therapeutics platform trial in stage 2B neuronal alpha-synuclein disease: Study design and timeline

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Background and Aims: To describe the study design and proposed timeline of the first interventional study in Neuronal α-Synuclein Disease (NSD).

Methods: P2P is a perpetual platform trial with a single Master Protocol dictating the conduct of the trial and regimen specific subprotocols outlining intervention specific aspects for each arm. Qualified participants will be recruited from the PPMI participants, based on NSD Stage 2B criteria (see Table 1). The study's Multiple Primary Endpoints include 1) DAT imaging as measured by the rate of progression in the mean striatum Specific Binding Ratio (SBR) and 2) rate of progression in the MDS-UPDRS part III score. Secondary endpoints include safety, tolerability and feasibility. The study will have an array of exploratory clinical (including digital) and biomarker measures. Participants will first be randomized in an equal manner among all of the regimen-specific sub-protocols for which they are eligible and then within the regimen to an active arm or placebo ($N=125$ per arm) in a K:1 ratio with K the number of active interventions. Intervention duration will be at least 24 months. The study is 90% powered to detect a slowing in either primary endpoint for each regimen, assuming a 30% slowing in DAT and a 40% slowing in MDS-UPDRS Part III.

Results: Interventions are being selected by a Therapeutic Evaluation Committee from >15 industry submitted applications. The study targets to start enrolment in the first 2 regimens in 2025.

Table 1. Data driven anchors for NSD-ISS

	Biologic anchors			Anchors of clinical signs or symptoms (stages 2A and 2B) and functional impairment (stages 3-4)[1,2]	
Stage	S	D[a]	G	Domain	Anchor(s)
Stage 0	-	-	*SNCA* [b]	—	—
Stage 1A	+	-	±	(1) Cognitive (2) Motor (3) Other non-motor	(1) MDS-UPDRS item 1.1 = 0; and (2a) Does not have subthreshold parkinsonism [c]; and (2b) is not on PD meds; and (3a) Does not have RBD; and (3b) is not hyposmic [d]
Stage 1B	+	+	±		
Stage 2A	+	-	±	(1) Cognitive (2) Motor (3) Other non-motor	(1) Item 1.1 = 1 AND MoCA ≥ 25; or (2a) Has subthreshold parkinsonism [c]; or (2b) is on PD meds; or (3a) Has RBD; or (3b) is hyposmic [d]
Stage 2B	+	+	±		
Stage 3	+	+	±	(1) Cognitive (2) Motor	(1a) Item 1.1 = 1 AND MoCA ≤ 24; or (1b) Item 1.1 = 2 AND MoCA ≥ 25; or (2) MDS-UPDRS-II = 3-13 AND either subthreshold parkinsonism [c] or PD meds
Stage 4	+	+	±	(1) Cognitive (2) Motor (3) Other non-motor	(1a) Item 1.1 = 2 and MoCA ≤ 24; or (1b) item 1.1 = 3 AND MoCA ≥ 25; or (2) MDS-UPDRS-II = 14-26; or (3) MDS-UPDRS-I (excluding item 1.1) = 13-24 [e]
Stage 5	+	+	±	(1) Cognitive (2) Motor (3) Other non-motor	(1a) Item 1.1 = 3 AND MoCA ≤ 24; or (1b) item 1.1 = 4 AND MoCA ≥ 25; or (2) MDS-UPDRS-II = 27-39; or (3) MDS-UPDRS-I (excluding item 1.1) = 25-36
Stage 6	+	+	±	(1) Cognitive (2) Motor (3) Other non-motor	(1) Item 1.1 = 4 AND MoCA ≤ 24; or (2) MDS-UPDRS-II ≥ 40; or (3) MDS-UPDRS-I (excluding item 1.1) ≥ 37

NSD is defined by presence of Alpha-Synuclein pathology, ultimately dopamine dysfunction, and stage dependent motor and non-motor clinical manifestations and related functional impairment. These participants were previously clinically defined as Parkinson's disease, Dementia with Lewy Bodies and Prodromal. The study is "nested" within the Parkinson's Progression Marker Initiative (PPMI) and sponsored by the MJFF.

Conclusion: We report the design of the first platform interventional study targeting NSD Stage 2B population.

Disclosure: In the last 12 months Tanya Simuni, MD has served as a consultant for AskBio, Amneal, Blue Rock Therapeutics, Critical Path for Parkinson's Consortium (CPP), Denali, General Electric, Kyowa, Neuroderm/ MTPA, Prevail/ Lilly, Roche, Sanofi, Sinopia, Takeda and Vanqua Bio. Dr. Simuni served on the ad board for AskBio, Amneal, Biohaven, Denali, GAIN, General Electric, Kyowa, MJFF, Neuron23, Parkinson Study Group, Prevail/ Lilly, and Roche. Dr. Simuni has served as a member of the scientific advisory board of Koneksa, Neuroderm/ MTPA, Sanofi and UCB. Dr. Simuni has received research funding from Amneal, Biogen, Neuroderm, Prevail, Roche, UCB and is an investigator for NINDS, MJFF, Parkinson's Foundation (Other authors disclosures to be updated if accepted).

EPO-754 | A closer look at eye movements in cervical dystonia

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Background and Aims: In the last few decades cervical dystonia (CD) has come under attention of experts in the field of movement disorders. The studies of its complex pathophysiology propose a disorganization within the motor cortex-basal ganglia-cerebellum axis i.e. network. For some time now, eye movements can serve as a good model for researching the motility of patients and thereby expand the knowledge about cervical dystonia.

Methods: 30 cervical dystonia patients and 30 matched healthy controls performed eye-movement examination including smooth-eye movements, prosaccade, antisaccade and memory saccade tasks on an eye tracker to assess automatic visual response.

Results: Cervical dystonia patients expressed poorer fixation ($p=0.02$) and target following ($p=0.04$) of smooth eye-movements on vertical axis, diminished maximum speed of prosaccades ($p=0.03$) which are of significant latency ($p=0.02$), more directional errors in the antisaccade task ($p=0.04$) and poorer execution of memory saccades testing ($p=0.002$). There were no changes in smooth eye-movements horizontally compared with healthy controls.

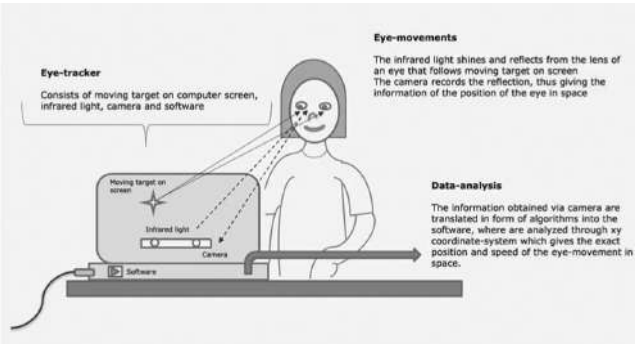

FIGURE 1 Representation of eye movements' analysis using an eye-tracker, original scheme.

Table 1. Comparison of eye-movements in cervical dystonia patients and healthy controls

Measured variables	Median (interquartile range) CD patients (n=30)	Healthy controls (n=30)	P*
Smooth eye-movements			
Horizontal eye-movement range 16 ms	0.584 (0.519 - 0.646)	0.544 (0.535 - 0.587)	0.16
Horizontal eye-movement fixation 16 ms	0.00810 (0.00653 - 0.0127)	0.00780 (0.00529 - 0.00967)	0.42
Vertical eye-movement range 16 ms	0.523 (0.471 - 0.627)	0.488 (0.470 - 0.514)	***0.04***
Vertical eye-movement fixation 16 ms	0.00971 (0.00606 - 0.0139)	0.00648 (0.00473 - 0.00874)	***0.02***
Horizontal eye-movement range 24 ms	0.574 (0.535 - 0.645)	0.545 (0.529 - 0.585)	0.09
Horizontal eye-movement fixation 24 ms	0.00413 (0.00291 - 0.00550)	0.00399 (0.00256 - 0.00550)	0.97
Vertical eye-movement range 24 ms	0.550 (0.463 - 0.672)	0.523 (0.482 - 0.574)	0.67
Vertical eye-movement fixation 24 ms	0.00515 (0.00219 - 0.00761)	0.00306 (.,00176 - 0.00433)	0.06
Prosaccades			
Latency	7.48 (7.28 - 7.98)	8.14 (7.49 - 8.75)	***0.02***
Maximum speed	2.90 (2.61 - 3.19)	3.21 (2.89 - 3.43)	***0.03***
Accuracy	3.57 (2.83 - 4.62)	3.33 (2.98 - 4.29)	0.46
Memory saccades			
Fixation length	235.94 (188.75 - 285.90)	210.96 (188.75 - 240.10)	0.08
Correct score onward	0.0 (0.0 - 4.0)	4.0 (0.75 - 6.0)	***0.008***
Correct score backward	0.0 (0.0 - 1.5)	3.0 (2.0 - 5.0)	***<0.001***
General score	0.0 (0.0 - 5.0)	8.0 (3.0 - 11.25)	***0.002***
Antisaccade testing			
Antisaccade latency	525.7 (482.4 - 548.0)	520.2 (461.5 - 589.9)	0.65
Correct scores per second	8.5 (1.0 - 12.0)	11.0 (8.5 - 14.0)	***0.04***
Number of corrections	0.0 (0.0 - 2.0)	1.0 (0.0 - 1.0)	0.48
Number of wrongful corrections	2.0 (0.0 - 6.0)	0.0 (0.0 - 1.0)	***0.04***
Percentage of incorrect viewing	75.0 (25.0 - 100.0)	50.0 (0.0 - 75.0)	***0.047***

*Mann-Whitney U test

Conclusion: Based on the obtained results and known anatomic connections, we assume a more significant pathophysiology of the interstitial nucleus of Cajal in CD patients than was previously known, considering altered vertical but not horizontal smooth-pursuit. Also, we suggest changes of saccadic inhibitory control in patients with CD at multiple levels, including dorsolateral prefrontal cortex and frontal eye fields and their projections to the superior colliculus, suggesting alterations of corticobasal networking.
Disclosure: Nothing to disclose.

EPO-755 | Pisa syndrome and botulinum toxin injection in paraspinal muscle ipsilateral to the bending site

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Background and Aims: The aim of this study was to evaluate the clinical and electromyographical effects of Botulinum toxin injections in patients with Parkinson's disease (PD) suffering from Pisa syndrome (PS).
Methods: We recruited 16 PD patients with PS from the Movement Disorders Unit of Trieste (Italy). Each patient was evaluated at baseline, 1 and 3 months after BoNT injection, which was ipsilateral to the bending site regardless of EMG activation. We recorded demographic, PD- and PS-related clinical variables, including PDQ-8 and PGIC scales, and back pain evaluation (VAS scale). Muscular hypo- and hyperactivity patterns were assessed using superficial EMG recording. Lateral bending angle of the spine was calculated on the planar view photographs as the angle between the vertical axis and a line connecting the fulcrum of the bent spine with the C7 spinous process.
Results: Sixteen outpatients showed an initial reduction in bending degrees followed by a reversion (6.5 ± 3, 5 ± 1.5, 6.7 ± 6 degrees at baseline, 1 and 3 months respectively), a substantial stability in PDQ-8 scores, and a reduction in back pain. Accordingly to 91 and 100% of the patients, at 1 and 3 months respectively, their condition globally improved (PGIC scores ≥3). Qualitative EMG signal analysis showed an almost uniform improvement in paraspinal muscles activation.
Conclusion: Our study shows an efficacy in bending angle reduction after 1 month from the treatment with a reversion after 3 months, and a subjective clinical improvement. This may indicate a benefit deriving from ipsilateral injection regardless of EMG activity.
Disclosure: Nothing to disclose.

EPO-756 | Selection of candidates for treatment with deep brain stimulation among patients with focal and segmental dystonia

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Background and Aims: Focal and segmental dystonia are commonly successfully treated with the application of botulinum toxin; however, a proportion of patients remains challenging. GPi deep brain stimulation (DBS) is successfully used in some of these patients, but their frequency and characteristics are still unknown.
Methods: We included 150 consecutive patients in cross-sectional study at the Neurology Clinic, Belgrade. A semi-structured survey was used to collect demographic and clinical data, relevant clinical scales to assess dystonia severity (BFMD) and psychiatric symptoms (HAMD; HAMA; Apathy scale). Current criteria were used to diagnose functional dystonia.
Results: Overall, patients were satisfied with the therapy: 74 (49.3%) felt better than 75%, and an additional 43 (28.7%) were 50% better compared to the period before starting botulinum toxin therapy. 33 (22%) respondents had an unsatisfactory therapeutic response (lower than 50%). These patients showed significantly worse scores regarding: BFMD, HAMD and HAMA. We further analyzed these patients found that 9 (6%) had purely functional dystonia, while further 9 (6%) were too old or had significant comorbities to be considered for DBS, thus leaving 15 (10%) potential candidates to be considered for DBS referral which showed no difference regarding duration and severity of the disease nor psychiatric symptoms severity, but they were significantly younger.
Conclusion: About 10% of the subjects with focal or segmental dystonia at the tertiary botulinum toxin center can be considered for DBS referral. Special precaution should be made to exclude patients with functional symptoms.
Disclosure: Nothing to disclose.

EPO-757 | Phenotypic heterogeneity of genetic forms of dystonia

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Background and Aims: Dystonia is a movement disorder characterized by continuous or intermittent muscle contraction that causes abnormal positions of body parts. It represents a clinically and

genetically very heterogeneous disease. More than 200 genes have been identified that are associated with different, mostly generalized forms of early-onset/infantile dystonia. The aim of this work is to describe the clinical characteristics and patterns of progression of different genetic forms of dystonia.

Methods: Carriers of DYT-TOR1A, DYT-THAP6 (isolated AD dystonia), DYT-GCH1 and DYT-SCGE (combined AD dystonia) mutations were included in the study. The data were obtained from the Registry of the Laboratory for Genetics, as well as from medical records. The assessment of the clinical picture was performed for each patient as typical or atypical based on the analysis of demographic data and phenotype analysis, which included data on initial presentation, progression and distribution of dystonia, presence of tremors, presence of other involuntary movements. Statistical processing included standard methods.

Results: Disease progression and dystonia spreading to unaffected regions occurred in all examined groups, according to specific patterns within the groups. There was no difference in the distribution of dystonia by region in DYT-TOR1A and DYT-THAP1 carriers. Additionally, atypical clinical presentation was described in all groups.

Conclusion: Our results indicate that two-thirds of patients with genetic forms of dystonia experience disease progression, while one-third of patients have signs of atypical manifestations. An adequate assessment of the clinical picture and recognition of the potential genetic basis of the disease significantly improves diagnostic and therapeutic strategies.

Disclosure: Nothing to disclose.

EPO-758 | Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) with novel mutation in SACS gene

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Background and Aims: Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) is a rare disease with cerebellar ataxia, peripheral neuropathy and pyramidal signs. It is caused by homozygous mutations in the SACS gene (1). It was first reported in the population of French descent in the Charlevoix Saguenay region of Quebec, Canada in 1978 (2). Over 200 pathogenic mutations have been described outside of Quebec (3, 4). ARSACS patients are not limited to a particular ethnic group (3, 4, 5). We present a patient with novel homozygous mutation in the SACS gene from Turkey.

Methods: Forty years old male, born of consanguineous marriage, presented with progressive ataxia and recurrent falls from 20 years of age. He has two cousins suffering from the similar symptoms. Neurological examination revealed ataxia, dysarthria, spasticity, walking difficulty, pes cavus deformity and polyneuropathy. Brain MRI scans show linear T2 and fluid attenuated inversion-recovery (FLAIR) hypointensities in the pons.

Results: Patient was diagnosed of Charlevoix Saguenay ataxia syndrome. Clinical exome sequencing revealed a homozygous frameshift mutation on exon 10 of SACS gene (NM_014363.6). The mutation, c.7720dup, p.Arg2574LysfsTer4 resulting in a stop codon and premature truncation of the protein.

Conclusion: This mutation is a novel variant that has not been published in the literature until now. According to the ACMG guidelines, as it causes the premature truncation, it can cause damaging effect. We present here a rare case of Charlevoix Saguenay ataxia that occurred secondary to a novel mutation in SACS gene from Türkiye.

Disclosure: There is no disclosure.

Neuropathies

EPO-759 | 3 Cases of canvas in a Spanish third level hospital

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Background and Aims: CANVAS (cerebellar ataxia, neuropathy and vestibular areflexia syndrome) is a recently genetically diagnosed disease that is caused by abnormal expansion in RFC1 gene. It typically presents in middle age with a combination of neuropathy, ataxia, vestibular disease and dry cough. Typical findings are: pure sensory axonal neuropathy and bilateral vestibular areflexia.

Methods: 3 cases of CANVAS confirmed with genetic study treated in our center.

Results: We present 3 patients with a mean age at onset of symptoms of 50.6 years. None of them had a family history of neurological disease or consanguinity. The average delay time from the onset of symptoms to the first evaluation was 4.6 years, with the reason for consultation being sensory alteration in two of them and walking instability in one of them. 67% had a history of cough years before presentation. 67% developed cerebellar symptoms during follow-up. In complementary tests, 100% had pure sensory axonal polyneuropathy and only one showed bilateral vestibular areflexia. The delay time until the genetic study was 4 years from the first visit. All 3 had homozygous expansion for AAGGG in the RFC1 gene with a number of expansions between 400–2000.

Conclusion: CANVAS syndrome is a relatively recent entity and it is interesting to know the forms of presentation when it comes to properly identifying patients. Our case series presents concordant and discordant data with respect to other series described, which is explained by the variability of presentation and evolution of these patients, which makes the diagnosis of suspected onset difficult.

Disclosure: Nothing to disclose.

EPO-760 | Longitudinal follow-up of neuropathy symptoms, neuropathy signs and gait in older adults from good aging in Skåne study

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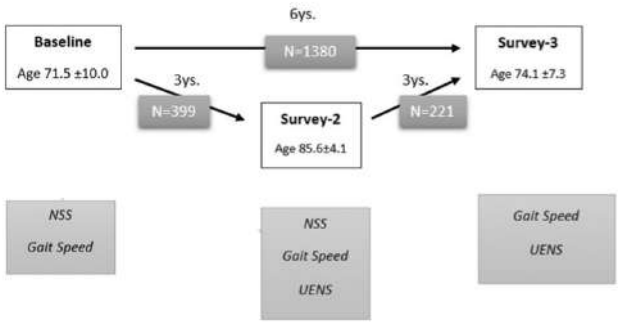
Background and Aims: We aimed to study an extent of neuropathy symptoms and their association with clinical signs of neuropathy and gait speed during 3–6 years follow-up.

Methods: Older adults ($n = 2805$, females 55%, mean age 71.5 ± 10.0 ys.) answered on questionnaire Neuropathy Scale Score (NSS), modified for self-assessment (max score18). At survey-2, 399 who reached at least 80 ys, were re-examined after mean 3.4 ys (age 85.6 ± 4.1) with NSS, Gait Speed and Utah Early Neuropathy Scale (UENS). After further 3 ys, all were invited to survey-3: 211 from the survey-2 and the rest of the baseline cohort, totally 1598 at mean age 74.1 ± 7.3 ys (figure below).

Figure: Good Aging in Scania Study flow chart of 3 surveys and examinations specified.



Results: At baseline, median NSS was 0p (0–13; iQR = 1; 41.4% had ≥1p) and was associated with decreased Gait Speed (<1 m/s in 8.5%) (OR = 1.40; 95% CI 1.27–1.54; $p < 0.00001$). At survey-2, NSS (median 1.0; 0–11; iQR = 3; 68.2% had ≥1p) was associated with higher risk of neuropathy (UENS ≥7p) (OR = 1.36; 95% CI 1.21–1.53; $p < 0.00001$) and Gait Speed < 1 m/s (OR = 1.54; 95% CI 1.31–1.81; $p < 0.00001$). Difference in NSS between survey-2 and baseline (mean = 1 ± 1.86; range: −4–8) was associated with higher risk of neuropathy (OR = 1.38; 95% CI 1.21–1.57; $p < 0.00001$) and Gait Speed < 1 m/s (OR = 1.49; 95% CI 1.25–1.77; $p < 0.00001$). NSS at the baseline was also associated with higher risk of neuropathy in 1598 subjects at survey-3 (OR = 1.23; 95% CI 1.12–1.34; $p = 0.00001$) and gait speed < 1 m/s (OR = 1.50; 95% CI 1.30–1.72; $p < 0.00001$). In 218 oldest old, NSS time-difference between survey-2 and baseline (mean 0.7; p ± 1.66; range: −4–7) was associated with neuropathy in survey-3 (OR = 1.61; 95% CI 1.24–2.01; $p = 0.0002$).

Conclusion: in general population of older adults, self-assessed Neuropathy Scale Score and it's time change was sensitive for future clinical signs of neuropathy and decreasing gait speed.

Disclosure: The Good Aging in Skåne (GÅS-SNAC) project, was supported by the Swedish Ministry of Health and Social Affairs, the county Region Skåne, the Medical Faculty at Lund University, and the Swedish Research Council (grant number 2013-8604, 2017-01613, 2021-01437).

EPO-761 | A new method to objectify the degree of spontaneous activity seen during electromyography study of denervated muscles

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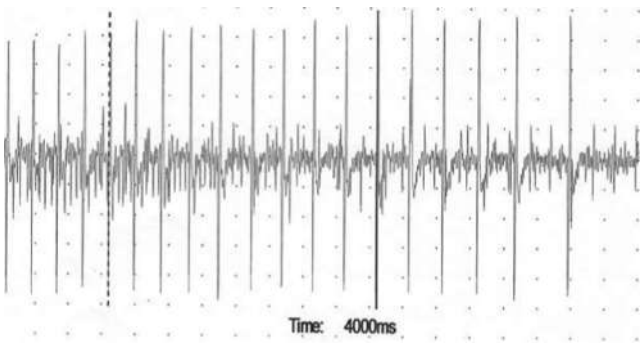
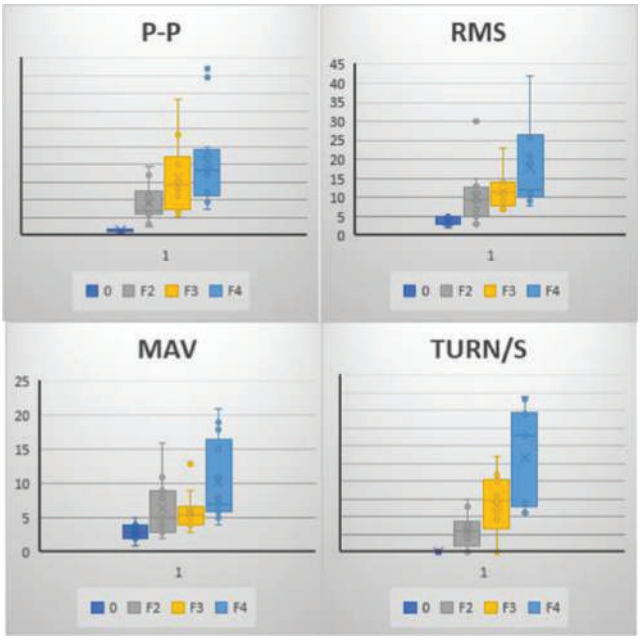
Background and Aims: The degree of spontaneous activity seen during electromyographic analysis of denervated muscles is conventionally defined by the electrophysiologist performing the procedure subjectively as mild, moderate, or severe. Discrepancy between physicians analyzing the quantity of spontaneous activity is not uncommon. The aim of this study is to create an EMG signal parameter capable of objectifying the degree of denervation activity of a given muscle through software analysis rather than subjective evaluation.

Methods: We analyzed the amount of spontaneous activity during the routine electromyographic study of patients referred for testing. We recorded the subjective evaluation of the quantity of spontaneous activity reported by the electrophysiologist. At the same time, we collected a 4 seconds epoch of that same activity. This epoch was incorporated in the electromyographic signal parameter analysis supplied by the manufacturers of the apparatus. The spontaneous activity was evaluated for the peak-to-peak value, root-mean-square, mean absolute value, and turns/second. We then correlated statistically the physician evaluation with the four parameters.

Results: The findings of the study confirm that the best objective electromyographic signal parameter reflecting the subjective evaluation of the experienced electrophysiologist was turns/second analysis of the epoch studied. The other three parameters did not correlate with the subjective evaluation.



Sample of EMG signal parameters recorded at time base: 200 ms and sensitivity: 50 uV/division.



The data collected for peak-to-peak value (P-P) uV, root-mean-square (RMS) uV, mean absolute value (MAV) uV, and turns/second through the software incorporated in the EMG machine from the manufacturer.

Conclusion: The turns/second electromyographic parameter seems to be the best electromyographic signal analysis reflecting the subjective opinion of the experienced electrophysiologist in defining the degree of denervation in a given muscle.

Disclosure: The authors have no conflict of interest and they did not receive any funding for this work.

EPO-762 | Small fiber dysfunction in chronic myeloid leukemia

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Background and Aims: In this study, we evaluated the frequency of small fiber dysfunction and the contribution of sympathetic skin response (SSR) in understanding small fiber function in patients with chronic myeloid leukemia (CML).

Methods: We evaluated all patients with CML who were receiving tyrosine kinase inhibitors (TKIs) and complained of neuropathic pain using a modified Toronto clinical neuropathy score (mTNS) and performed sensory and motor conduction studies. Based on clinical and nerve conduction studies, patients with large fiber neuropathy were excluded. In the remaining patients, we evaluated palmar and plantar SSRs and compared them with the findings of 13 healthy individuals.

Results: There were 18 patients with suspected small fiber dysfunction. The mean amplitude of the palmar and plantar SSR were lower in the patient group than those in the control group ($p=0.199$ and $p<0.001$, respectively). Comparing patients with CML and healthy individuals, ROC curve analysis showed the area under the curve was 0.64 for palmar and 0.94 for plantar SSR. If the plantar SSR amplitude cut-off value was 114 μV, sensitivity, and specificity were 67.1% and 50%, respectively. However, comparing patients with or without small fiber dysfunction, the area under the curve was low, and no cut-off value distinguished these groups.

Conclusion: Here, we report that dysfunction of small fibers can occur during CML and the use of TKIs. Plantar SSR is a nonspecific method that may be used in screening. The awareness of small fiber dysfunction and evaluation with nerve conduction studies, including SSRs in suspected patients are essential.

Disclosure: Nothing to disclose.

EPO-763 | Unveiling subclinical autonomic dysfunction in coeliac disease

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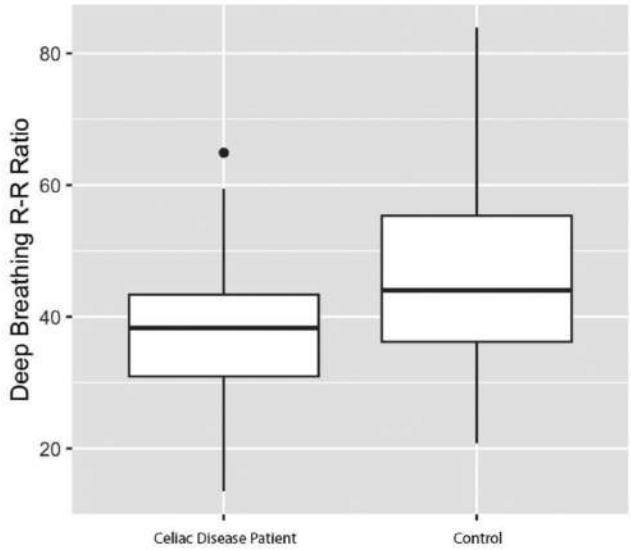
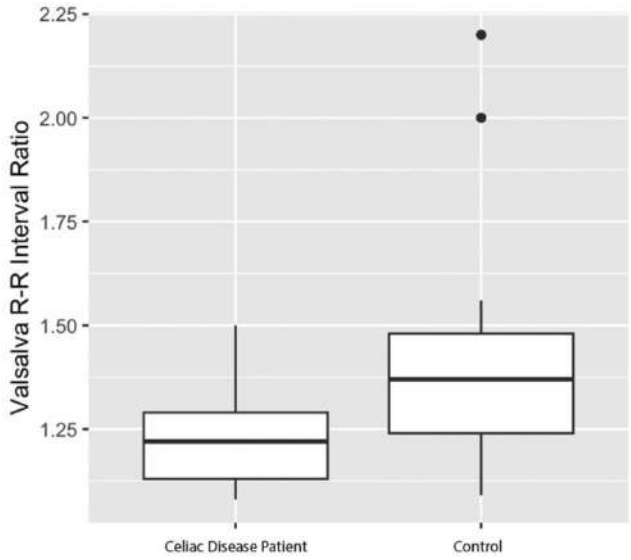
Background and Aims: Celiac disease (CD) patients can exhibit dysautonomia. Early detection can be crucial for timely intervention and managing complications such as syncope. This study aims to identify subclinical autonomic changes in CD patients using heart rate variability and sympathetic skin response tests, compared to healthy controls.

Methods: Serial CD patients from our gastroenterology outpatient clinic and matched controls underwent testing for sympathetic skin response and heart rate variability (including standing up and valsalva 30:15 ratio, and R-R interval ratios during normal and deep breathing) using the Natus Dantec Keypoint Focus device. Statistical analysis in R 4.3.2 included Welch's *t*-test and Mann-Whitney *U* test for means, Shapiro-Wilk test for normality, and descriptive statistics.

Results: The study included 38 CD patients (mean age 31.81 years, 33 females) and 30 controls (mean age 30 years, 20 females). CD patients had a mean disease duration of 5.26 years. IgA transglutaminase antibodies were positive in 15 patients, indicating lack of response to gluten-free diet. CD patients showed significantly lower deep breathing and valsalva R-R interval ratios compared to controls ($p=0.0065$-d$=0.706$ & $p=0.0011$-d$=0.40$). Median nerve proximal and distal CMAP amplitudes were significantly lower in IgA positive CD patients ($p=0.0092$-d$=0.83$ & $p=0.0065$-d$=0.706$).



Deep breathing R-R interval ratios.



Valsalva R-R interval ratios.

Conclusion: CD patients exhibit lower valsalva and deep breathing R-R interval ratios, suggesting subclinical autonomic dysfunction. Additionally, higher median nerve CMAP amplitudes correlate with diet unresponsiveness in CD patients. These findings underscore the need for further research and clinical monitoring.
Disclosure: Nothing to disclose.

EPO-764 | Motor unit number estimation (MUNE) test as assessment tool for motor impairment in Charcot Marie tooth disease

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Background and Aims: Charcot-Marie-Tooth Disease (CMT) represents the most common form of hereditary neuropathy, often burdened by a significant motor impairment. Several clinical validated scales are used to evaluate the degree of disability and to estimate the progression of the disease. The aim of our study has been to evaluate the correlation between electromyography estimation of the residual motor units (MUNE), in targeted muscles, and data obtained by an extensive clinimetric assessment, in different CMT subtypes.
Methods: 29 CMT patients (11 males and 18 females, median age 52,45-SD = 13,90, median disease duration 28,93 years -SD = 17,11) were recruited, including CMT1, CMT2 and HNPP subtypes. For all patients MUNE calculation and clinimetric evaluation by means of CMTNSv2 and CMT-FOM scales were done.
Results: In CMT2 patients, statistically significant correlations were found between CMT-FOM sub-items scores (right/left dorsiflexion, left/right plantar flexion and "4 Stair Descend), CMTNSv2 total score and MUNE values (on Tibialis Anterior muscle). In CMT1 patients, statistically significant correlation between Tibial MUNE value and "4 Stair Climb" sub item score was observed; in HNPP patient no correlations were observed.
Conclusion: MUNE has proven useful for quantifying denervation, highlighting a direct correlation with clinimetric evaluation, in most severe forms of CMT. In less disabling forms, such as HNPP, MUNE appears to be less useful, due to the absent of clear correlations with the result obtained on the clinimetric scales. In future studies MUNE should be considered a surrogate laboratory marker to monitor disease course, also in a clinical trial setting.
Disclosure: Nothing to disclose.

EPO-765 | Neurophysiological outcomes of Rituximab responsive inflammatory neuropathies

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Background and Aims: Rituximab (RTX) significantly improves the clinical outcome of selected cases of inflammatory polyneuropathies (IPN) resistant to standard treatments. Here we present the preliminary data of a retrospective study we are conducting at the

Neurological Unit of Pisa University Hospital, aiming to characterize the neurophysiological effects of RTX on IPN.

Methods: The following data are collected: a) diagnosis of IPN; b) clinical, laboratory and demographical data; c) Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score before and after (6 months) RTX treatment; d) electrophysiological data before and after (6 months) RTX treatment. Electroneurography (ENG) parameters measured are: conduction velocity (CV), distal latency (DL) and amplitude (Am).

Results: Eight IPN patients (38% males; mean age 62.6 and SD 10.7 years) were included. Remarkable improvements were observed in in the whole group, with the mean CV and Am increased by 23% and 26% respectively, and DL reduced by 26%. Only two patients did not show a significant response to RTX, with no or limited changes observed after the treatment. Whole group INCAT was significantly lower post RTX treatment ($p = 0.042$).

Conclusion: The longer disease duration of the two non-responder patients (10 and 7 years) compared to the other subjects (3 years) might partially explain their poorer clinical and ENG outcome. This ENG-based study of RTX-treated IPN patients may aid in identifying individuals most likely to benefit from the therapy and refining optimal treatment timelines.

Disclosure: Nothing to disclose.

EPO-766 | Quantitative sudomotor axonal reflex test in patients with chemotherapy induced polyneuropathy

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Background and Aims: Chemotherapy induced polyneuropathy (CIPN) is one of the common neurological complications that can occur in patients undergoing cancer treatment. While research on risk factors for CIPN has been conducted, there is limited research specifically focused on small fiber neuropathy (SFN). In this study we conducted quantitative sudomotor axon reflex test to evaluate SFN in CIPN patients. Then, we aimed to identify predictors of SFN by analyzing independent variables.

Methods: This is a retrospective observational study conducted at a single institution. Clinical and electrophysiological variables between groups with SFN and without SFN (non-SFN) were analyzed using *t*-tests, Mann-Whitney tests, and chi-square tests. Logistic regression analysis was performed for variables that showed significant differences.

Results: A total of 102 patients with CIPN included in the study. Among them, 25 patients had SFN and 77 patients did not. When comparing the two groups, significant differences were observed in age ($p = 0.0422$), gender ($p = 0.0221$), history of diabetes ($p = 0.0791$), and history of radiation therapy ($p = 0.0035$). On the other hand, variables such as duration of cancer, duration of chemotherapy, type of chemotherapy agents, and number of chemotherapy agents did not show significant differences. Quality of Life Questionnaire – Chemotherapy Induced Peripheral Neuropathy (QLQ-CIPN20) and the results of the nerve conduction study also did not show significant differences. In logistic regression analysis, the only significant predictor was the history of radiation therapy.

Conclusion: Older age, male, history of diabetes mellitus, and having not been treated with radiation therapy is related with SFN in CIPN patients. Among them, radiation therapy was the most significant factor.

Disclosure: There is no conflict of interest.

EPO-767 | Exploring etiologies and diagnostic precision in hypoglossal neuropathy cases

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Background and Aims: Isolated neuropathy of the hypoglossal nerve is a rare cranial neuropathy, typically arising as a secondary condition linked to lesions in one of its five nerve segments (nuclei, cisternal segment, hypoglossal canal, extracranial portion, and tongue segment).

Methods: This study presents a multicentric series involving consecutive patients seeking medical attention for unilateral tongue paralysis. Comprehensive otorhinolaryngological examinations and craniocervical MRI scans were conducted. In cases where these assessments yielded negative results, electromyography was subsequently performed.

Results: The study comprised six patients (4 female, aged 57–84), with all cases detailed in Table 1. Notably, two patients exhibited hypoglossal nerve compression—Pt1 due to synovial cyst in the atlanto-occipital joint, and Pt5 with a clival bone lesion linked to multiple myeloma. Pt2, despite a negative MRI, displayed electromyogram indications of bulbar amyotrophic lateral sclerosis (ALS), and she progressed to bilateral tongue paralysis within a month and full bulbar involvement within 3 months. Pt3 presented with hypoglossal compression at the carotid artery, a unique manifestation of carotid extracranial dissection. Pt4, experiencing idiopathic XII neuropathy, fully recovered within a month. Finally, Pt6 showed a vascular vertebral artery loop at the cisternal nerve portion and was ultimately diagnosed with microvascular XII neuropathy due to multiple vascular risk factors. He demonstrated clinical stability after a thorough examination and several months of follow-up.

Table 1. Patients with unilateral isolated neuropathy of the hypoglossal nerve

	Relevant Comorbidities	Final Diagnosis	Clinical Follow-up
Pt1. Female, 77	None	**Synovial cyst in the atlanto-occipital joint**, occupying the hypoglossal canal	Stability
Pt2. Female, 84	None	**Amyotrophic lateral sclerosis**	Bilateral progression in one month. Bulbar ALS debut
Pt3. Male, 63	Intervened splanchnic aneurysm	**Extracranial carotid artery dissection** with external mural hematoma compressing the hypoglossal nerve	Stability
Pt4. Female, 57	None	**Idiopathic neuropathy**	Full recovery
Pt5. Female, 74	Multiple Myeloma	**Multiple Myeloma lytic lesion** in the lower half of the clivus with meningeal extension, affecting the hypoglossal canal.	Neurological stability. Multiple Myeloma progression
Pt6. Male, 76	Smoker. Hypertension.	**Microvascular** / compressive due to vascular vertebral artery loop at the cisternal nerve segment	Stability

TABLE 1 Patients with unilateral isolated neuropathy of the hypoglossal nerve.

Conclusion: While hypoglossal neuropathy is uncommon, clinicians should remain vigilant for potential secondary etiologies. In instances where routine MRI testing proves inconclusive, electromyography and diligent follow-up play pivotal roles in ensuring an accurate diagnosis.

Disclosure: Nothing to disclose.

EPO-768 | Neurofilament light chain as a universal biomarker in neuropathies

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[1]Riga Stradinš University, Rīga, Latva; [2]Children's Clinical University Hospital, Rīga, Latvia

Background and Aims: Neurofilaments, specifically their light chains (NfL), are released following neuroaxonal injuries. Charcot–Marie–Tooth disease (CMT) is a hereditary neuropathy with no effective treatments or sensitive markers available for clinical use. Chronic autoimmune neuropathies arise from an immune response against peripheral nervous system antigens. NfL levels have potential as biomarkers for both conditions, and this study seeks to assess and compare NfL levels to aid in clinical differentiation and improve patient care.

Methods: In this study, a total of 44 Charcot–Marie–Tooth disease (CMT) patients, 34 individuals with chronic autoimmune neuropathy, and 44 control subjects were included. Plasma neurofilament light chain (NfL) concentrations were quantified using the Single molecule array (Simoa) NfL assay. CMT diagnoses relied on genetic testing, while diagnoses for CIDP and MMN followed the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria.

Results: Sex and age distribution did not significantly differ among the groups. Both CMT and autoimmune neuropathy patients exhibited significantly higher NfL levels than controls ($p < 0.05$). Importantly, there was no significant difference in NfL levels between the two patient groups ($p = 0.22$).

Conclusion: Our study confirms elevated NfL levels in CMT, CAN, and SS neuropathy patients compared to controls. Remarkably, despite the distinct nature of these neuropathies, NfL levels did not significantly differ among the patient groups. These findings underscore the potential of NfL as a universal biomarker and warrant further exploration in neuropathology research.

Disclosure: This research has been developed with financing from the Latvian Science Council, Project Discovering biomarkers of disease progression and variability in Charcot-Marie-Tooth neuropathy, No lzp-2021/1-0327.

EPO-769 | Abstract withdrawn

EPO-770 | Temporal kinetics of sensorimotor and autonomic recovery in Guillain Barre syndrome

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Background and Aims: Guillain-Barré syndrome (GBS) is characterized by rapidly progressive quadriparesis with or without sensory or autonomic dysfunction. There is paucity of information regarding recovery pattern in GBS. We evaluate the temporal kinetics of recovery and its pattern among demyelinating (AIDP) and axonal (AMAN) forms.

Methods: Patients with GBS diagnosed on clinical, laboratory and neurophysiological criteria, were included and disabilities were evaluated on Hughes score. Motor, sensory, cranial nerve and autonomic recovery days were recorded and compared among AIDP and AMAN at 3 months. Early recovery was defined as an improvement ≥2 Hughes grades within 4 weeks of symptom onset and late recovery as improvement beyond 4 weeks.

Results: 42 patients were analyzed. Median age was 31 years and 26.2% were females. Autonomic dysfunction recovered in all and at the earliest with median of 12 days (5–69); followed by bulbar weakness and facial weakness with median of 15 days (2–81) & 19 days (4–86) respectively. Sensory function improved over a median period of 20 days (5–66). Motor recovery occurred in 17 (40.5%) patients with median of 65 days (20–90). Dysautonomia occurred more frequently in AIDP (68% vs 10%; $p = 0.03$) than AMAN. Recovery patterns were comparable in AIDP and AMAN. 20 (47.6%) patients had early recovery and proportion of patients in demyelinating vs axonal were similar.

Conclusion: The neurological recovery in GBS occurred first in autonomic followed by bulbar, facial, sensory, and motor functions. The recovery is comparable between AMAN and AIDP.

Disclosure: Nothing to disclosure.

EPO-771 | A 15-year retrospective analysis of Guillain Barre syndrome in the adult population of the Maltese Islands

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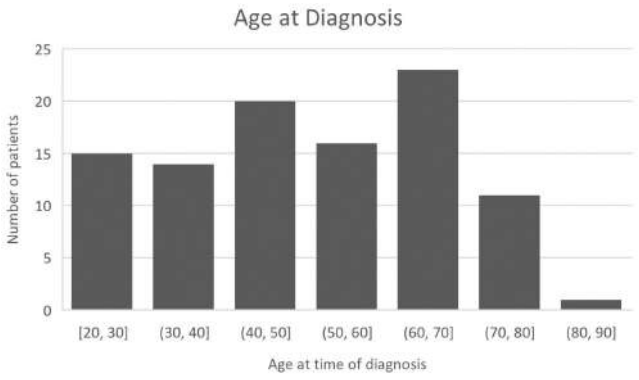
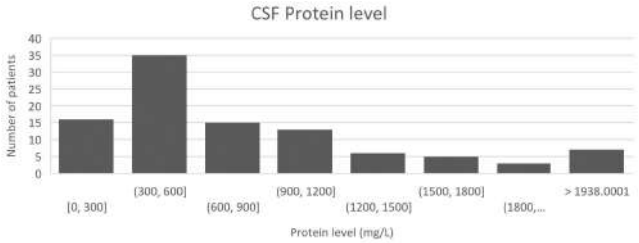
Background and Aims: Guillain Barre Syndrome (GBS) has a worldwide overall incidence rate of 1–2 cases per 100,000 people per year 1. It typically presents with ascending lower limb weakness, associated with hypo/areflexia. Most patient require hospitalization and active treatment with IVIg of Plasma Exchange. The aim of the study is to retrospectively analyze the adult cohort of patients who were admitted with GBS in the Maltese Islands.
Methods: Data were retrospectively collected from National Registries and discharge summaries. Demographic details, infectious screens, lumbar puncture results, nerve conduction study results, treatment regimens and outcomes were collected.
Results: A total of 100 patients were diagnosed with GBS; M = 68. The median age was 53 years. The average length of inpatient acute hospital care was 22.1 days (±32.4SD) (Chart 1). 60% had a previous infection documented. All patients underwent lumbar puncture, most of which happened within 48 hours of admission. 55% of patients had albuminocytological dissociation, with a protein level of >500 mg/L) (Chart 2). 72% were discharged home, 24% needed rehab, 2% passed away during their inpatient stay and 2% required admission to a long-term facility.



Age distribution of our local cohort.



CSF protein levels.

Conclusion: The Maltese population has a similar incidence rate of GBS with a relatively low mortality. Clinical correlation between CSF protein level, presence of positive serum anti-gangliosides and length of hospital stay, and long-term outcomes is being sought.
Disclosure: Nothing to disclose.

EPO-772 | Charcot-Marie-tooth type 2P in a Spanish family with the novel variant in the LRSAM1 gene: p.Gln698_Gln701del

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Background and Aims: Charcot-Marie-Tooth disease (CMT) is the most common hereditary neuropathy. The CMT2 subtype is typically caused by mutations in MFN2 and GDAP1; other genes such as LRSAM1 are exceptional. LRSAM1 mutations specifically cause CMT2-P, characterized by progressive sensory-motor neuropathy. Twelve mutations in LRSAM1 causing CMT2-P have been documented, but each one has been reported only in a single individual or family. Here, we present a Spanish family with dominant CMT2-P associated with a novel mutation in LRSAM1 recently identified in a single study in French families.
Methods: Analysis of clinical, electrophysiological, and laboratory findings of patients diagnosed with CMT2-P and carriers of the c.2093_2104del mutation in LRSAM1 gene.
Results: Eight patients within a single family were identified, with onset spanning 23–52 years. Pes cavus were the onset symptom in 5 patients. Currently, they exhibit distal weakness in upper limbs (1 patient), lower limbs (3 patients), or both (3 patients). Bilateral atrophy of hand interossei muscles and short extensor muscle of toes was observed. Achilles areflexia was evident in all patients, with patellar areflexia in 5. Seven experienced lower limbs hypoesthesia, and 3 neuropathic pain. A sensory predominant axonal polyneuropathy was observed in all patients, with a motor component in 5. Exome sequencing revealed the heterozygous pathogenic variant c.2093_2104del (p.Gln698_Gln701del) in the LRSAM1 gene.
Conclusion: This study reports for the first time a Spanish family afflicted by the p.Gln698_Gln701del variant in the LRSAM1 gene causing CMT2-P. The presence of pes cavus and axonal sensory polyneuropathy are characteristic features of this disease.
Disclosure: None.

EPO-773 | Clinical outcomes, disease course, and QoL in patients with multifocal motor neuropathy: iMMersioN, study in progress

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Background and Aims: Multifocal motor neuropathy (MMN) is a rare, peripheral, immune-mediated, chronic neuropathy resulting from motor nerve conduction block due to IgM auto-antibodies leading to axonal degeneration and progressive disabling asymmetric limb weakness with absence of sensory loss. Data on patient experience and clinical management of MMN are limited to small cohorts and retrospective analyses. There is a need to further understand MMN diagnosis, disease course and management and to characterise the healthcare resource use of patients with MMN.
Methods: iMMersioN (NCT05988073), a global, prospective, longitudinal study, will enrol approximately 150 participants. No investigational medicinal product will be administered. Participants will be observed as they receive standard of care treatments. Site visits will coincide with regular MMN treatment visits and will occur approximately every 3 months, and participants will be followed for up to 24 months. In certain countries, optional blood samples may be collected from participants.
Results: The objectives of the iMMersioN study are: to characterise MMN participant profiles, assess disease management and disease course, including outcomes measures such as MMN-RODS, MMRC-10, and adjusted INCAT, estimate the economic burden and impact of MMN on quality of life, and collect data on relevant disease biomarkers such as autoantibody titers against gangliosides, components of the complement cascade, and a marker of neurological degeneration. The first participant was enrolled on 29 November 2023.
Conclusion: iMMersioN is an ongoing global, prospective, longitudinal study to examine clinical outcomes, disease course, resource utilization and health-related quality of life in adult patients with MMN.
Disclosure: SP received lecture honoraria from argenx, Viatris, Pfizer, Teva Actavis, Berlin-Chemie Menarini, Mylan, Wörwag, ADOC, Remedica and Salveo; research grants from argenx, Kedrion Biopharma and Octapharma; consultant fees from argenx, Dianthus Therapeutics and Mylan; and travel grants from Octapharma, Kedrion Biopharma, Teva Actavis, Sanofi Genzyme, Pfizer, Roche, ADOC, Wörwag, Medis, and Berlin-Chemie Menarini; and reports no other conflicts of interest outside or related to this work. LQ received research grants from Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS/CIDP Foundation International, UCB and Grifols; speaker or expert testimony honoraria from CSL Behring, Novartis, Sanofi Genzyme, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, argenx, UCB, LFB, Avilar Therapeutics, Octapharma and Roche; serves at Clinical Trial Steering Committee for Sanofi Genzyme; and was Principal Investigator for UCB's CIDP01 trial. SA nothing to disclose. IVW, EP, IVH, MH, CA-B are employees of argenx. OVS works as a consultant for argenx. GS, MV work as consultants for argenx and PPD. JA has received consulting honoraria from argenx, Alexion, Akcea, CSL Behring, Johnson & Johnson, Grifols, Takeda, and Sanofi.

MS and related disorders 7

EPO-774 | Abstract withdrawn

EPO-775 | Nocturnal melatonin ingestion alleviated dynamic postural imbalance and muscle weakness in multiple sclerosis

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Background and Aims: Endogenous melatonin (MEL) deficiency in patients with multiple sclerosis (PwMS) was linked to pain and fatigue that induce postural imbalance and muscle weakness. Exogenous MEL has been shown to present anti-fatigue and analgesic effects. Despite this association between physical and perceptual disorders, no study has examined the acute effect of MEL intake on dynamic postural stability and muscle strength in PwMS. This study aimed to investigate the effect of nocturnal MEL ingestion on dynamic postural control and leg muscle strength the following morning in PwMS.
Methods: Fourteen PwMS (28.36 ± 6.81 years) were assessed before and after nocturnal ingestion of 6-mg MEL or placebo (PLA). A force platform was used to evaluate dynamic postural balance in the frontal and sagittal planes. Leg muscles strength (5-sit to stand test (5-STST)), fatigue (Hooper index), nociceptive pain (visual analogue scale (VAS)), and neuropathic pain neuropathic pain 4 questions (DN4)) were also evaluated.
Results: MEL decreased posturographic parameters compared with PLA [frontal plane: center of pressure (CoP) path length (CoPL): 7.56% ($p = 0.02$), mean CoP velocity: 11.1%, ($p = 0.00003$); sagittal plane: only CoPL: 9.1% ($p = 0.005$)]. MEL reduced duration of 5-STST, and scores of VAS and DN4 compared with PLA (8.19% ($p = 0.008$), 84.44% ($p = 0.04$) and 37.69% ($p = 0.023$), respectively). Compared

with PLA, MEL alleviated fatigue (42.29% ($p=0.044$)) and enhanced sleep quality (30.2% ($p=0.012$)).

Conclusion: A single dose of MEL enhanced dynamic postural stability and lower-extremity muscle strength probably through alleviating pain, fatigue, and sleep disorders in PwMS.

Disclosure: Nothing to disclose.

EPO-776 | Incidence of relapses after meningococcal vaccination in clinical trials of eculizumab and ravulizumab in AQP4+ NMOSD

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Background and Aims: Ravulizumab and eculizumab are complement C5 inhibitors (C5ITs) approved for anti-aquaporin-4 antibody-positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD). Because C5ITs are associated with increased *Neisseria meningitidis* infection risk, patients are generally advised to be vaccinated ≥2 weeks before receiving C5ITs; however, vaccination may further activate the complement pathway. Patients with complement-mediated diseases, including NMOSD, may experience increased signs and symptoms of their underlying disease when vaccinated before C5IT initiation. We report on relapses occurring within 4 weeks of meningococcal vaccination administered before initiating C5IT in patients screened in CHAMPION-NMOSD (NCT04201262) and enrolled in PREVENT (NCT01892345).

Methods: Patients analyzed included those with vaccination data who were screened in CHAMPION-NMOSD, irrespective of screening outcome, and those randomised to placebo or eculizumab in PREVENT (vaccination data unavailable for screen failures). Outcomes were relapses occurring within 4 weeks of last meningococcal vaccination and before study drug initiation.

Results: In CHAMPION-NMOSD ($N=71$), 1 enrolled patient was excluded from this analysis because of vaccination before AQP4+ confirmation. Among remaining patients (57 enrolled; 13 screen failures), 2/70 (2.9%) patients experienced a relapse; both were screen failures. In PREVENT, 3.1% (3/96) of eculizumab and 10.6% (5/47) of placebo patients had a relapse.

Conclusion: This retrospective analysis indicates a low relapse incidence (2.9%–3.1%) within 4 weeks of meningococcal vaccinations before C5IT initiation and up to 10.6% for those randomised to placebo. Available information precludes determination as to whether relapses observed are attributable to meningococcal vaccination or inherent relapse risk among patients with AQP4+ NMOSD.

Disclosure: All authors are employees of Alexion, AstraZeneca Rare Disease and hold stock options in AstraZeneca. This study was funded by Alexion, AstraZeneca Rare Disease. Medical writing and editorial support were provided by James Banigan, PhD, CMPP, and Melissa Austin of Apollo Medical Communications (Guilford, CT), part of Helios Global Group, with funding from Alexion, AstraZeneca Rare Disease.

EPO-777 | MS-STAT2 (UCL cohort) baseline analysis: ABILHAND and nine-hole peg test in secondary progressive multiple sclerosis

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Background and Aims: Upper limb (UL) dysfunction affecting 80% of people with MS is associated with reduced independence and quality of life. The Nine-Hole Peg Test (9HPT) is an important progressive MS clinical trial measure, ABILHAND is a 23-item patient reported outcome measure (PROM) covering UL function, shown to correlate variably with the 9HPT depending on the trial mean/median EDSS. Given the ease with which PROMs can be collected, it is important to assess their potential to predict trial relevant clinically reported measures.

Methods: Blinded ABILHAND total scores were calculated, logits calculated using rehab-scales.org, and analysis with reciprocal 9HPT performed using Spearman's correlation and linear regression.

Results: ABILHAND data from 232 trial participants (female $n=177$, male $n=54$), median EDSS of 6.0 (4.0 to 6.5) was analysed. The mean dominant hand 9HPT was 34.1 s, and non-dominant was 34.4 s. Correlation between ABILHAND total score and reciprocal 9HPT was moderate (rho −0.53). There was not a significant change when subgrouping into low/high EDSS groups; or scoring only the easy/difficult ABILHAND items. ABILHAND total scores accounted for variance of: 18% of the 9HPT dominant hand, 27% of the non-dominant hand, and 27.8% of the combined result.

Conclusion: ABILHAND has moderate negative correlation with 9HPT. The discrepancy in hand variance accountability may reflect the implied practical bimanual functionality assessed in the ABILHAND items, and relatively reduced functional reserve of the non-dominant hand. However ultimately the variance was similar when 9HPT results were combined. Longitudinal information will be available late 2024/early 2025 to explore this relationship in more detail.

Disclosure: In the last 3 years, JC has received support from the Health Technology Assessment (HTA) Programme (National Institute for Health Research, NIHR), the UK MS Society, the US National MS Society and the Rosetrees Trust. He is supported in part by the NIHR University College London Hospitals (UCLH) Biomedical Research Centre, London, UK. He has been a local principal investigator for a trial in MS funded by MS Canada. A local principal investigator

for commercial trials funded by: Ionis and Roche; and has taken part in advisory boards/consultancy for Biogen, Janssen, Lucid, Merck, NervGen, Novartis and Roche. The other authors have no disclosures related to this work.

EPO-778 | Autologous hematopoietic stem cell transplantation (AHSCT) in relapsing multiple sclerosis (RMS): A real-world study

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Background and Aims: In recent years treating MS patients early and efficaciously has become prevalent. Literature data agree that a better treatment response occurs when therapy starts in the early phase. The use of AHSCT in MS evolved, passing from a "rescue therapy" in patients who failed all the available DMTs, to an earlier use. No guidelines exist about its correct placement in drugs sequencing; due to its safety profile, AHSCT is usually reserved to patients with hyperaggressive onset or poor responder to highly efficacious therapies. Aim of the study: to describe a series of 24 RMS patients who received AHSCT in our Center.

Methods: 24 RMS patients underwent AHSCT between 2001 and 2023; 23 had a relapsing remitting course, 1 had a relapsing progressive course. Two out of 24 had an aggressive onset. Clinical and demographic characteristics are presented in table 1. 15 patients received BEAM+AGT as conditioning regimen, 1 received BEAM without ATG; 1 patient received only BEAM and subsequently underwent a second AHSCT.

Results: Median EDSS changed from 2.0 at the time of AHSTC to 1.5 at the last follow up visit. 62.5% patients were in NEDA-3 status at the last visit. Limiting the analysis to patients who received BEAM+AGT as conditioning regimen, 82.3% was in NEDA-3 status at the end of follow up. No major adverse event occurred.

Table 1: Patients' characteristics

PATIENTs	
F/M	18/6
Disease phenotype (n°)	RR (23); RP (1)
Age at AHSCT	18 - 46 years (median 28 years)
Disease duration at AHSCT	0.5-16.7 years (median 6.8 years)
EDSS at AHSCT	1.0 - 9.0 (mean 3.2; median 2.0)
N° of previous DMTs	0-5 (median 2)
Follow up after AHSCT	0.5-20.6 years (median 8 years)

RR: relapsing remitting
RP: relapsing progressive

Conclusion: AHSCT represents a highly efficacious treatment in patients with aggressive disease course. Careful selection and both hematological and neurological evaluation should be performed in order to better define risks and benefits.

Disclosure: SM received speaker honoraria from Biogen, Merck, Sanofi, Novartis, Roche. FS received honaria for talking from Novartis. RB received compensation from Novartis, Sanofi, reimbursement from Bristol Myers, Janssen. MLR received compensation from Novartis and Merck. DQ received compensation from Merck and Novartis and reimbursement from Merck, Roche, Novartis and Biogen. AO has nothing to disclose. MDG has nothing to disclose. AB served on the scientific advisory board of Almirall, Bayer, Biogen, Genzyme; received speaker honoraria from Biogen, Novartis, Sanofi, grant support from Almiral, Biogen, Associazione San Luigi Gonzaga ONLUS, Fondazione per la Ricerca Biomedica ONLUS, Mylan, Novartis and the Italian Multiple sclerosis Society. MM received compensation from Alexion and Novartis. ADS received honoraria from Biogen, Novartis, Roche, sanofi, Merck, Alexion and Sandoz and has been reimbursed by Merck, Biogen, Sanofi, Novartis and Roche for attending conferences.

EPO-779 | The remyelinating potential of non-invasive neuromodulation and its effects on cognition

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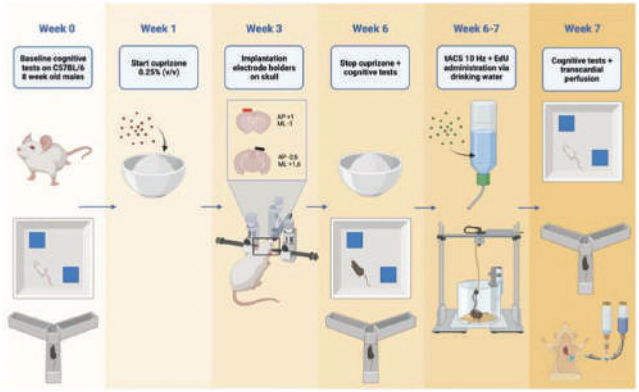
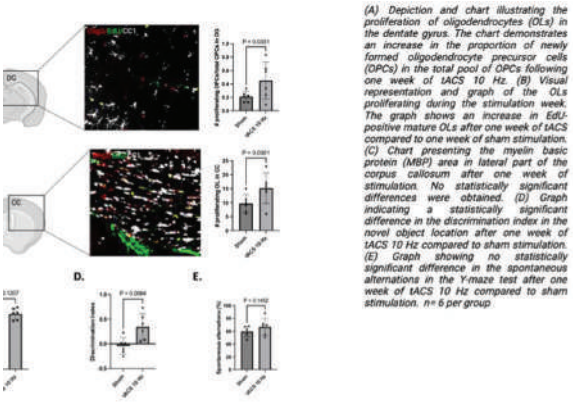
Background and Aims: Previous preclinical studies have revealed that neuronal activity can enhance remyelination and that different patterns of neuronal activity can be sensed by oligodendrocytes. These techniques, however, are not translatable to people with MS due to their invasive nature. In that regard, we intend to investigate the potential of tACS at different frequencies in the cuprizone model.

Methods: Eight-week-old mice receive a cuprizone diet for six weeks enabling demyelination whereafter the mice are reverted to a normal diet allowing partial remyelination. During the withdrawal phase, mice receive either tACS at one, five or 10 Hz or sham stimulation for a week. Readouts include cognitive tests such as the novel object location task and the y-maze as well as immunohistochemistry.

Results: Preliminary results indicate that one week of tACS at 10 Hz leads to improved cognition as demonstrated by improvements in the discrimination index during the novel object location task ($p = 0.0064$). The improvements were not associated with enhanced remyelination in the corpus callosum ($p = 0.1207$). However, the number of mature oligodendrocytes colocalizing EdU was increased in the corpus callosum after one week of tACS 10 Hz compared to sham stimulation ($p = 0.0301$).



Overview of the project.



(A) Depiction and chart illustrating the proliferation of oligodendrocytes (OLs) in the dentate gyrus. The chart demonstrates an increase in the proportion of newly formed oligodendrocyte precursor cells (OPCs) in the total pool of OPCs following one week of tACS 10 Hz. (B) Visual representation and graph of the OLs proliferating during the stimulation week. The graph shows an increase in EdU-positive mature OLs after one week of tACS compared to one week of sham stimulation. (C) Chart presenting the myelin basic protein (MBP) area in lateral part of the corpus callosum after one week of stimulation. No statistically significant differences were obtained. (D) Graph indicating a statistically significant difference in the discrimination index in the novel object location after one week of tACS 10 Hz compared to sham stimulation. (E) Graph showing no statistically significant difference in the spontaneous alternations in the Y-maze test after one week of tACS 10 Hz compared to sham stimulation. n= 6 per group

Summary of the results.

Conclusion: One week of tACS at 10Hz during the withdrawal phase of cuprizone leads to improved spatial working memory. While we do not show increased remyelination, we do report an acceleration of maturation of OLs within the OLs proliferating in the corpus callosum. Future experiments will confirm whether these findings can be confirmed and whether different stimulation frequencies might be more effective in remyelination.

Disclosure: Thomas Scheinok received a travel grant from Merck of 250 euros for the EAN congress in 2022. Other authors have nothing to disclose.

EPO-780 | Effectiveness of telemedicine neurologic examination in real-life settings

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Background and Aims: The importance of telemedicine applications in neurology practice has been widely recognized during the COVID-19 period, although there is no clear scientific evidence about the feasibility of general neurological examinations performed with telemedicine. In this study, we aimed to determine the effectiveness of telemedicine neurologic examination (TNE) in real-life conditions and in various disease groups.

Methods: In this multicenter, prospective, and cross-sectional study, patients with various neurological diagnoses were first evaluated face-to-face. These patients were then evaluated by a randomly assigned physician via TNE in terms of 42 different components performed with video conferencing tools used by the public in daily life. These components were scored as categorical variables. Fleiss-Kappa analysis was used for interrater agreement.

Results: The study included 93 patients 64 of whom were female. Among all, 39 patients had demyelinating diseases, 15 headaches, 9 movement disorders, 6 dementia, 8 neuromuscular diseases, 6 epilepsy, 5 strokes, and 4 other neurological disorders. During the in-person examination, 17.2–50.5 percent of the patient population had abnormal neurological findings in four different domains.

The telemedicine exam had almost perfect interrater agreement in 4 domains (Kappa > 0.8), substantial agreement in 16 domains (Kappa = 0.6–0.8), moderate agreement in 10 domains (Kappa = 0.4–0.6), and slight agreement in 8 domains (Kappa = 0.2–0.4). Although a rather heterogeneous distribution was observed in all neurological examination domains, the best performance was observed in cranial nerve examinations, paresis testing, and cerebellar system examinations.

Conclusion: Our study provides scientific evidence that many components of the neurological examination can be effectively implemented with telemedicine.

Disclosure: Nothing to disclose.

EPO-781 | Conversational agent engagement patterns among individuals with MS: A retrospective analysis of the mHealth application

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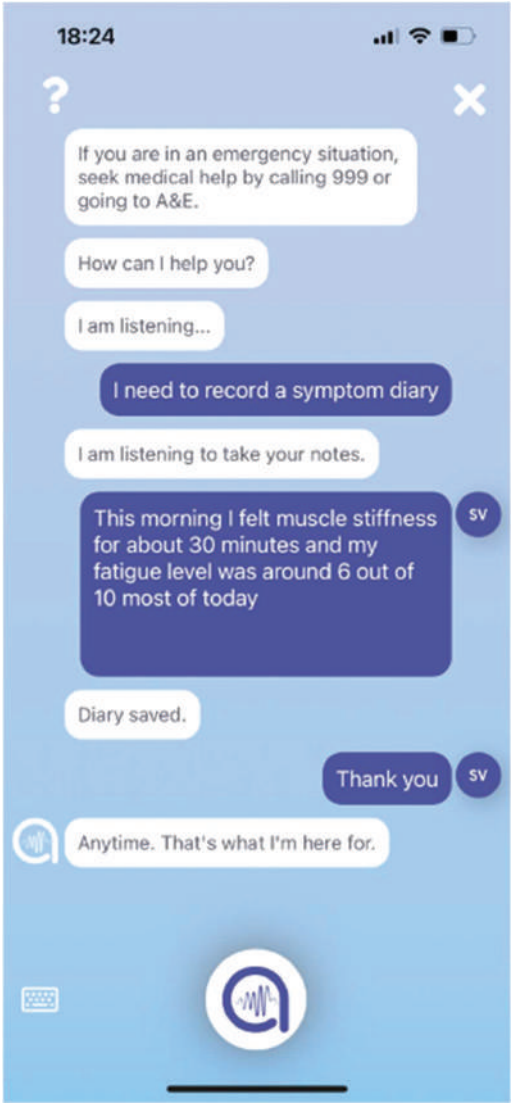
Background and Aims: This study analyzes the engagement patterns of MS-diagnosed individuals with "Albert MS+" a mHealth application tailored for MS self-management and remote monitoring, with conversational agent (CA) support.

Methods: We retrospectively analyzed the data based on the intent classification during conversations with CA such as accessing health information, recording clinical parameters, treatment-related queries, small talk, and fallbacks.

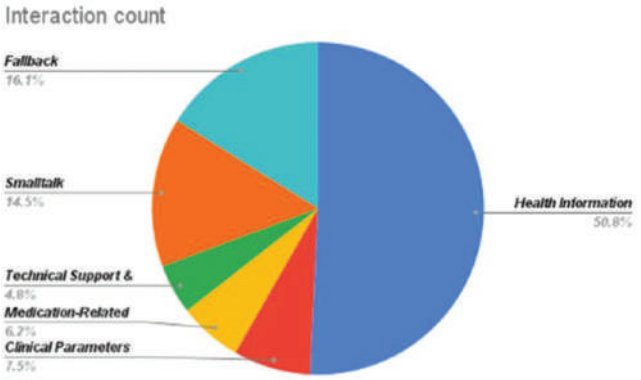
Results: A total of 263 individuals diagnosed with MS for up to 20 years were enrolled to use Albert. Out of these, 125 participants interacted with the CA 1196 times between 2022 and 2023. The demographic profile showed an average age of 36.3 years with a predominance of females (72.57%) and a high educational background, as 69.6% are university graduates. The average duration since diagnosis was 7.5 years. Health Information accounted for 50.8% of total interactions. Within this category, the specific queries around MS, telehealth, and pharmacy information represent significant areas of user engagement indicating a high demand for accessible health-related information. Clinical parameters and medication-related topics together made up 13.7% of interactions. Smalltalk constituted 14.5% of the interactions. Fallbacks comprised 16.1% of interactions, this highlights opportunities for improving the agent's understanding and response accuracy.

Intent Category	Definition	Conversation examples
Health Information	This category includes interactions about health advice or medical knowledge specifically related to Multiple Sclerosis (MS). Example: - Ask MS-related health questions, - Show pharmacy on duty, - Get a telehealth appointment	User: Is there a specific diet that's recommended for someone with MS? CA: There's no one-size-fits-all diet for MS. Some individuals with MS follow specific diets, like the Mediterranean diet or low-saturated fat diets, to manage their symptoms. You can consult with a nutritionist in the app or your healthcare provider on your next visit for personalized advice. Also, you can watch the video in the app that provides useful dietary tips for MS patients. User: Thank you.
Clinical Parameters	This category focuses on tracking and recording clinical data related to MS or other health metrics such as blood pressure, blood glucose level Example: - Record a symptom diary - Record blood pressure or glucose level, - Upload a clinical document (e.g. lab report)	User: I'd like to track my MS symptoms over time. CA: Keeping a symptom diary can be very helpful. You can log your symptoms, their severity, and any factors you think might be contributing to them. We also have a feature in the app that allows you and your physician to track your symptoms and view trends over time. Would you like to start by recording today's symptoms? User: Yes, that would be great. CA: I'm listening ...
Medication - Related	Actions related to the management and understanding of medications, supplements, or treatments, applicable to routine health maintenance or MS-specific management. Example: - Record medication, - Mark medication as taken, - Show daily medication schedule	User: I need to record my new medication. CA: Can you tell me the name of the medication? User: Fingolimod. CA: Your medication is saved as Fingolimod. You can edit it later from the My Health menu. How often should I remind you this? User: Once a day. CA: What time will you be taking it? User: 9 a.m. CA: I recorded your medication info and set a reminder
Non-clinical	Casual interactions and system guidance to ensure a comfortable and supportive user experience, these address general inquiries and navigate uncertainties. Example: -Fallback, -Smalltalk, -Technical Support & Guidance	User: [Attempts to speak, but the speech is unclear and not transcribed correctly] CA: I'm sorry, I didn't catch that. Could you please repeat what you just said? User: [Attempts to speak again, but the speech is still unclear and not transcribed correctly] CA: It seems we're having trouble understanding your message. I apologize for the inconvenience. If you're experiencing an urgent issue, it's important to contact a healthcare professional directly or dial emergency services. Remember, this platform is not a substitute for professional medical advice, diagnosis, or treatment. Please try to rephrase your concern or reach out to your healthcare provider for immediate assistance.

Categories of intents created by the patients using the app.



An example of a clinical parameter recorded by a patient via conversational agent.



The distribution of intent categories.

Conclusion: The analysis underscores the conversational agent's role in providing health information, and supporting self-management and indicates a potential to enhance user experience by improving its response capabilities.
Disclosure: Nothing to disclose.

EPO-782 | Prognostic biomarkers of silent progression in multiple sclerosis (MS): Report from an Italian cohort

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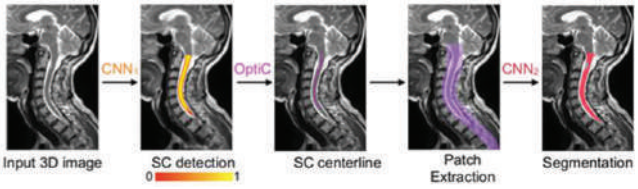
Background and Aims: Silent progression is a central topic in MS, with a lack of prognostic indicators. This study aims to discern radiological and biochemical markers to identify silent progressors from relapsing-remitting MS (RR-MS).
Methods: A total of 42 untreated RR-MS subjects were enrolled. Twenty-two out of 42 were identified as silent progressors (SiPr) (Cree et al., 2019). Each patient underwent a 3-Tesla Magnetic Resonance Imaging (MRI) at diagnosis. Serum levels of neurofilaments light chains (Nfl) and Glial Fibrillary Acidic Protein (GFAP) were assessed on 29 subjects. Comparison between groups were analyzed using Student *t*-tests or the non-parametric Mann-Whitney test. Univariate and multivariate linear regression analysis were performed to assess association between different neuroradiological quantitative data and being SiPr.
We used Spinal Cord Toolbox (SCT) software to acquire cervical spinal cord volumes at C2-C3 from T1-weighted MRI images. SCT created a 3D mask, and convolutional neural networks (CNN) facilitated spinal cord segmentation.
Results: At the univariate analysis lesion load, count of cortical and spinal lesions, choroid plexus volume, and cervical spinal cord volume resulted predictors of silent progression. However, at the multivariate analysis, only the number of spinal cord lesions was a significant predictor of silent progression. No significant differences in Nfl and GFAP levels were noted across groups.



	OR	95%CI		p (<0.05)
Number of lesions	1.04	1.01	1.07	**0.022**
Lesion load	1.13	1.02	1.25	**0.019**
Cortical lesions	1.24	1.05	1.46	**0.010**
Spinal lesions	5.72	2.08	15.67	**0.001**
Paramagnetic Rim Lesions	14.24	0.92	219.75	Not significant (0.057)
NchP	3.70	1.13	12.20	**0.031**
Cervical volume	0.80	0.67	0.96	**0.016**

Univariate analysis of radiological characteristics among non-SiPr and SiPr. OR: odds ratio; CI: confidence intervals; NchP: normalized choroidal plexus volume.

Conclusion: The study highlights spinal cord lesions as key predictors of silent progression in MS. SiPr presented a more enlarged choroidal plexus compared to non-SiPr patients, suggesting a chronic inflammatory state and an impairment of periventricular remyelination. Identifying RR-MS patients with worse prognosis and faster progression from onset could enable targeted therapeutic interventions for improved outcomes.
Disclosure: Nothing to disclose.

EPO-783 | Cognitive and neuropsychological features among patients with multiple sclerosis and epilepsy

V. Pozzilli[1]; C. Tortorella[2]; L. Prosperini[2]; S. Ruggieri[2]; S. Haggiag[2]; C. Gasperini[2]; A. Cruciani[1]; F. Capone[1]; V. Di Lazzaro[1]; L. Celani[1]; G. Evangelista[3]; G. De Luca[3]; S. Cipollone[3]; V. Tomassini[3]; F. Dono[3]
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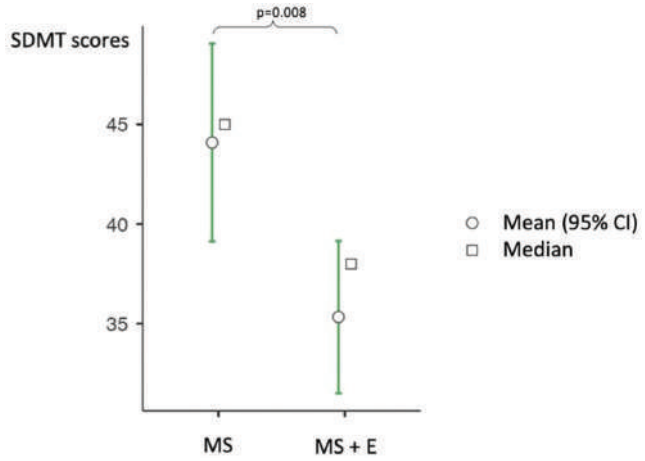
Background and Aims: Epilepsy is 2–3 fold more common in patients affected by multiple sclerosis (pwMS) compared to the general population. Currently it is not elucidated whether patients with MS and epilepsy (MS+E) exhibit distinct cognitive and neuropsychological features compared to MS patients.

Methods: Our study aimed to assess the cognitive and neuropsychological impact of epilepsy on MS. Data including clinical features of MS, epilepsy, and medications were collected. Neuropsychological tests including the brief cognitive assessment for MS (BICAMS), the general anxiety disorder-7, beck's depression inventory and symptom checklist-90 for psychiatric morbidity were administered.
Results: kkThirty-three MS+E patients and 33 MS controls matched for age, sex and MS duration were included. MS+E individuals showed lower processing speed ($p < 0.01$) and visuospatial memory scores ($p = 0.03$). Seizure onset timing influenced seizure freedom, as in those who manifested their first seizure within 1 year of MS onset had higher seizure freedom rates ($p = 0.03$). Slowing and/or epileptic activity in at least one EEG were associated with elevated psychological distress. In MS+E patients, higher levels of psychological distress were associated to lower verbal learning test abilities ($p = 0.04$). Compared to the general population, MS+E patients yielded higher scores in somatization, depression, anxiety, phobia, paranoid ideation, and psychoticism ($p < 0.001$), with phobia deviating the most from normative values.



Symbol digit modalities test (SDMT) scores in patients with MS + E (epilepsy) compared to MS.

Conclusion: Epilepsy in MS is associated to worse cognition and psychological morbidity, particularly phobia. This suggests a need for comprehensive patient care, possibly addressing the neuropsychological aspect. Larger studies are needed to confirm such findings.
Disclosure: Nothing to disclose.

EPO-784 | Assessing spatio-temporal pattern of thalamic damage in multiple sclerosis patients

V. Penati[1]; E. Portaccio[1]; A. Caporali[1]; M. Betti[1]; C. Ballerini[1]; C. Fabbiani[2]; R. Bonacchi[3]; E. Fainardi[2]; E. De Meo[1]; M. Amato[1]
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Background and Aims: Thalamic atrophy is one of the earliest changes occurring during multiple sclerosis. Several pathogenetic mechanisms underlying thalamic damage have been hypothesized including Wallerian degeneration from white matter lesions (WM) and cerebrospinal fluid (CSF)-immunocytotoxic factors mediated damage. We aim to identify long-term trajectories of thalamic nuclei damage and the contribution of its progression in determining clinical disability and cognitive impairment.
Methods: A cohort of 108 MS patients underwent annual 3T MRI scans (3DT1- and T2-weighted images) and clinical/cognitive assessments for up to 8 years from disease onset. Thalamic nuclei segmentation was performed using Freesurfer 7.2.0. Growth models by alternating conditional expectation evaluated long-term thalamic volume changes. Linear regression models determined the relationship between thalamic damage progression and clinical disability and cognitive decline.
Results: Bilateral thalamic nuclei adjacent to CSF exhibited a slower, steady volume loss, while those near white matter demonstrated rapid progression. Using growth models, we identified a relative progression index (γ), reflecting shared variance in thalamic nuclei volumes. Significant correlations were found between γ and clinical disability, information processing speed, and executive functions.
Conclusion: The study confirms heterogenous pathogenetic mechanisms in thalamic damage: Wallerian degeneration due to macroscopic white matter damage and CSF-cytotoxic mediated damage. The identified index (γ) effectively links thalamic damage to cognitive impairment and clinical disability, suggesting its potential as a biomarker for disease monitoring and aiding in treatment strategy identification.
Disclosure: Nothing to disclose.

EPO-785 | Carotid intima media thickness, neutrophil to lymphocyte ratio, and platelet to lymphocyte ratio in multiple sclerosis

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Background and Aims: Limited evidence suggests that carotid intima-media thickness (cIMT) and neutrophil-to-lymphocyte ratio (NLR) increase in patients with MS. Furthermore, platelet-to-lymphocyte ratio (PLR) can increase in neuroinflammatory and autoimmune diseases, and it is better interpreted when measured along with other biomarkers, such as NLR. We aimed to assess cIMT, NLR, and PLR levels and their possible correlation in patients with MS.

Methods: We included 110 patients and 110 healthy controls in this case-control study. All participants underwent complete history taking, and general and neurological examination. Expanded Disability Status Scale was used to assess disability. cIMT was measured with B-mode ultrasound images, 10 mm before the bifurcation of the common carotid artery.

Results: NLR, PLR, and cIMT were significantly increased in patients with MS, compared to healthy controls ($p < 0.001$). Among patients with MS, higher cIMT ($p < 0.001$) was significantly associated with older age ($p < 0.001$), higher BMI ($p < 0.001$), higher EDSS scores ($p = 0.005$), older age of disease onset ($p < 0.001$) and SPMS type ($p = 0.003$). Further linear regression analysis revealed that cIMT was marginally associated with higher NLR values ($p = 0.055$). After controlling for confounding factors, cIMT was significantly associated with NLR ($p = 0.047$), and not with PLR ($p = 0.2$). The cut-off value of mean cIMT (sensitivity: 84%; specificity: 49%) for discriminating mild-to-moderate and severe disability was calculated as 0.5.

Conclusion: Higher cIMT levels are significantly associated with higher NLR levels. cIMT could be used as a simple, rapid, and cost-effective inflammatory marker for MS disability. Further multicenter studies with larger sample sizes are needed to validate the findings of this study.

Disclosure: Nothing to disclose.

Neuro-ophthalmology/neuro-otology

EPO-786 | A case series of five fulminant idiopathic intracranial hypertension (IIH) patients at a tertiary care hospital

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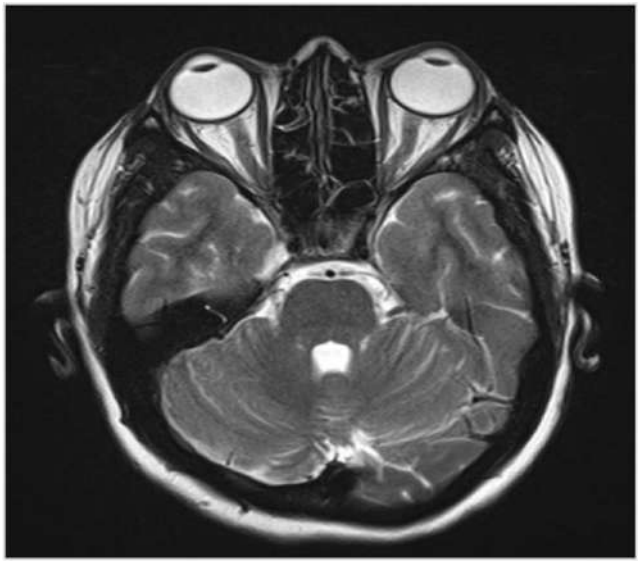
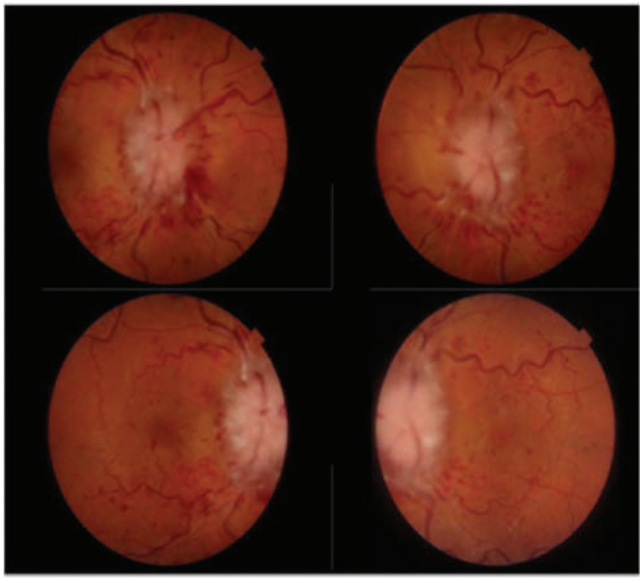
Background and Aims: Fulminant IIH, presents with abrupt symptom onset and signs of intracranial hypertension, progressing to rapid vision decline within four weeks.

Methods: This case series evaluates clinical, ophthalmological, and radiological features in five non-obese female patients aged 28–40 years.

Results: Comprehensive evaluation of these patients, revealed symptoms like acute migranous headache, nausea, diplopia and transient visual obscurations (TVO's). Progression to near-total blindness occurred swiftly within 14 days, with one patient experiencing this within 48 hours. Uniform grade 4 papilledema was observed, including two cases with associated peripapillary hemorrhages. The CSF opening pressure ranged from 35 to 45 cm of H_2O. Optical coherence tomography (OCT) illustrated increased retinal nerve fiber layer (RNFL) thickness. MRI findings aligned with IIH, coupled with evidence of transverse sinus stenosis. Optic nerve sheath diameter (ONSD) measured by MRI exceeded 6mm in all cases. Four patients underwent medical management with acetazolamide and temporary CSF drainage for ongoing rapid visual loss. One patient underwent delayed optic nerve sheath fenestration after conservative management. Notable improvements in headache, nausea, and TVO's with subjective visual function improvement. Visual fields remained severely altered.



MRI consistent with IIH.



Papilledema with peripapillary hemorrhage.

TABLE: CLINICAL, OPTHALMOLOGICAL AND RADIOLOGICAL PARAMETERS

	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5
AGE	33	29	35	40	28
BMI	22 kg/m2	21.6 kg/m2	22 kg/m2	23.7 kg/m2	22.5 kg/m2
VISUAL ACUITY & EOM	Hand movement; B/L lateral rectus palsy	Hand movement; B/L lateral rectus palsy	Hand movement; B/L lateral rectus palsy	Hand movement; B/L lateral rectus palsy	Hand movement; B/L lateral rectus palsy
FUNDOSCOPY	grade 4 papilledema	grade 4 papilledema	grade 4 papilledema+ peripapillary hemorrhage	grade 4 papilledema+ peripapillary hemorrhage	grade 4 papilledema
OCT	RNFL thickening	RNFL thickening	RNFL thickening	RNFL thickening	RNFL thickening
CSF OPENING PRESSURE	38 cm H2O	35 cm H2O	40 cm H2O	45 cm H2O	42 cm H2O
MRI	consistent with IIH*	consistent with IIH*	consistent with IIH*	consistent with IIH*	consistent with IIH*
MR VENOGRAPHY	U/L transverse sinus stenosis	U/L transverse sinus stenosis	B/L transverse sinus stenosis	B/L transverse sinus stenosis	U/L transverse sinus stenosis
ONSD	6.1 mm	6.1 mm	6.3 mm	6.3 mm	6 mm

* MRI findings in IIH: optic nerve tortuosity, flattened posterior aspect of sclera, dilated perioptic sheath, partially empty sella

Conclusion: Fulminant IIH, characterized by distinctive traits, is not universally linked to obesity. Acute symptoms, near-total blindness, grade 4 papilledema, significantly elevated CSF opening pressure, and raised ONSD can help initiate swift identification and management thereby preventing potential permanent visual loss. Immediate medical therapy with temporary CSF drainage is vital in cases of anticipated intervention delay.

Disclosure: Nothing to disclose.

EPO-787 | Clinical and multimodal imaging findings in traumatic optic neuropathy

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Background and Aims: Traumatic optic neuropathy (TON) is a grave complication of cranio-orbital injury, causing visual involvement. The severity may range from simple contusion to complete avulsion of the optic nerve. We review clinical presentation and multimodal imaging findings in TON.

Methods: Retrospective review of patients with the diagnosis of TON. Clinical records of patients treated in ophthalmology department of Habib Bourguiba Hospital were collected.

Results: Our study included 8 patients with an average age of 22,2 years comprising 7 males and 1 female. All patients complained of sudden vision loss following blunt ocular trauma. Neurological examination was normal in all patients. The TON was unilateral in all cases. Visual acuity was limited to counting fingers in all cases with an afferent pupillary defect. Fundus examination showed signs of partial optic nerve avulsion in two patients, was normal in others. Optical coherence tomography showed a disruption of optic nerve axons in two patients diagnosed with optic nerve avulsion and was normal in 6 cases. Orbital scan revealed orbital fractures in two patients with a bony fragment adjacent to the optic nerve in one case. Six patients received high-dose corticosteroid. Improvement of visual acuity was achieved in one case.

Conclusion: The diagnosis of TON is clinical, based on visual acuity impairment with the afferent pupillary defect. Optical coherence tomography reveal the disruption of optic nerve axons at the scleral rim in optic nerve avulsion. There is no consensus in the management of TON and visual recovery is uncertain.

Disclosure: Nothing to disclose.

EPO-788 | The condition of vestibular and auditory function in patients with established endolymphatic hydropsis

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Background and Aims: One of the causes of recurrent cochleovestibular syndrome is endolymphatic hydrops (EH) in Meniere's disease (MD). The study was to assess vestibular and auditory function in patients with a fixed EH according to MRI data.

Methods: 32 patients with MD were examined (of the criteria of the Barany Society, 2015) 21 women and 11 men, average age 53.22 ± 12.6 years). 2 groups were identified: definite MD (DMD), $n = 17$ and probable MD (PMD), $n = 15$. Tonal threshold audiometry (TTA), vestibulometry with functional tests (de Klein's test, hyperventilation, Valsalva, Dix-Hallpike, McClure-Pagnini) with registration of spontaneous (SN) and provocative nystagmus (PN), brain MRI and inner ear (IE) with delayed intravenous or transtympanal by contrast.

Results: The TTA data the average value of the hearing threshold on the affected side in the DMD group – 47.08 ± 23.18 dB, in the PMD group – 36.31 ± 22.25 dB, ($p > 0.05$). SN was registered in 2 (12%) of 17 and PN in 9 (53%) patients with DMD. In the PMD group SN was not registered, in 5 (35%) PN was registered on the lesion side. Significant vestibular hyporeflexia on the hearing loss side was detected in 100% patients with DMD and PMD. In the PMD group brain MRI and IE did not reveal MR signs of EH. In the DMD group MRI revealed EH in 8 (47%) of 17 patients ($p < 0.05$) on the affected side it corresponded (100%) to the detected hearing loss and vestibular hyporeflexia.

Conclusion: The results obtained make it possible to objectify the EG during subcompensation, which is confirmed by MRI diagnostics.

Disclosure: Nothing to disclose.

EPO-789 | Clinical and evolutionary characteristics of optic neuritis inaugurating multiple sclerosis: About 38 Algerian patients

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Background and Aims: Optic neuritis (ON) is a frequent clinical presentation in multiple sclerosis (MS), which may be inaugural or occur during the course of the disease, and is considered in the literature to be a factor with a good prognosis. We describe the clinical and evolutionary characteristics of optic neuritis in 38 Algerian patients.
Methods: Prospective longitudinal descriptive and analytical study over a 3-year period in the neurology department of the CHU annaba Algeria, involving patients over 15 years of age presenting with inaugural ON alone or associated with other neurological signs.
Results: Out of 79 patients, 38 were diagnosed with clinically defined MS according to the 2017 McDonald criteria; sex ratio F/M = 4.42, mean age 29.39 ± 10.61 years; ON was acute in 86. 8%, unilateral in 84.21%, painful in 81.57%, Uhthoff's phenomenon was present in only 6 patients, distance visual acuity was <1/10th in 31.81%, fundus appearance was normal in 68.18%, neurological examination revealed multifocal CNS involvement in 55.28%, orbital MRI was performed in only 11 patients, with ON found in 8; brain MRI met Barkhoff criteria in 68.42%, with active lesions in 6 patients; spinal cord MRI was pathological in over half of cases, dominated by cervical myelitis; symptomatic treatment based on high doses of corticosteroid was initiated in 76.3%, with a good response in the majority of cases.
Conclusion: This study enabled us to assess the characteristics of ON inaugurating MS in an Algerian population; Is ON in MS really a good prognostic factor?
Disclosure: Nothing to disclose.

EPO-790 | An exceptionally uncommon stroke syndrome: A case of cortical deafness

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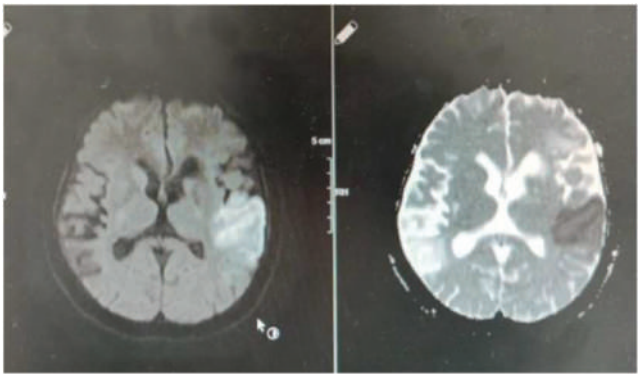
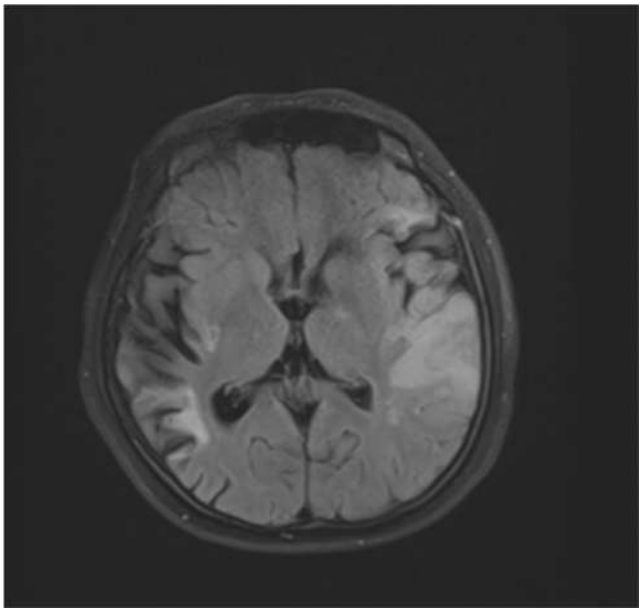
Background and Aims: Cortical deafness is an extremely rare condition that arises from bilateral cortical lesions in the primary auditory cortex. Its main clinical manifestation is a sudden bilateral hearing loss. Diagnosis is challenging due to its rarity and similarity to other language and communication disorders, such as Wernicke's aphasia, auditory agnosia, or pure word deafness.
Methods: Case report.
Results: We present a 33-year-old female with an acute onset of complete bilateral hearing loss. The hearing loss was attributed to a subacute cortical infarction at the level of the superior and transverse temporal gyri on the left, and an older cortical infarction at a similar location on the right. The etiology of these recurrent cardioembolic infarcts was her mechanical heart valve.



Initial diffusion MR.



MRI, 3 months.

Conclusion: Both the peripheral and central auditory pathways must be intact for proper hearing. Auditory signals from each ear are evaluated bilaterally in the cerebral cortex. Therefore, for a complete hearing loss, there must be damage to both auditory cortices, the Heschl's gyri. As a result, stroke-induced deafness is an exceptionally uncommon situation that should be kept in mind in a patient presenting with acute bilateral hearing loss to treat appropriately and to prevent permanent disability.
Disclosure: Nothing to disclose.

EPO-791 | "Complete external ophthalmoplegia" as an adverse reaction to Adalimumab

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Background and Aims: "Complete external ophthalmoplegia" refers to the inability of the eyes to move conjugately in all gaze positions. It is caused by damage to the brainstem conjugate gaze control nuclei.
Methods: A 51-year-old male, treated with Adalimumab for primary uveitis suffered sudden horizontal binocular diplopía two weeks after Adalimumab administration, which was firstly orientated as microangiopathic IIIpc palsy. He was found two weeks later with a sudden worsening with a complete external ophthalmoplegia. The patient was admitted to the neurology department for study.
Results: In 2017, a magnetic resonance imaging (MRI) conducted in context of the uveitis, revealed a subcortical small hyperintense lesion. A follow-up MRI one week after the initial clinical presentation identified a small hyperintense lesion located parasagittally in the dorsal tegmentum of the pons. Another MRI during admission (15 days later) demonstrates an increase in size of the lesion, showing diffusion restriction. The cerebrospinal fluid (CSF) exhibited mild pleocytosis. Rest of the ancillary tests were normal. The patient received high-dose methylprednisolone for five days, showing favorable evolution of symptoms. Due to suspicion of adverse drug reaction, Adalimumab was discontinued. Subsequent follow-up MRI shows an inflammatory activity regression.
Conclusion: We report a case of an adverse reaction to Adalimumab consisting of brainstem inflammation with complete external ophthalmoplegia. Anti-TNF-alpha therapy is not indicated in patients with central demyelinating diseases. Our patient had a previous suspicious lesion so that may not have been the best option.
Disclosure: No conflicts of interest.

EPO-792 | Abstract withdrawn

EPO-793 | Vestibular perceptual thresholds in patients with persistent postural perceptual dizziness

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Background and Aims: Persistent postural perceptual dizziness (PPPD) is a common functional disorder. It is characterized by a chronic sensation of dizziness which is exacerbated by upright posture. PPPD usually evolves as a consequence of a vestibular or other illness. With standard vestibular testing being usually normal in those patients with PPPD we studied whether there are changes in vestibular perception.
Methods: 12 patients with PPPD were assessed, 10 males, 2 females (mean age 60 years). The diagnosis of PPPD was established according to the criteria of the Bárány Society from 2017. 23 healthy controls were assessed, 11 males, 12 females (mean age 42.3 years). Vestibular perceptual thresholds were determined for yaw-plane rotations with randomly presented half cosine stimuli. Patients were assessed for handedness, Dizziness Handicap Inventory (DHI), Ten-item personality inventory (TIPI) and Hospital Anxiety and Depression scale (HADS).
Results: Vestibular perceptual thresholds in PPPD patients did not significantly differ from those of normal controls. There was no correlation between age and elevated thresholds. The number of trials needed to determine the respective threshold was not related to lower threshold values. Handedness was not correlated with direction errors when indicating motion perception. There was no correlation between DHI values and high or low thresholds.
Conclusion: Patients with PPPD did not differ from normal controls regarding vestibular perceptual threshold values for yaw-plane rotations. There was no correlation between age and threshold value.
Disclosure: Nothing to disclose.

EPO-794 | Neurological aspect of peripapillary retinal nerve fiber layer changes analysis in idiopathic intracranial hypertension

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Background and Aims: Papilledema is a biomarker of the elevated intracranial pressure (ICP), observable in fundoscopy. Optic Coherence Tomography (OCT) is a superior method that provides valuable real-time information about retinal nerve fiber layers (RNFL) and uneven RNFL distribution and thickness, with more density in the temporal circumpapillary bundle (Figure-1). This allows us to observe sequential changes even before the formation of overt papilledema and diagnose Idiopathic Intracranial Hypertension (IIH) in its early stages.
Methods: In this study, we have enrolled 4 patients whose OCTs were suggestive of elevated ICP based on Sajjadi et al 2017 patterns. Their investigation included: ICP measurement by lumbar puncture (LP), circumpapillary RNFL thickness assessment in temporal, superior, nasal and inferior (TSNI) quarters (Figure-1) and Brain Magnetic Resonance Imaging (MRI). As normal people and patients with overt papilledema can be diagnosed definitely, they have been excluded from our study.

Results: As demonstrated in table-1 Despite all cases having elevated ICP, case 2 and 3 had RNFL thicknesses were in the normal chart and case 1 had minimal elevation in RNFL thickness and surprisingly case 4 had generalized depression.

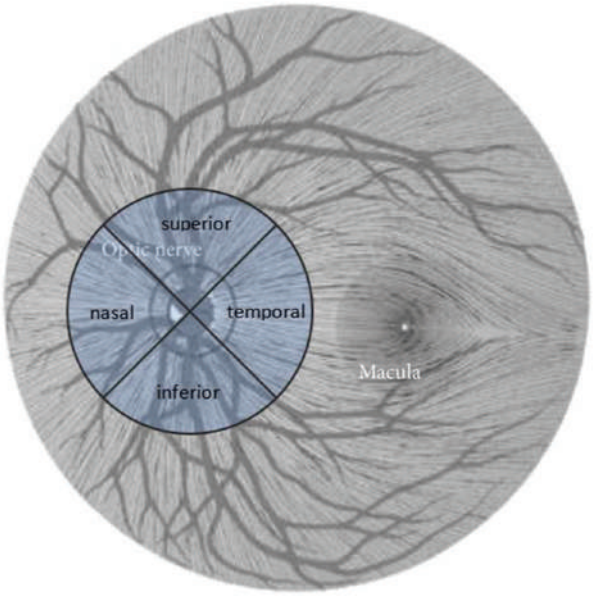

Figure 1: the radiation of RFNL and maculopapillary bundle – peripapillary section is divided into temporal, superior, nasal and inferior quadrants

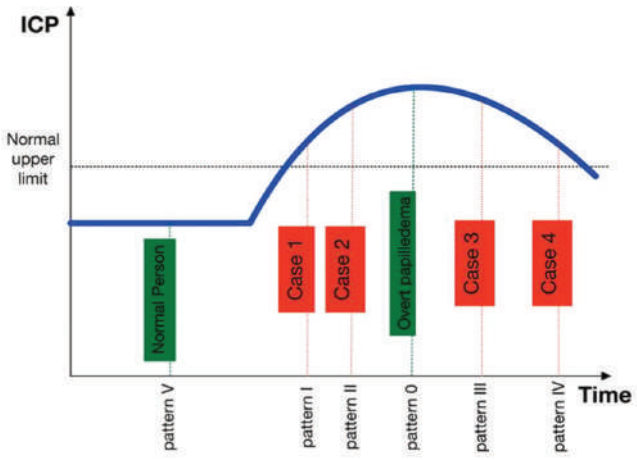

Figure 2: Allocated Sajjadi patterns and presented cases in Rising ICP progression diagram from normal case to increasing ICP and then Normal pressure hydrocephalus with decreased ICP due to pressure redistribution to solid tissues.

Patterns	RNFL thickness in TSNIT quadrants				CSF pressure incremental progress	Reversible RNFL damages	Reversible brain damages
	T	N	S	I			
0	↑↑	↑↑	↑↑	↑↑	Rapid progression	Variable	Variable
1-case 1	↑↑	↑	↑		Slow progression	Yes	Variable
2-case 2	↑	↑	↑	↑	Slow progression	Yes	Variable
3-case 3	↔	↑	↑	↔	Variable	Variable	Variable
4-case 4	↓	↓	↓	↓	Variable	No	Variable
5	↔	↔	↔	↔	-	-	-

***Table 1:** In detail RNLF thickness analysis per each Sajjadi patterns and RICP progression timeline, ophthalmic and brain damage reversibility (↑: elevation, ↓: depression, ↔: normal thickness)*

Conclusion: As demonstrated in table-1 Despite all cases having elevated ICP, case 2 and 3 had RNFL thicknesses were in the normal chart and case 1 had minimal elevation in RNFL thickness and surprisingly case 4 had generalized depression.

Disclosure: Nothing to disclose.

EPO-795 | The diagnostic potential of mesosystolic notch in transcranial Doppler for reversible cerebral vasoconstriction syndrome

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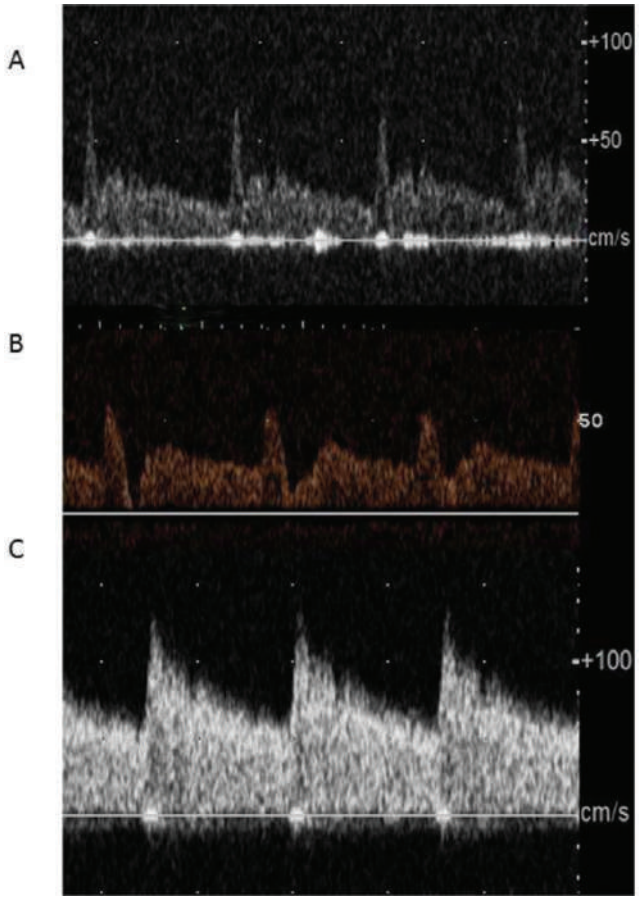
Background and Aims: Reversible Cerebral Vasoconstriction Syndrome (RCVS) poses diagnostic challenges due to its manifestation through severe headaches and dynamic vascular abnormalities, with confirmation typically requiring invasive procedures like arteriography, computed tomography angiography (CTA), or magnetic resonance angiography (MRA). The centripetal evolution of vasospasm and the absence of specific clinical criteria hinder early detection.

Methods: In our center, we systematically employed transcranial Doppler (TCD) in suspected RCVS cases, obtaining crucial information on velocity, Lindegard index, and flow turbulences. To assess TCD's diagnostic potential, we conducted a one-year survey of all TCD examinations, with a specific focus on suspected RCVS cases. A total of 191 TCD examinations were performed, including 38 on 23 patients with suspected RCVS.

Results: Within the cohort, a distinctive TCD flow pattern was identified in four cases, characterized by a mesosystolic notch reaching the baseline or elevating the pulsatility index, notably within seven days of headache onset in three patients. Despite subnormal arteriography results in two cases, only two out of the four patients received a confirmed RCVS diagnosis. TCD, however, normalized during follow-up in all four cases.



Illustrations depicting deep mesosystolic notches in two patients diagnosed with reversible cerebral vasoconstriction syndrome (A and B), contrasted with a typical cerebral artery flow pattern observed in a normal case (C).

Conclusion: This study highlights the potential diagnostic significance of a mesosystolic notch on TCD in RCVS, offering a non-invasive and easily repeatable criterion for early detection and follow-up monitoring. Although not universally conclusive, the presence of a mesosystolic notch on TCD may serve as a pathological finding associated with RCVS, providing valuable insights for early diagnosis and supporting clinical decision-making to prevent exacerbation of conditions when observed.

Disclosure: Nothing to disclose.

EPO-796 | Analgesia-related dizziness

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Background and Aims: Dizziness and vertigo are frequent symptoms reported in migraine during spontaneous and triggered attacks. Medication-Overuse Headache is a type of secondary headache that could be attributed to frequent use of analgesia in patients with an underlying headache. Our impression is patients with vestibular symptoms of unknown cause may have a migrainous biology and potentially frequent use of painkillers. Our aim was to study the relationship between analgesia and vertigo in a migraine cohort.

Methods: This study is part of the prospective cohort questionnaire-based IMPARTS at King's College Hospital. We did a cross-sectional analysis from February-September 2023. We used SPSS 28 and generalised linear models including linear and binomial (normal and logit functions, respectively), adjusted for normality as appropriate. Presence of vertigo or total score in the Situational Vertigo Questionnaire were dependent variables. Presence of triptans, NSAIDs, opioids, paracetamol and medication overuse were selected as predictors.

Results: The consumption of paracetamol was a predictor for a higher score of vertigo in patients that describe dizziness ($n=96$, $\beta=0.56$, $p=0.045$). The remaining painkillers and the presence of overuse, and none the predictors for the presence of dizziness, were significant. Medication overuse had a slightly higher percentage in the group that reported dizziness (24% vs 20%, NS).

Conclusion: The consumption of analgesia, specifically that of paracetamol, may be related with the presence of more vertiginous symptoms in those patients that report dizziness in spontaneous attacks. More power is needed to determine if those symptoms are due to "Medication-Overuse Dizziness".

Disclosure: Nothing to disclose.

EPO-797 | Extrapulmonary tuberculosis presenting as diplopia in an immunocompetent patient

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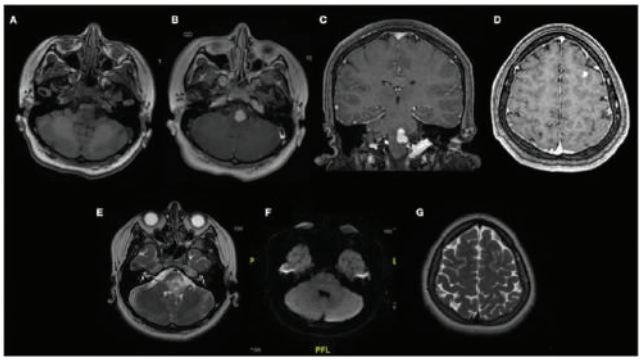
Background and Aims: Extrapulmonary tuberculosis, accounting for 10–15% of cases, can manifest in various forms, including central nervous system involvement. While meningitis is the more common presentation, it is essential to consider tuberculoma in the differential diagnosis of cerebral masses, particularly in immunocompetent individuals.

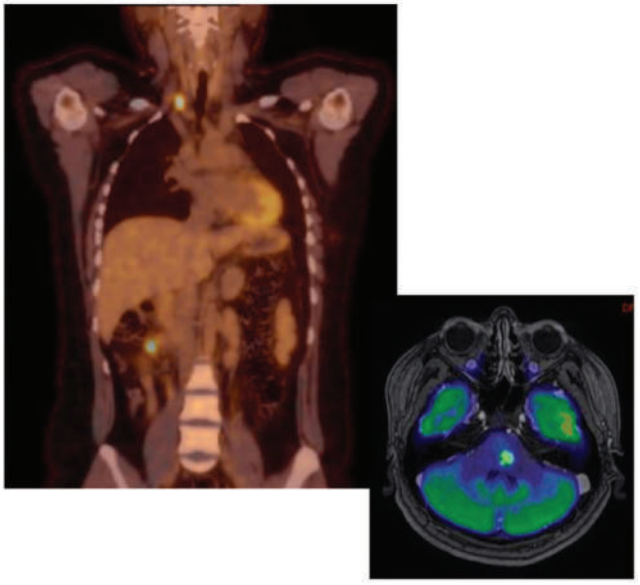
Methods: We report an 18-year-old woman with no significant medical history, presenting to the emergency department with a two-week history of binocular diplopia. Physical examination revealed left sixth cranial nerve paralysis.

Results: Blood analysis and cranial CT scan yielded no significant findings. Brain MRI identified a 1.8 cm oval lesion in the left bulbar region extending into the pons, accompanied by extensive vasogenic edema. Cerebrospinal fluid analysis showed no biochemical, cytological, or microbiological abnormalities. PET-CT revealed lesions with heightened glucose metabolism in the bulb and axillary regions. Ultrasound-guided fine-needle aspiration of lymphadenopathy demonstrated histiocytic groups on a necrotic background with cellular

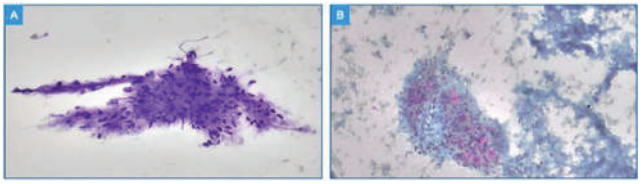
debris, indicative of necrotic granuloma. PCR on the sample tested positive for Mycobacterium Tuberculosis, and Quantiferon was also positive. Upon further inquiry, relatives reported a history of tuberculosis during pregnancy. One year of quadruple anti-tuberculous therapy led to symptom remission and lesion resolution.



Focal lesion with oval morphology, measuring 1.8 cm, located in the bulbar region with extension towards a hypointense protuberance in T1-weighted sequence (A). The lesion homogeneously enhances in T2-weighted sequences (B, C), with extensive perilesional.



Whole-body FDG-F18 PET-CT revealing a lesion in the brainstem with increased glycolytic metabolism and hypermetabolic supraclavicular right lymph nodes. Additionally, smaller nodes with metabolism are observed in the high right paratracheal region.



A. Cytological staining with Giemsa reveals a cluster of cells with broad cytoplasm and oval-shaped nuclei, suggestive of histiocytes. B. Papanicolaou-stained cytology displays a cluster of histiocytes on a necrotic background, indicative of a necrotic gr.

Conclusion: This case highlights the atypical presentation of extrapulmonary tuberculosis in an immunocompetent patient, emphasizing the importance of considering infectious etiologies in the differential diagnosis of neurological manifestations and brain masses. Early detection and treatment are critical in mitigating the associated high morbidity and mortality.

Disclosure: Nothing to disclose.

EPO-798 | The influence of virtual reality on the optokinetic nystagmus parameters in patients with stroke

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Background and Aims: Using virtual reality (VR) in patients with stroke rehabilitation is a promising way for motor and oculomotor function recovery. Pathophysiological similarity of motor disorders after stroke and oculomotor phenomena makes it possible to use the oculomotor function assessment as a non-invasive method for rehabilitation effectiveness evaluation. We aimed to assess the dynamics of optokinetic nystagmus (OKN) under the influence of VR training.

Methods: We examined oculomotor function in 23 patients, using electronystagmography, to explore vertical and horizontal OKN. We registered OKN twice in every patient: before the first training in VR, and after the last one. OKN fast and slow phase amplitude and velocity were measured and analyzed before and after training.

Results: There was a noticeable decrease in asymmetry coefficient (CA) for all horizontal OKN phases characteristics ($p=0.06$). CA of fast phase amplitude before starting VR training was 11%, at the end of the course – 5%. CA of OKN slow phase amplitude decreased from 32% to 5% ($p<0.05$). CA of OKN slow phase velocity decreased from 23% to 7%, $p<0.05$. Also, we discovered absent vertical optokinetic nystagmus (OKN) in 18/23 (78%) patients before training. In 6 patients out of 18 (33%) restoration of the vertical OKN was detected after VR training course.

Conclusion: OKN abnormalities in stroke are common. OKN registration may be used to assess the effectiveness of VR in rehabilitation. Vertical OKN restoration and eye movement asymmetry decrease after VR training demonstrates significant restorative potential of VR for oculomotor functions in patients with stroke.

Disclosure: Nothing to disclose.

EPO-799 | Effect of duration and severity of migraine on ocular structures

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Background and Aims: Migraine is a complex neurovascular disorder. The pathophysiology of the disease suggests that duration and severity lead to more ocular changes. We investigate the effect of duration and severity of migraine on macular thickness using optical coherence tomography (OCT).
Methods: A cross-sectional case-control study conducted at the Habib Bourguiba University Hospital in Sfax. This study included migraine patients and control subjects. Mean macular thickness measurements (MMT) was performed by OCT. Years of evolution were recorded. Severity was assessed using the MIDAS (Migraine Disability Assessment Scale) and MIGSEV (migraine severity scale) scores.
Results: One hundred and twenty eyes from 60 patients (60 eyes in the migraine without aura (MWoA) group and 60 eyes in the migraine with aura (MWA group) were included. Control group included 30 age and gender matched healthy participants (60 eyes). The mean duration of migraine was 12.27 ± 5.88 years. According to the MIGSEV score, migraine was considered of intermediate severity in 43.3% and 50% of MWoA and MWA patients respectively. According to the MIDAS score, migraine caused moderate disability (Grade III) in 43.3% and 26.7% of MWoA and MWA patients respectively. OCT revealed a significant reduction in both groups compared to the control group. Prolonged disease duration was not associated with decreased MT. The severity was the determinant factor of MMT.
Conclusion: Migraine has strong effect on the macular structures. The duration of the disease does not affect the MMT, while the severity has a stronger effect on MMT.
Disclosure: Nothing to disclose.

EPO-800 | The impact of the frequency and the duration of migraine attacks on macular thickness

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Background and Aims: Migraine episodically leads to the activation and sensitization of the trigeminovascular system leading to vasoconstriction not only of cerebral blood vessels but also of retinal blood vessels. We investigate the frequency and the duration of migraine attacks on macular thickness (MT) using optical coherence tomography (OCT).
Methods: This study aimed to compare MT, measured using OCT, among patients diagnosed with migraine with aura (MWA) and migraine without aura (MWoA), compared to healthy controls. The mean MT (MMT) and pericentral quadrants was measured conforming to the segmentation of the Early Treatment Diabetic Retinopathy Study.
Results: One hundred and twenty eyes from 60 patients (60 eyes in the MWoA group and 60 eyes in the MWA group) were included. The control group consisted of 30 age- and gender-matched healthy participants (60 eyes). The frequency of attacks was between one and four per month in 66.7% of MWoA and 56.7% of MWA. The frequency of attacks was between 4 and 12 hours in 50% and 76.7% of MWoA and MWA respectively. The frequency of attacks was correlated with the MMT, superior parafoveal thickness, and superior, nasal and inferior perifoveal thickness in both groups, while the attack duration does not affect the MMT.
Conclusion: Migraine patients with and without aura are prone to have damages in MT. In our study, the thinning of MT is significantly influenced by the duration of migraine attacks than their duration.
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 4

EPO-801 | Assessment of sympathetic sudomotor function in myotonic dystrophy type 1 with electrochemical skin conductance

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Background and Aims: Myotonic dystrophy type 1 (MD1) is an autosomal dominant disease caused by an expansion of CTG repeats. One of the most controversial manifestations consist of its potential autonomic involvement. The electrochemical skin conductance (ESC) is a non-invasive neurophysiologic technique, which has been considered a reliable tool in the assessment of small-fibre neuropathy caused by diabetes mellitus, hereditary ATTR amyloidosis, Fabry disease, and amyotrophic lateral sclerosis.
Methods: ESC measurements were prospectively investigated in 18 consecutive MD1 patients (8 males, 44%) with a median age of 46 years (1st–3rd IQR, 37–55), that were compared with a group of 24 age and sex-matched healthy subjects as controls. Their nerve conduction studies were normal and none of the individuals had a previous history of diabetes or was taking any anticholinergic medication.
Results: ESC values from MD1 patients did not differ from controls: hands [74 μS (1st–3rd IQR, 67–78) vs 79 μS (1st–3rd IQR, 67–85, $p = 0.27$)] and feet [81 μS (1st–3rd IQR, 77–85) vs 81 μS (1st–3rd IQR, 78–85, $p = 0.87$]. No significant correlation was found between hands and feet ECS measurements and the disease duration or

number of CTG repeats, as well as between feet ESC and anterior tibialis weakness ($p > 0.05$).

Conclusion: This innovative technique does not confirm the potential involvement of cholinergic unmyelinated postganglionic sympathetic C fibres in patients with DM1. An altered function of the target organ due to smooth muscle compromise seems to be a possible explanation for those manifestations rather than the primary involvement of the autonomic nervous system.

Disclosure: Nothing to disclose.

EPO-802 | Identification of novel plasma biomarkers for myasthenia gravis prognostication

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Background and Aims: Myasthenia Gravis (MG) is an antibody-mediated neurological disease characterized by potentially life-threatening muscular fatigability. Currently, there are no established prognostic biomarkers predicting outcomes, and the understanding of the underlying immunopathogenesis is limited.

Methods: Plasma from 60 newly diagnosed MG patients and 51 age- and sex-matched healthy controls (HCs) were assayed on the Olink EXPLORE 1536 panel, measuring 1460 pre-selected soluble proteins. Protein expression was calculated as relative NPX values, and corrected for age, sex, and sample handling. Groupwise expression differences were calculated using post-hoc ANOVA test. Prognostic power was determined using survival analyses investigating time to remission (defined as quantitative MG score, QMG, ≤2 and no rescue treatment within 3 months).

Results: Baseline characteristics of patients were: Average age 59.5 years (SD 18.6), 36.7% females, 88.3% AChR+, QMG 5.9 (SD 4.4) and 86.7% were untreated. Significant differences between MG patients and HC were observed in nine proteins, with the strongest association observed for oligodendrocyte myelin glycoprotein (OMG; adj. $p < 0.0001$), which aside the nervous system also is expressed in leukocytes. Four of the nine proteins were associated to the STAT1/3 pathway. Altered expression of proteins linked to T-cell activation and migration were significantly associated with earlier remission within one year from sampling, including increased CCL27 and ITGAV expression, and decreased CLEC4D expression (all adj. $p = 0.033$).

Conclusion: We observed plasma proteins differentially expressed between new-onset MG and matched HC. Additionally, we identified proteins linked to T-cell activation and migration as potential biomarkers of medium-term disease remission.

Disclosure: SB has received in non-restricted research grants from UCB Pharma and Janssen, not related to this study. FP has received research grants from Janssen, Merck KGaA and UCB, and fees for serving on DMC in clinical trials with Chugai, Lundbeck and Roche, and preparation of expert witness statement for Novartis.

EPO-803 | Sensitivity to change and meaningful change thresholds of the quick motor function test (QMFT) in Pompe disease

N. van der Beek[1]; A. Sjöström-Bujacz[2]; C. Daskalopoulou[3]; D. Papageorgiou[3]; K. An Haack[4]; V. Gallego[5]; P. DasMahapatra[5]; N. Thibault[5]; A. Zaher[6]; N. Armstrong[5]; M. Kruijshaar[1]; A. van der Ploeg[1]

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Background and Aims: QMFT is a 16-item validated scale for assessing motor function in Pompe disease. Objectives were to determine whether QMFT was sensitive to changes in patient's status and inform on meaningful change thresholds (MCTs) for within-patient change.

Methods: Using blinded, pooled data from COMET (NCT02782741) study of late-onset Pompe disease (LOPD), sensitivity to change was examined from baseline to Week 49. Mean QMFT total score was investigated among those who improved, worsened, and remained unchanged based on other collected and theoretically related clinical outcomes assessments (COAs) via Kruskal-Wallis analysis. Spearman correlations of changes between QMFT and COAs were also examined. CMT for within-patient change was estimated via anchor approaches, based on anchors with appropriate correlations (>0.371 corresponding to d = 0.8), and distribution approaches (0.5 standard deviation [SD] and standard error of measurement [SEM] to estimate a lower bound; minimal detectable change [MDC] for upper bound).

Results: Sensitivity to change was indicated, due to the expected pattern between changes in QMFT and most COAs (Table 1) and high correlations between QMFT and the COAs (Table 2). Summary statistics for change scores for improvement ranged from mean/median of 3.0–8.0 points (Table 3). Distribution results were 0.5 SD = 5.16 points; SEM = 3.94 points; and MDC = 10.92 points. Considering the above, the within-patient MCT for improvement ranged from 5.16 to 10.92 points.

Table 1: Sensitivity to change: Mean change from baseline to Week 49 for Quick Motor Function Test (QMFT) total score by clinical outcomes assessments

Anchor/Clinical Outcomes Assessments	Anchor group	N	Least Squares Means[1]	Standard Error	95% Confidence Interval	*P*-value
12-Item Short Form Health Survey Version 2 – Physical Health Component Summary	Improvement *(change≤6)*	23	5.99	2.43	[1.15–10.83]	0.044
	No change *(-6<change<6)*	55	3.65	2.26	[-0.84–8.15]	-
	Worsening *(change≥6)*	8	2.34	2.78	[-3.19–7.87]	-
Patient Global Impression of Change Subscales*						
Ability to perform daily activities	Improvement	47	4.61	2.27	[0.08–9.13]	0.051
	No change	28	3.41	2.43	[-1.43–8.25]	-
	Worsening	8	0.01	2.77	[-5.52–5.53]	-
Disease-related symptoms	Improvement	56	4.50	2.26	[0.00–8.99]	0.032
	No change	19	3.32	2.48	[-1.62–8.26]	-
	Worsening	8	-0.17	2.74	[-5.63–5.29]	-
Mobility (walking, running, climbing stairs)	Improvement	45	4.73	2.28	[0.19–9.27]	0.020
	No change	26	2.21	2.44	[-2.65–7.08]	-
	Worsening	12	2.04	2.61	[-3.15–7.23]	-

*"Improvement" - "Somewhat/Moderately/A great deal better. No change - "No change." Worsening - "Somewhat/Moderately/A great deal worse."
[1]Models included anchor groups, baseline QMFT, randomization stratification factors, sex, age, and country.

Table 2: Sensitivity to change: Correlations of change from baseline to Week 49 between Quick Motor Function Test (QMFT) total score and other clinical outcomes assessments

Clinical Outcomes Assessments	N	r
PDIS Difficulty Performing Activities domain	**88**	**-0.394**
SF-12 v2 physical component summary (PCS)	88	0.299
Gait, Stair, Gower's Maneuver, and Chair Composite Functional Assessment (GSGC)		
Time to walk 10 meters (Gait)	88	-0.234
Time to climb 4 stairs (Stair)	88	-0.137
Time to stand from sitting on the floor (Gower's Maneuver)	88	-0.350
Time to stand from sitting position in a chair (Chair)	88	-0.158
Total score	88	-0.240
Patient Global Impression of Change		
Ability to perform daily activities	88	0.368
Disease-related symptoms	88	0.309
Mobility (walking, running, climbing stairs)	88	**0.382**

PDIS, Pompe Disease Impact Scale; SF-12 v2, 12-Item Short-Form Health Survey version 2; 6MWT, 6-Minute Walk Test; r, Spearman correlation coefficient is presented; bolded correlations met criteria for the estimation of meaningful change threshold.

Table 3: Summary statistics for QMFT total change from baseline to Week 49 by anchor categories needed for the estimation of meaningful change threshold for QMFT

Anchor	Anchor group	N	Mean	Standard Deviation	Q1	Median	Q3	95% Confidence Interval of the Mean
Pompe Disease Impact Score - Difficulty Performing Activities	Improvement (change≤-1)	8	7.25	5.34	2.00	8.00	12.50	[2.79–11.71]
	No change (-1<change<1)	36	2.25	4.35	-0.50	2.00	4.00	[0.78–3.72]
	Worsening (change≥1)	1	-1.00	NC	-1.00	-1.00	-1.00	NC
Patient Global Impression of Change Subscales*								
Ability to perform daily activities	Improvement	47	4.23	5.09	0.00	4.00	8.00	[2.74–5.73]
	No change	28	2.21	4.09	-0.50	1.50	5.50	[0.63–3.80]
	Worsening	8	0.50	2.73	-2.00	0.50	3.00	[-1.78–2.78]
Mobility (walking, running, climbing stairs)	Improvement	45	4.49	4.68	1.00	4.00	8.00	[3.08–5.90]
	No change	26	1.50	4.24	-1.00	1.00	4.00	[-0.21–3.21]
	Worsening	12	2.00	4.75	-1.00	1.00	2.50	[-1.02–5.02]

"Improvement meant "Somewhat better," "Moderately better," or "A great deal better." "No change meant "No change." "Worsening meant "Somewhat worse," "Moderately worse," or "A great deal worse."

Conclusion: QMFT appeared sensitive to change in ambulatory LOPD patients. MCTs for within-person improvement can be used to interpret change in this population. However, further investigation is needed among more patients across the spectrum of disease severity.

Disclosure: The study was funded by Sanofi. Nadine van der Beek has received consulting fees, speaking fees, and fees for attending meetings and advisory boards by Sanofi. Nicole Armstrong, Kristina An Haack, Víctor Gallego, Pronabesh DasMahapatra, Nathan Thibault, and Atef Zaher are employees of Sanofi and may own Sanofi stock. Aleksandra Sjöström-Bujacz, Christina Daskalopoulou and Dimitrios-Paraskevas Papageorgiou are employees of IQVIA and serve as consultants to Sanofi. Michelle Kruijshaar declares no conflicts of interest. Ans van der Ploeg received funding for research, clinical trials, and advisory fees from Sanofi-Genzyme, Amicus Therapeutics, BioMarin, Ultragenyx, Sarepta, Audentes, and Spark Therapeutics working on enzyme replacement therapy or next-generation therapies in the field of Pompe disease, other lysosomal storage diseases, or neuro-muscular disorders, under agreements with the Erasmus MC University Medical Center and the relevant industry.

EPO-804 | Efficacy, safety, and factors predicting response in Rituximab therapy for generalised myasthenia gravis

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Background and Aims: Rituximab (RTX) is an anti CD20 monoclonal antibody approved for use in refractory generalised Myasthenia Gravis (gMG). We aimed to assess the efficacy, safety, and factors predicting response in RTX therapy for gMG.

Methods: A retrospective observational study was conducted at our centre. Case notes of patients with gMG treated with rituximab from 2019 to 2023 were analysed. Positive outcomes were recorded if, at six months a) a reduction of at least 2 points in MG Activities of Daily Living (ADL) or 3 points in MG composite scale occurred, or b) if at one year – treatment escalation was not required, or c) if either prednisolone or intravenous immunoglobulin were weaned.

Results: Of the 32 patients included in the study, 26 (81.2%) were female and 6 were male. Eighteen (56.2%) were acetylcholine receptor antibody positive (AchR) and thirteen were muscle-specific kinase (MuSK) antibody positive. Mean age at start of treatment was 46.8 years (range 25–76) and mean disease duration was 13.2 (±10) (range 1 to 47). Patients had previously received an average of 4 immunosuppressive agents (range 1–7). Twenty (62.5%) patients responded to RTX. 76.9% (10/13) of the MuSK positive group responded compared to 50% (9/18) of the AchR positive cohort. Age and thymectomy were unrelated to outcomes while time to treatment of less than 10 years was correlated to positive outcome. A multi-morbid patient died of COVID-19 two months after treatment.

Conclusion: Rituximab is effective in MuSK gMG but variably effective in AchR gMG.

Disclosure: 1. Nothing to disclose 2. Has received travel support from UCB and been on an advisory board for Alexion 3. Nothing to disclose 4. Nothing to disclose 5. Nothing to disclose 6. Has received speakers fees and travel support from Argenx and served on an advisory board for UCB.

EPO-805 | Abstract withdrawn

EPO-806 | Patient characteristics and exacerbations in incident myasthenia gravis: Analysis of US commercial insurance claims data

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Background and Aims: The incident myasthenia gravis (MG) population in the United States (US) is not well-characterized. Many patients experience exacerbations despite the use of conventional immunosuppressive treatments; however, this has not been studied in detail.

Methods: This retrospective analysis used Inovalon claims data to estimate the incidence of MG among adults aged ≥18 years in the US for 2019. Patient characteristics, treatment utilization patterns, and exacerbation frequency were assessed in the incident population.

Results: We identified 1,372 incident patients with MG, corresponding to a raw incidence rate of 4.9 per 100,000 persons, and an adjusted incidence of 5.2 per 100,000 after extrapolating to the US population. More than half (56.9%) of the patients were women, and the median age for women (58 years) was lower than for men (62 years). Hypertension was the most common comorbidity,

occurring in 50.4% of patients. Among 920 patients who received medication, 773 (84.0%) received acetylcholinesterase inhibitors. Among 1,204 incident patients with ≥1 year of continuous follow-up, 387 (32.1%) experienced exacerbations, with the majority experiencing ≥3 exacerbations. Median (interquartile range [IQR]) time to first exacerbation was 7 (60) days, and in patients with >1 exacerbation, the median (IQR) time from the first to subsequent exacerbation was 25 (42) days.

Patient characteristic	Incident cohort (N=1,372)
Women, n (%)	781 (56.9)
Median age (IQR), years	
Women	58 (25)
Men	62 (17)
Comorbidities, n (%)[a]	
Hypertension	692 (50.4)
Hyperlipidemia	410 (29.9)
Type 2 diabetes	307 (22.4)
Gastroesophageal reflux disease	284 (20.7)
Hypothyroidism	250 (18.2)
Chronic pain	241 (17.6)
Vitamin D deficiency	194 (14.1)
Anxiety disorder	167 (12.2)
Obesity	158 (11.5)
Obstructive sleep apnea	183 (13.3)
Geographic region	
Northeast	255 (18.6)
South	472 (34.4)
Midwest	346 (25.2)
West	280 (20.4)
Puerto Rico	18 (1.3)
Unknown	1 (<0.1)

[a]Patients may have >1 comorbidity. IQR, interquartile range.

TABLE 1 Demographics and baseline characteristics of the incident population.

	Incident cohort (N=1,372)
Total unique patients who received treatment in 2019	920 (67.1)
Medication use among those who were treated	
Acetylcholinesterase inhibitors	773 (84.0)
Neostigmine	10 (1.1)
Pyridostigmine	767 (83.4)
Immunosuppressants	204 (22.2)
Azathioprine	93 (10.1)
Cyclophosphamide	3 (0.3)
Cyclosporine	1 (0.1)
Methotrexate	15 (1.6)
Mycophenolate	107 (11.6)
Tacrolimus	4 (0.4)
Oral steroids	538 (58.5)
Prednisone	538 (58.5)
Biologics	130 (14.1)
Eculizumab	8 (0.9)
Immunoglobulin	109 (11.9)
Ravulizumab	0
Rituximab	17 (1.9)
Tocilizumab	0
Plasmapheresis	30 (3.3)

[a]Patients may have been treated with multiple medications.

TABLE 2 Treatment utilization in the incident population.

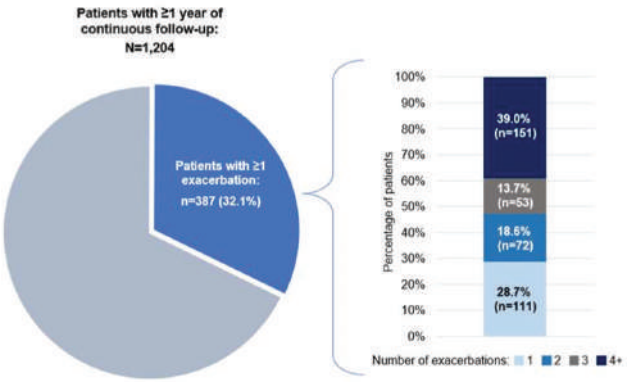

FIGURE 1 Number of MG exacerbations in incident patients with ≥1 year of follow-up.

Conclusion: The estimated incidence of MG among adults in the US was 5.2 per 100,000 persons. Approximately one-third of patients experienced exacerbations within a year, with >50% of those patients having ≥3 exacerbations. These findings highlight the unmet need for targeted therapies that provide sustained symptom control.
Disclosure: This analysis was funded by Immunovant, Inc. PMO is an employee of Immunovant, Inc. JA has nothing to disclose. JW is an employee of Roivant Sciences, Ltd. BV is an employee of Roivant Sciences, Ltd. JS is an employee of Immunovant, Inc. LAMW is an employee of Immunovant, Inc.

EPO-807 | Characterisation of patients with myasthenia gravis in France: A cluster analysis of patients from the SPOON study

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Background and Aims: The SPOON study was an online patient survey about living with myasthenia gravis (MG). The present analysis aimed to identify potential patient subgroups with different disease characteristics and experiences, and to document their aspirations about living with MG.
Methods: Cluster analysis was performed using ascending hierarchical clustering. The characteristics of each cluster were described. Differences in characteristics between clusters were tested using the χ^2 or Student's *t*-test as appropriate.
Results: The cluster analysis included 255 participants. Three clusters were identified, which accounted for 52.5% of the inertia in the

sample (Figure 1). Characteristics of the clusters are described in Table 1. Cluster 1 ($n=83$; 32.5%), mostly comprising women (86%) diagnosed at an older age than cluster 3, appears to be the one most affected by MG, with 78% of the patients with current symptom exacerbation and a heavier burden of disease. Cluster 2 ($n=44$; 17.3%) mostly comprises men diagnosed later in life with a lower disease burden. Cluster 3 is the largest cluster ($n=128$; 50.2%) and is principally women (94%) diagnosed at a younger age than cluster 1, with stable disease (96.9% without current symptom exacerbation), a moderate disease burden and relatively low psychological burden. Aspirations about living with MG are similar across clusters: for all clusters, the main aspiration is to be more physically active (Figure 2).

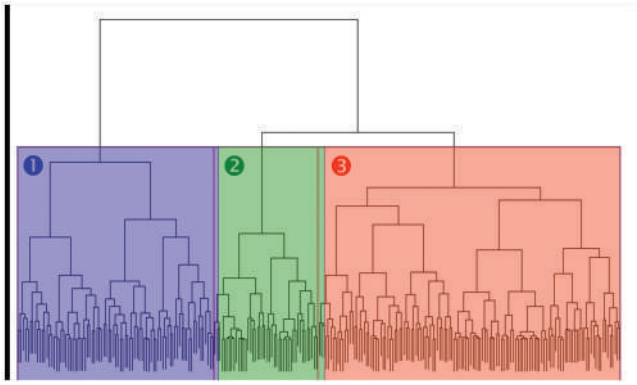

FIGURE 1 Cluster dendrogram obtained after hierarchical ascending classification.

	Cluster 1 n=83	Cluster 2 n=44	Cluster 3 n=128	P value
Gender : women/men (n, %)	68 (**86%**) / 11 (14%)	3 (7%) / 40 (**93%**)	116 (**94%**) / 8 (6%)	**<0.001**
Age at diagnosis - Mean (SD) **(years)**	42 (15)	55 (15)	36 (18)	**<0.001**
Time since diagnosis: ≤ 3 years (n, %)	30 (38%)	10 (23.3%)	29 (23.2%)	0.055
Current symptom exacerbation(n, %)	64 (**78%**)	1 (2.3%)	4 (3.2%)	**<0.001**
HADS Anxiety scale (21 points)				**<0.001**
Mean (SD)	9.5 (4.6)	5.6 (3.4)	8.3 (3.9)	
Probable anxiety (score ≥11), n (%)	37 (**45.6%**)	5 (11.6%)	31 (24.8%)	
HADS Depression scale (/21 points)				**<0.001**
Mean (SD)	9.7 (3.7)	5.6 (3.7)	6.4 (3.5)	
Probable depression (score ≥11), n (%)	37 (**45.7%**)	3 (7%)	18 (14.5%)	
MG-ADL profile (/24 points) - Mean (SD)	**8.3** (3.4)	3.7 (3)	4.6 (3.2)	**<0.001**
MG-QoL-15R scale (/30 points) - Mean (SD)	**18.3** (5)	8.7 (5.6)	12.4 (6.2)	**<0.001**
Disease acceptability (PASS question) (yes: n(%))	8 (9.8%)	36 (**83.7%**)	84 (**66.7%**)	**<0.001**
Neuro-QoL fatigue item bank (/100 points)				
Mean (SD)	**58.1** (6.4)	49.3 (9.0)	52.2 (7.8)	**<0.001**
No problem (t-score ≤45), n (%)	3 (3.8%)	14 (**32.6%**)	21 (16.7%)	
Mild problems (t-score 46 - 55), n (%)	14 (17.7%)	18 (41.9%)	55 (**44.3%**)	
Moderate problems (t-score 56-65), n (%)	55 (**69.6%**)	10 (23.3%)	47 (37.9%)	
Severe problems (t-score >65), n (%)	7 (8.9%)	1 (2.3%)	1 (0.8%)	

TABLE 1 Characteristics of the clusters.

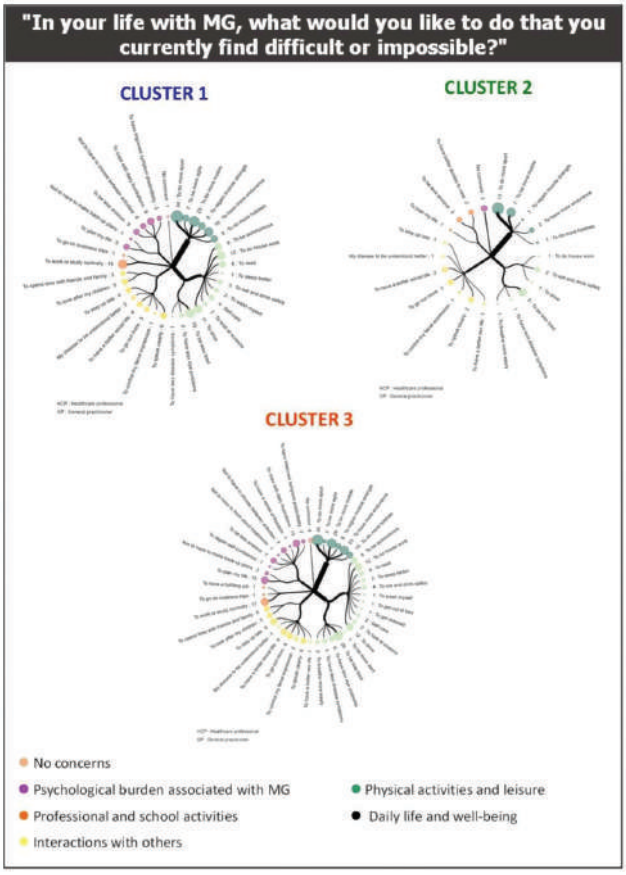

FIGURE 2 Domains and dimensions of patients' aspiration with respect to MG.

Conclusion: Three clusters were identified defined by gender and disease stage. Regardless of cluster, patients' aspirations were similar, centered on physical activity.

Disclosure: This study was funded by UCB Pharma. A Crochard, P-E Villy and A Richard are employees of UCB Pharma. Other authors declare no conflict of interest.

EPO-808 | Long-term safety and efficacy of subcutaneous efgartigimod PH20: Interim results of the ADAPT-SC+ trial

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Background and Aims: Efgartigimod, a human IgG1 antibody Fc-fragment, reduces IgG levels through neonatal Fc receptor blockade. In the ADAPT-SC study, subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) was shown to be noninferior in total immunoglobulin G reduction compared with intravenous (IV) efgartigimod. Participants completing ADAPT-SC or enrolled in ADAPT+ were eligible for the ongoing ADAPT-SC+ open-label extension, which sought to evaluate long-term safety, tolerability, and efficacy of efgartigimod PH20 SC in participants with gMG.

Methods: Efgartigimod PH20 SC 1000 mg was administered in cycles of 4 once-weekly injections. Subsequent cycles were initiated ≥28 days from the last dose based on clinical evaluation. MG-ADL score assessed clinical efficacy.

Results: Through December 2022, 179 participants received ≥1 dose of efgartigimod PH20 SC, with a mean (SD) treatment and follow-up time of 395 (116) days, resulting in 193 participant-years of follow-up. Treatment-emergent adverse events (TEAEs) were predominantly mild/moderate. The most frequent TEAEs (Table 1) were injection site erythema (29.1%), COVID-19 (22.3%), and headache (20.1%). TEAEs, serious TEAEs, and infections did not increase with subsequent cycles through Cycle 9 (Figure 1). Improvement from cycle baseline (mean [SE] improvement at Week 4) was observed in Cycle 1 in MG-ADL total score (−4.0 [0.24]) with consistent and repeatable improvements seen through Cycle 9 (Figure 2), and the number of participants achieving minimal symptom expression (MSE) at any time in each cycle ranged from 35.5% to 43.5%.

	Efgartigimod PH20 SC (n=179; PYFU=193.4)	
	ER[a]	n (%)
Any TEAE, n (%)	9.0	152 (84.9)
Any TEAE grade ≥3, n (%)	0.4	36 (20.1)
Any serious TEAE, n (%)	0.3	33 (18.4)
Any injection site reaction, n (%)	3.2	82 (45.8)
Any infection, n (%)	1.0	91 (50.8)
Fatal event[b], n (%)	<0.1	4 (2.2)
Discontinued study treatment owing to TEAEs[c], n (%)	<0.1	4 (2.2)
Most commonly observed TEAEs[d], n (%)		
Injection site erythema	1.7	52 (29.1)
COVID-19	0.2	40 (22.3)
Headache	0.6	36 (20.1)
Nasopharyngitis	0.2	28 (15.6)
Diarrhea	0.2	24 (13.4)
Injection site pain	0.2	21 (11.7)
Injection site pruritus	0.2	19 (10.6)
Injection site bruising	0.2	18 (10.1)

ER, event rate; MG, myasthenia gravis; PYFU, participant-years of follow-up; TEAE, treatment-emergent adverse event.
[a]ER was calculated as number of events per total PYFU. [b]Fatal events (metastatic renal cell cancer, cardiac arrest, pulmonary mass, and COVID-19/respiratory failure) were not related to efgartigimod PH20 SC treatment, as determined by investigators. [c]Treatment discontinuation due to metastatic renal cell cancer (Cycle 1, death), cardiac arrest (Cycle 2, death), COVID-19/respiratory failure (Cycle 3, death), and MG crisis (Cycle 1). [d]Most frequent TEAEs occurring in >10% of participants receiving efgartigimod PH20 SC.

TABLE 1 Summary of TEAEs.

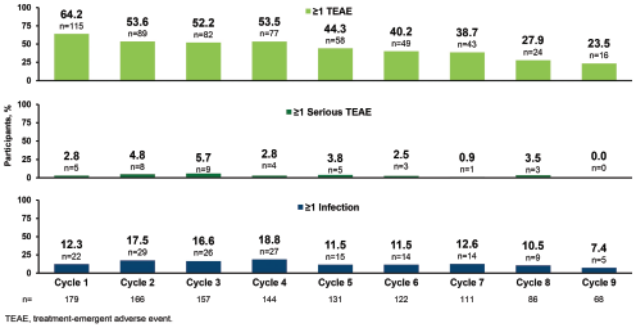

FIGURE 1 TEAEs by Cycle.

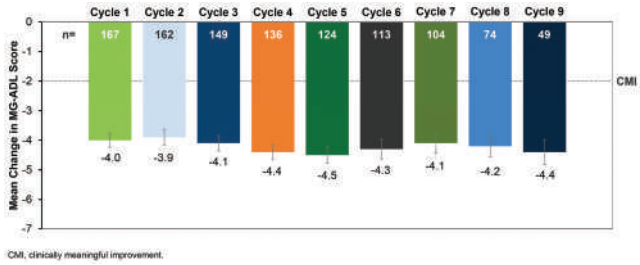

FIGURE 2 Mean Change in MG-ADL From Study Baseline at Week 4.

Conclusion: Treatment with multiple cycles of efgartigimod PH20 SC was well tolerated and efficacious, consistent with efgartigimod IV in ADAPT/ADAPT+.

Disclosure: Multiple relationships financial and non-financial nature for authors JLDB, JFH, YL, TV, DK, SS, BVH, JP, MH, KU, FS, HW, RM, and ECV stated at point of presentation.

EPO-809 | BCMA-targeted CAR T cell therapy in the management of refractory myasthenia gravis

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Background and Aims: Chimeric antigen receptor (CAR) T cell therapy shown promise in treating hematologic malignancies and autoimmune diseases. This study reports an ongoing Investigator-initiated trial (IIT) involving B-cell maturation antigen (BCMA)-targeted CAR T therapy for refractory myasthenia gravis (MG) patients with anti-acetylcholine receptor (AChR) antibodies positive.

Methods: The study enrolled seven patients (3 females and 4 males) with a median quantitative myasthenia gravis score (QMGS) of 15 (range: 11–27), a median age of 50 years (range: 24–64), and a median disease duration of 4 years (range: 1.25–11). After lymphodepletion, autologous BCMA-targeting CAR T cells were administered as a single infusion at doses ranging from 1.7×105/kg to 10×105/kg.

Results: The results showed all patients developed grade 1 or 2 Cytokine Release Syndrome (CRS), and no neurotoxicity syndrome was observed. The most common adverse events of grade 3 or higher were hematologic toxicity. One patient was infected with the COVID-19 virus but recovered rapidly after supportive therapies. The expansion of CAR T cells in vivo was associated with clinical symptom improvement and normalization of laboratory parameters, including serum anti-AChR IgG. MG syndromes remission was achieved in all seven patients after 3 months, and the median QMGS decreased to 5 (range: 0–11) from 15 at baseline (range: 11–27). During a median follow-up of 4 months (range: 3–10 months), drug-free remission was maintained after CAR T cell administration.

Conclusion: In conclusion, the study demonstrated that BCMA-targeted CAR T therapy is a safe and effective treatment for refractory MG.

Disclosure: Nothing to disclose.

EPO-810 | Late-onset Pompe disease: Patient journeys from symptom onset to diagnosis

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Background and Aims: Pompe disease is a rare neuromuscular disorder caused by deficiency of acid alpha-glucosidase, leading to lysosomal glycogen accumulation and consequential progressive muscle weakness, respiratory dysfunction, and functional disabilities. Pompe disease has a broad clinical spectrum in terms of affected body systems, symptom onset age, and progression rate. We aim to describe the path from symptoms onset to diagnosis in late-onset Pompe disease (LOPD) to gain a better understanding of the diagnostic journey.

Methods: Data about demographic, clinical pre-diagnosis symptoms, and diagnostic experience were collected by independent researchers during a 30-minute pre-interview survey and 60-minute telephone interview with patients or their caregivers.

Results: 56 patients with Pompe disease were interviewed; 51 had LOPD. Main demographic/clinical characteristics are given in Table 1. Frequencies of pre-diagnosis symptoms are summarised in Figure 1; the most frequent was lower limb weakness (86% [44/51] patients). Patients with earlier symptoms in life received a quicker diagnosis than older ones; 75% (9/12) aged 1–9 years were diagnosed within 2 years of symptoms versus 36% (14/39) aged ≥10 years. Most patients (66% [33/51]) were referred by healthcare professionals to neuromuscular specialists/neurologists with a final diagnosis made mainly by neuromuscular specialists (39% [20/51]) and neurologists (31% [16/51]) often as part of a team of physicians (Figure 2). Key tests leading to diagnosis: muscle biopsy ($n=18$), genetic testing ($n=12$), blood panel ($n=8$), dry blood spots ($n=5$), liver biopsy ($n=1$). Around one-third of patients were misdiagnosed before Pompe disease was confirmed.

	Patients with LOPD (N=51)
Males/females, n (%)	23 (45) / 28 (55)
Region, n (%)	
Europe	22 (43)
Japan–Asia Pacific	11 (22)
United States	10 (20)
South America	5 (10)
Middle East	3 (6)
Age at interview, years	
Mean (SD)	39 (18.1)
Median (min, max)	38 (4, 67)
Age group 1–9 years	
Age at symptom onset, years (n=12)	
Mean (SD)	2.6 (2.5)
Median (min, max)	2 (0, 9)
Age at diagnosis, years (n=10)	
Mean (SD)	3.9 (2.9)
Median (min, max)	2.5 (1, 9)
Age group ≥10 years	
Age at symptom onset, years (n=39)	
Mean (SD)	26 (13.3)
Median (min, max)	23 (10, 50)
Age at diagnosis, years (n=41)	
Mean (SD)	34 (12.6)
Median (min, max)	33 (10, 62)
SD, standard deviation	

TABLE 1 Demographic and clinical characteristics of patients with LOPD.

FIGURE 1 Frequency of pre-diagnosis symptoms of Pompe disease mentioned by patients at interview.

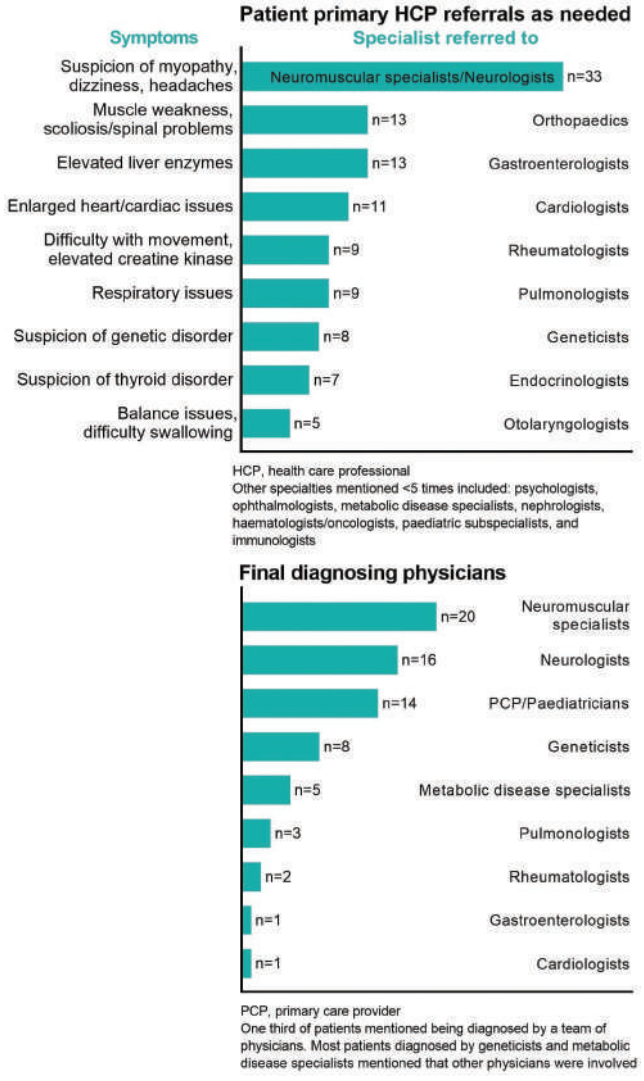

FIGURE 2 Diagnosis referrals in patients with LOPD and final diagnosing physicians.

Conclusion: These findings underline the need to raise worldwide awareness of Pompe disease symptoms and improve diagnostic pathways.

Disclosure: Funding: Sanofi Rafael Jenaro Martínez Marín has received travel expenses from Sanofi. Andrew Doerr and Rebecca Gould are employees of Fulcrum Research Group, which was contracted by Sanofi to conduct the research for this study. Jennifer Heuterman and Pamela Rajasekhar are employees of Sanofi and hold stock/stock options in Sanofi.

EPO-811 | Near fiber segment jitter in the diagnosis of myasthenia gravis

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Background and Aims: Near fiber EMG (NFEMG) focuses on the activity of muscle fibers close to the electrode, can be applied to routinely acquired needle EMG, and offers the ability to semi-automatically assess neuromuscular junction stability in a conceptually similar manner to single fiber EMG (SFEMG).

Methods: NFEMG was blindly applied to SFEMG recordings of 50 patients tested at BIDMC in the prior 18 months. In those without myopathy or neuropathy, we performed 10-fold cross validation using two E-Ref-based NFEMG jitter value thresholds to establish the performance of several different criteria for classifying patients as MG or non-MG, compared to clinical diagnosis, in each of the 10 testing sets as well as the full cohort.

Results: 12 of 50 patients were diagnosed clinically as MG after SFEMG testing (3 diagnosed as myopathy, 1 as neuropathy). Of those without myopathy or neuropathy, the sensitivity for detecting MG using NFEMG was 100% while the specificity ranged from 89% to 95% (mean of 90%). When testing on the whole cohort, sensitivity and specificity were 100% and 94%.

Conclusion: NFEMG performs well in diagnosing MG. Due to the ease of application to routine EMG and the minimal need for training, NFEMG may represent an effective screen prior to referring for SFEMG or as a viable alternative diagnostic test when SFEMG is not available, potentially addressing a significant global healthcare disparity.

Disclosure: Nothing to disclose.

EPO-812 | Natural history of distal and myofibrillar myopathies assessed by clinical and technological outcome measures (Dista-Myo)

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Background and Aims: Dista-Myo is an international multicentre longitudinal study that integrates validated motor function scales with novel technological tools for gait and strength assessment in patients with distal (DM) and myofibrillar myopathies (MFM). The study aims to gather natural history data and build a new toolbox for the evaluation of these disorders.

Methods: Patients were assessed by Motor Function Measure (MFM-32), timed tests and dexterity tests as functional outcome measures; technological outcome measures included Myotools for muscle strength evaluation, and wireless insoles for gait analysis.

Results: Forty-seven patients were assessed at baseline. Ninety-six% showed reduced MFM-32 scores, while 65% underperformed on 6MWT. Most patients presented impaired distal muscle strength (80% at ankle dorsiflexion, 92% at ankle plantar-flexion, 50% at grip and pinch level). Metrics extracted from gait analysis significantly differed between patients and controls and correlated with distal muscle strength and functional scores. Preliminary analysis of the changes at 12 months showed a mild but significant decrease in MFM-32 scores and MyoTools strength values compared to baseline, with a moderate responsiveness.

Conclusion: Baseline results showed heterogeneous impairment in the global motor function in our cohort of patients with DM and MFM. Distal muscle weakness and gait ability were efficiently captured by the combination of functional and digital outcome measures. MyoTools are promising digital tools able to define the extent of weakness even in severely affected patients and to capture changes in longitudinal studies.

Disclosure: This work has been funded by AFM Telethon (Grant to GT #23493).

EPO-813 | Assessing the suitability of the Neuro-QoL fatigue to evaluate fatigue in patients living with myasthenia gravis

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Janssen Global Services, LLC

Background and Aims: Generalized myasthenia gravis (gMG) is a rare, chronic, autoantibody-mediated neuromuscular disease characterized by fatigable muscle weakness. The objectives of this research were to identify an appropriate patient-reported outcome (PRO) measure to assess fatigue in patients living with gMG and to conduct patient interviews to evaluate the content validity of the measure.

Methods: A literature review identified the Neuro-QoL Fatigue as a suitable candidate PRO to assess fatigue in gMG. Twenty-three interviews were conducted with adults living with gMG. All participants were recruited from the United States via research partners following IRB approval. Each interview explored the symptoms and impacts of gMG on participants' daily lives. The last 8 interviews included debriefing of the Neuro-QoL Fatigue to determine its appropriateness for use in gMG. Interviews were recorded and transcribed verbatim, and data were thematically analyzed.

Results: All participants reported experiencing fatigue as part of their experience with gMG and that fatigue impacted their ability to carry out daily life activities and participation limitations. Among those asked to provide bothersome ratings, 80% ($n = 12$ of 15) reported that fatigue was their most bothersome symptom. The debriefing exercise demonstrated that nearly all participants interpreted the Neuro-QoL Fatigue instructions, items, and recall period as intended.

Table 1. Interview participant demographic characteristics (n=23)

Characteristic	Interview sample (n=23)
Age, mean years (median, range)	53.4 (51, 29-81)
Duration of MG diagnosis mean years (median, range)	9.7 (6, 1.2 -62)
Sex n (%)	
Male	10 (43.5)
Female	13 (56.5)
Race/ethnicity n (%)	
African American	2 (8.7)
Caucasian	19 (82.6)
Hispanic	2 (8.7)
Education n (%)	
High school diploma	3 (13.0)
Some college	5 (21.7)
Technical or Associate's degree	3 (13.0)
College degree	8 (34.8)
Professional or advanced degree	4 (17.4)
Employment n (%)	
Employed full-time	4 (17.4)
Retired	7 (30.4)
Unable to work due to disability	11 (47.8)
Unemployed	1 (4.3)
Frequently reported symptoms n (%)	
Fatigue, tiredness, exhaustion, weakness	23 (100.0)
Double vision	13 (56.5)
Difficulty chewing/swallowing	8 (34.8)
Difficulty breathing/shortness of breath	6 (26.1)
Droopy eyelid	6 (26.1)
Vocal changes	3 (13.0)
Pain	2 (8.7)

MG Research Participant Characteristics.

Table 2. Neuro-QoL Fatigue Cognitive Debriefing Item-Level Insights (n=8)

Item concept	Item interpreted as intended	Reported as relevant to the patient's experience with gMG
	n (%)	
Felt exhausted	8 (100)	8 (100)
No energy	8 (100)	8 (100)
Felt fatigued	8 (100)	8 (100)
Too tired to do chores	8 (100)	8 (100)
Too tired to leave the house	8 (100)	8 (100)
Frustrated by being too tired	8 (100)	8 (100)
Felt tired	8 (100)	8 (100)
Limited social activity because too tired	8 (100)	8 (100)
Needed help doing usual activities because of fatigue	8 (100)	8 (100)
Sleep during the day	8 (100)	8 (100)
Trouble starting things	8 (100)	7 (87.5)
Trouble finishing things	8 (100)	8 (100)
Too tired to walk	8 (100)	8 (100)
Too tired to eat	8 (100)	8 (100)
Needed to rest during the day	8 (100)	8 (100)
Felt weak all over	8 (100)	8 (100)
Needed help doing usual activities because of weakness	8 (100)	8 (100)
Limited social activity because physically weak	8 (100)	8 (100)
Forced self to get up and do things	7 (87.5)	7 (87.5)

Cognitive Debriefing Item-Level Insights.

Conclusion: Fatigue is a bothersome symptom of gMG that limits patients' abilities to participate in daily life. The interview insights support the content validity of the Neuro-QoL Fatigue in gMG patients. Future research will focus on evaluating the psychometric properties of the Neuro-QoL Fatigue in the gMG population.

Disclosure: Sheryl Pease and Kayla Scippa are employees of Janssen Global Services, LLC This study was sponsored by Janssen Global Services, LLC.

EPO-814 | Very late onset myasthenia gravis with an unexpected high titer of AChR Abs: A new serological subtype?

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Background and Aims: Very late onset myasthenia gravis (VLOMG) (onset ≥65 years) is typically associated with low titers of acetylcholine receptor antibodies (AChR Abs), consistent with the age-related thymic atrophy. This study investigates the occurrence and characteristics of VLOMG patients with high levels of AChR Abs at diagnosis.

Methods: We performed a registry-based search for VLOMG patients with longitudinal follow-up between 2008–2023. Clinical data were collected through our MG-database.

Results: Of 69 VLOMG patients we identified 11 (15.9%) with a titer of AChR Abs ≥100 nM/L (radioimmunoprecipitation assay), 9 male and 2 female, with age at onset ranging from 65 to 85 years (mean: 75.2). AChR Abs titers ranged from 116 to 433 nM/L (mean: 217). There was no association with thymoma. All patients had generalized MG with prominent bulbar involvement. Two patients required intensive care unit monitoring. Plasmapheresis and/or intravenous immunoglobulin were necessitated in 9/11 patients. All patients were treated with prednisolone with prompt clinical response, while one received rituximab for refractory bulbar symptoms. The majority received concomitant non-steroidal immunosuppression. At the last follow-up, 9/11 patients had achieved a post-intervention status of minimal manifestations or better.

Conclusion: Patients in this serological subgroup present clinical and therapeutic characteristics of typical VLOMG patients. However, the unexpected high titer of AChR Abs raises concern about residual thymic lymphoid follicles, a possible but rare finding in LOMG. This could not be confirmed, as none of our patients underwent thymectomy. Another plausible explanation could be the presence of autoantibodies targeting multiple AChR subunits. The latter warrants additional analysis of Abs subunit specificity.

Disclosure: Nothing to disclose.

EPO-815 | Long term follow up of late-onset Pompe disease (LOPD) treated with alglucosidase alfa: The Italian experience

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Background and Aims: Pompe Disease is due to deficiency of the lysosomal enzyme acid alfa-glucosidase (GAA), with large phenotypic variability. An enzymatic replacement therapy (ERT) has been available since 2006, with different individual responses. Considering the new emerging therapies, it is important to collect information

on large patients' cohorts to define subgroups with homogeneous characteristics and their prognostic factors.

Methods: Fifteen Neuromuscular Centers, afferent to the Italian Myology Association (AIM), collected data from 90 LOPD patients (1–72 y, median 47) ERT-treated for 10 years; for 39 of them, data at 15 years were available.

Results: At baseline, 6MWT results were wide-ranging (60–814 m); 13/79 patients needed ventilatory support. FVC% values paralleled 6MWT results, with few exceptions. After 10 y, 6/77 patients had lost ambulation, and additional 3/30 after 15 years. Baseline 6MWT was <250 m in 8/9 of them. After 15 y, 9/27 patients were still stable, whereas 18 patients had worsened (66.6%). Age at start of therapy <18 y was a positive factor (85% stable after 15 y, against 7.31% treated aging >40 y). Five/32 patients (15.6%) with an initial FVC >80% started NIV after 10 y, compared to 21/34 (61.76%) with an initial FVC <80%. After 15 y, 16/39 patients (41.02%) were still ventilator-free.

Conclusion: Our results confirm the large variability of clinical course and ERT responses in LOPD patients, with about 30% patients stable after 15 years (most of them with an early-stage start of therapy), and a variable type and degree of decline in the others. A careful individual evaluation is requested in every patient when discussing the switch to alternative therapies.

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ABSTRACT

ePosters Virtual

EPV-001 | Neuroanatomical basis of overlapping symptoms in nonfluent and logopenic primary progressive apashia

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EPV-002 | Prognostic role of hemoglobin variation in anterior circulation ischemic stroke treated with mechanical thrombectomy

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EPV-003 | The effect of kidney function on plasma NfL, and p-tau 181 in a community-based cohort: The Shanghai aging study

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EPV-004 | Longitudinal changes of plasma phosphorylated tau 217 in a hospital-based cohort: The Shanghai Memory Study

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EPV-005 | Abstract withdrawn

EPV-006 | Bilateral watershed infarcts due to hypoperfusion in the context of drug abuse: Case report

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EPV-007 | Major haemorrhage risk in non-valvular atrial fibrillation under anticoagulation: Comparison of DOACs and VKAs

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EPV-008 | Dysregulated homeostasis of serum D-serine and glycine mirrors cognitive dysfunction in frail older subjects

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EPV-009

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EPV-010 | Efficacy and safety of clipping versus coiling for unruptured intracranial aneurysms: A comprehensive meta-analysis

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EPV-011 | Functional connectivity as biomarker of cognitive decline

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EPV-012 | Impact of Alzheimer's disease severity on quality of life of patients and their caregivers in the United States

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EPV-013 | Genetics of cerebral small vessel disease: A POLG-mutation case report

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EPV-014 | Facilitators and barriers of telemedicine use for the elderly with cognitive disorders: A systematic review

D. Kontaxopoulou; E. Angelopoulou; E. Stanitsa; K. Vourou; E. Smaragdaki; S. Fragkiadaki; J. Papatriantafyllou; L. Stefanis; S. Papageorgiou

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EPV-015 | Markers of cerebral thrombotic complications in polycythemia vera

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EPV-016 | Markers of cerebral thrombotic complications in essential thrombocythemia

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EPV-017 | Risk of recurrences and development of neurological diseases in patients with a history of transient global amnesia

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EPV-018 | Hearing loss increases the risk for cognitive impairment in elderly people in Western Romania

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EPV-019 | Fall risk in elderly with insomnia in Western Romania

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EPV-020 | Late-life depression and subsequent dementia: Results from a Tertiary Referral Hospital in Portugal

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EPV-021 | Plasma tau in iatrogenic cerebral amyloid angiopathy: It is not simply a matter of brain trauma

G. Pollaci[1]; B. Storti[2]; L. Zapparoli[3]; A. Potenza[1]; A. Zuleta[4]; G. Marinoni[1]; G. Gorla[1]; T. Carrozzini[1]; M. Catania[5]; L. Gatti[1]; A. Bersano[2]

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EPV-022 | Analysis of abeta-40 and abeta-42 in patients with iatrogenic cerebral amyloid angiopathy: A diagnostic hypothesis

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EPV-023 | NOACs vs. antiplatelets in ESUS with AF predictors: Meta-analysis

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EPV-024 | Testing the feasibility of the European diagnostic workflow for MCI disorders in clinical practice: Study-design

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EPV-025 | Comprehensive genetic screening of early-onset dementia patients in Southern Italy cohort: A five case series

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EPV-026 | Autonomic dysfunction in Parkinson's disease

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EPV-027 | Validation of the Italian recommendations for the biomarker-based diagnosis of mild cognitive impairment: Study design

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EPV-028 | Investigating the background of impaired visuomotor abilities in patients with mild cognitive impairment

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EPV-029 | Epidemiological study on potential protective factors for dementia in a small Italian village

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EPV-030 | Exploring the connection between dysautonomia and neuropsychiatric symptoms in Alzheimer's disease

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EPV-031 | C9Orf72-related neurodegenerative disorders: Clinical spectrum in a Spanish cohort

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EPV-032 | Improved automated quantification of temporal lobe volume for early diagnosis of AD using high resolution 3D MRI

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EPV-033 | Effect of left presupplementary iTBS stimulation on clinic and electrophysiology in Parkinsonian speech disorder

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EPV-034 | Insular and limbic abnormal functional connectivity in de novo Parkinson's disease patients with autonomic dysfunction

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EPV-035 | Predicting rTMS outcomes in Alzheimer's disease: Exploring initial clinical parameters for personalized insights

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EPV-036 | PSEN-1 mutation in early-onset alzheimer disease with spastic paraparesis: Experience from Pisa and literature review

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EPV-037 | Satisfaction of transdermal rivastigmine "two per week" in caregivers of Alzheimer's patients

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EPV-038 | Neuroimaging biomarkers in Alzheimer's disease continuum and CSF sTREM2: Longitudinal study

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EPV-039 | PSEN1 pathogenic variant in a patient with a family history of suspected prion disease: A case of likely misdiagnosis

F. Barros; M. Lima; M. Pereira; A. Novo; I. Baldeiras; I. Santana; J. Durães
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EPV-040 | BIOmarkers in NEuropsychiatric SYmptoms (BIONESY): A multicenter nation survey

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EPV-041 | Five patients with early onset dementia of TREM2 mutation in a Turkish family

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EPV-042 | Mismatch learning in virtual reality (VR) technology in older adults – A pilot-study

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EPV-043 | Effects of an OX2R agonist on hippocampal tau in human P301S mutant tau transgenic mice

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EPV-044 | RT-QUIC: A rapid diagnostic tool for probable Creutzfeldt-Jakob disease – Insights from two clinical cases

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EPV-045 | Nocturia and sleep dysfunction in Parkinson's disease

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EPV-046 | Primary angiitis of the central nervous system – Clinical case

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EPV-047 | A study on Metaphor comprehension deficit in patients with mild cognitive impairment in Bengali speaking population

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EPV-048 | Correlation between routine hemogram inflammatory biomarkers and cognitive impairment

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EPV-049 | Tackling sex and gender inequalities in effective treatment and support: Findings from a narrative review study

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EPV-050 | Off-road cycle lanes can reduce the sex and gender differences in risk of dementia and are cost-saving

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EPV-051 | Dementia specialized care units in adverse healthcare scenarios: Initial experience, working areas and future potential

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EPV-052 | Shared biological mechanisms between Alzheimer's disease and sepsis: An in silico analysis

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EPV-053 | Sentence reading comprehension in patients with mild cognitive impairment with Lewy bodies

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EPV-054 | Frequency and severity of cardiovascular autonomic dysfunction in myasthenia gravis patients

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EPV-055 | Fatigue and autonomic symptoms in chronic inflammatory demyelinating polyneuropathy – Pilot study

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EPV-056 | Young-onset dementia: Portrait of a tertiary outpatient clinic

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EPV-057 | Alcoholism as a risk factor for frontal AD

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EPV-058 | Association between cerebrovascular reactivity and CSF/plasma biomarkers in Alzheimer's disease

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EPV-059 | A rarity knocking on the clinic door – Ross syndrome

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EPV-060 | Effect of oral dimethyl fumarate treatment on orthostatic hypotension in multiple sclerosis patients

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EPV-061 | The effectiveness of dementia prevention programs: A systematic review and meta-analysis for 61,457 patients

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EPV-062 | Diagnosis of mild cognitive impairment in primary care in the era of plasma biomarkers and anti-amyloid therapies

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EPV-063 | Autonomic responses in electroconvulsive therapy: Understanding the neurophysiological basis of ejaculation

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EPV-064 | Circulatory shock associated with left insular stroke and chronic steroid treatment

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EPV-065 | Brain hemorrhage or edema in U.S. veterans with Alzheimer's disease prescribed antiplatelet and anticoagulant therapy

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EPV-066 | More than just a transient memory loss: TGA as a first presentation of neurodegenerative disease

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EPV-067 | Factors affecting clinical improvement in patients diagnosed with possible normal pressure hydrocephalia

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EPV-068 | The efficacy of a home-based, augmented reality dual-task platform for cognitive-motor training for elderly patients

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EPV-069 | Clinical and autonomic characteristics in patients with postural tachycardia syndrome

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EPV-070 | Autonomic dysfunction in patients with Epilepsy

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EPV-071 | Effects of obstructive sleep apnea syndrome associated with aging: Preventing dementia – biomarker research

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EPV-072 | Plasma ptau species, neuronal and glial biomarkers for evaluating Brain health in ageing

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EPV-073 | The clinical overlap between frontotemporal dementia (non-fluent variant PPA) and Corticobasal syndrome: A case report

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EPV-074 | Is almería reaady for lecanemab?

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EPV-075 | Diagnosis of functional cognitive disorder – Misguided by imaging findings, psychiatric and family history?

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EPV-076 | Effect of treatment for head & neck tumor on autonomic nervous system

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EPV-077 | Correlation of gait characteristics to cognitive status during dual-task walking in elderly subjects of different ages

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EPV-078 | A single blind rct in india on effectiveness of adjunct cognitive stimulation therapy on cognitive outcomes in dementia

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EPV-079 | A prenatal filamin a deficiency as a possible protective mechanism in Alzheimer's disease progression. A case study

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EPV-080 | Cognitive deterioration between Alzheimer's dementia and Parkinson's disease dementia

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EPV-081 | Dementia and associated caregiver family burden in a North Indian cohort: An observational study

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EPV-082 | The "claustrum sign" in covid-19 AND Alzheimer's disease: A case report

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EPV-083 | Longitudinal objective and self-reported cognitive function in subjective cognitive decline

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EPV-084 | Drug-induced reversible cerebral vasoconstriction syndrome: A real-world evidence

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EPV-085 | Saccadic eye movement task can differentiate functional cognitive disorder from mild cognitive impairment

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EPV-086 | Development of a brief intervention to address z-hypnotic overuse among older adults

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EPV-087 | Alteration of blood biomarkers in Alzheimer's dementia with vascular lesions

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EPV-088 | Slow wave sleep and dementia: A systematic review and critical analysis

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EPV-089 | Colour memory in mild cognitive impairment and Alzheimer's disease

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EPV-090 | Spectrum of vascular cognitive impairment according to the type of brain vascular damage

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EPV-091 | TPS – Are there new perspectives in treatment of AD?

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EPV-092 | Potential applications of software supporting the early detection of cognitive disorders and dementia in diagnostics

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EPV-093 | Efficacy and safety of gantenerumab in the treatment of Alzheimer's disease: A systematic review and meta-analysis

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EPV-094 | Digital biomarkers from diffusion MRI to monitor white matter abnormalities in Alzheimer's disease

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EPV-095 | Correlation of hippocampal volume with memory impairment in Alzheimer's disease

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EPV-096 | Pupillary light reflex testing may specify the location of visual tract lesions in patients with multiple sclerosis

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EPV-097 | Cohort study of the effects of occupation and environmental tobacco smoke on Alzheimer's disease

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EPV-098 | Correlation of CSF index of blood–brain barrier with visual rating scale of brain MRI

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EPV-099 | Clinical, radiological and biomarker analysis of single center Creutzfeld-Jacob disease patients

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EPV-100 | Clinical peripheral nerve examination in older adults with respect to risk factors and peripheral circulation

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EPV-101 | Rare case of acute middle cerebral artery stroke with ipsilateral hemiplegia and uncrossed corticospinal tracts

E. Abi Fadel[1]; T. El Khoury[2]; A. Nassif[2]; S. Iskandar[1]; H. Al Khuder[1]; W. Ayoub[1]; M. El Dassouki[1]; A. Shatila[1]
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EPV-102 | Evaluation of atrial cardiopathy in embolic stroke of undetermined source in elderly subjects with acute ischemic stroke

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EPV-103 | Post-transcatheter aortic valve implantation stroke: an analysis of risk factors, characteristics and clinical outcomes

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EPV-104 | Neurological findings in patients with organic acidemias

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EPV-105 | Carotid Eagle syndrome: A possible cause for undeterminated ischemic stroke cases

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EPV-106 | Acute recanalization therapy for ischemic stroke during pregnancy and puerperium

A. Richardt[1]; K. Aarnio[1]; A. Korhonen[1]; K. Rantanen[1]; L. Verho[2]; S. Curtze[1]; H. Laivuori[3]; M. Gissler[4]; M. Tikkanen[5]; P. Ijäs[1]

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EPV-107 | Radiological eligibility of patients presenting with hyperdense MCA sign for mechanical thrombectomy

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EPV-108 | The effect of anodal tDCS on post-stroke cognitive impairment in the acute phase: A pilot study

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EPV-109 | The early mobilization decision after an acute stroke: An umbrella review

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EPV-110 | A 'salted pretzel' after a car accident

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EPV-111 | The role of autophagy in the adaptation of neurons to chronic hypoxia

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EPV-112 | Mechanical thrombectomy in acute ischemic stroke: Predisposing factors for hemorrhagic transformation

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EPV-113 | Circadian effects on stroke outcomes after clot retrieval – An exploratory analysis

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EPV-114 | Reperfusion therapy vs. conservative management in acute stroke patients with premorbid disability: Retrospective study

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EPV-115 | Markers of damage to the blood–brain barrier and brain in cerebral small vessel disease with cognitive impairments

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EPV-116 | Carotid plaque MRI: Effects of plaque features on embolic complications and cognition after carotid artery stenting

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EPV-117 | Decompressive craniectomy, for Whom? When? How Much?

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EPV-118 | Precipitating factors in Moyamoya angiopathy, it's profile and implications: An experience from eastern India

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EPV-119 | Acute incidental cerebral microinfarcts may predict ischemic stroke in patients with cancer

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EPV-120 | Acute incidental cerebral microinfarcts are common in patients with antiphospholipid syndrome

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EPV-121 | The current profile of elderly Tunisian stroke patients

C. Khiari; E. Jarrar; A. Rekik; K. Jemai; S. Naija; A. Hassine; S. Ben Amor
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EPV-122 | Chronic cognitive deficits among aneurysmal subarachnoid hemorrhage survivors

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EPV-123 | Outcome predictors of posterior circulation ischemic stroke: A retrospective, single centre study

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EPV-124 | Gait disorders in cerebral small vessel disease: The role of cerebrospinal fluid flow and venous drainage impairment

L. Dobrynina; E. Bitsieva; A. Byrochkina; M. Tsypushtanova; A. Makarova; M. Zabitova; K. Shamtieva; Y. Akhmetshina; V. Trubitsyna
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EPV-125 | CT perfusion in acute-onset global aphasia: A powerful tool to make a proper diagnosis

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EPV-126 | Moyamoya presenting with tremor and bilateral symmetrical hyperintensities of the corticospinal tracts

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EPV-127 | Neurodevelopmental disorders in pediatric patients with myotonic dystrophy type 1

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[1]Pirogov Russian National Research Medical University, Moscow, Russian Federation; [2]Lomonosov Medical Scientific and Educational Center of Moscow State University, Moscow, Russian Federation; [3]Russian Federation Research Centre for Medical Genetics, Moscow, Russian Federation

EPV-128 | Reversible cerebral vasoconstriction syndrome. Number of cases

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EPV-129 | Abstract withdrawn

EPV-130 | Endothelin-1 in embolic stroke of undetermined source patients with non-stenosing intracranial atherosclerotic plaques

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EPV-131 | Double subclavian steal syndrome as manifestation of Erdheim-Chester

J. Finsterer
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EPV-132 | What happens after transient global amnesia? A longitudinal population-based study

F. Gabriele[1]; M. Foschi[1]; F. De Santis[1]; D. Ciuffini[1]; F. Conversi[1]; E. Colangeli[2]; B. Orlandi[2]; F. De Santis[2]; R. Ornello[1]; S. Sacco[1]
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EPV-133 | From 0 to 100 – Loop recorder implantation on stoke unit

F. Wagner; S. Brodoehl; C. Klingner; A. Günther; C. Geis; C. Klingner
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EPV-134 | Giant cell arteritis and inflammatory cerebral amyloid angiopathy – distinct or related diseases? A case report

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EPV-135 | Comparing ischemic strokes treated in extended and conventional times in the city of Pisa. A one-year outcomes analysis

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EPV-136 | Increasing incidence of posterior reversible encephalopathy syndrome: 23-year experience in a third-level hospital

G. Cabañas Engenios; R. Sainz Amo; N. Mena García; R. Pastor González; M. Campos Jiménez; P. Garay Albizuri; B. Martínez García; D. Pérez Gil; I. Corral Corral
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EPV-137 | Evaluation of the relationship of systemic inflammatory index with prognosis in patients with acute ischemic stroke

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EPV-138 | Do infarct volumes influence stroke heart syndrome (SHS) after mechanical thrombectomy (MT)?

G. Prandin; L. Mancinelli; F. Palacino; E. Vincis; G. Furlanis; P. Caruso; M. Naccarato; P. Manganotti
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EPV-139 | Niemann-Pick disease type C: Phenotypic variability

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EPV-140 | Internal carotid artery occlusion with stroke: Outcomes of emergent carotid endarterectomy and intravenous thrombolysis

R. Herzig[1]; S. Ostrý[2]; V. Kunešová[3]; A. Kondé[4]; M. Kovář[5]; R. Jura[6]; J. Fiksa[7]; P. Geier[8]; O. Škoda[9]; P. Vaško[10]
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EPV-141 | Factors influencing the early neurological deterioration in intracranial branch atheromatous diseases

I. Deguchi; S. Fujiwara; N. Arai; T. Nakagami; R. Kimura; K. Oryu; K. Watanabe; Y. Kato; T. Hayashi; S. Takahashi; S. Suda
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EPV-142 | Limb ischemia and ischemic stroke as a presentation of Kounis Syndrome

I. Del Pino Díaz; P. Guirado Ruiz; R. Calle Calle; I. Villegas Rodríguez
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EPV-143 | Next generation sequencing and whole-exome sequencing of patients with spontaneous cervical artery dissections

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EPV-144 | Factors influencing the outcome of stroke due to M1 occlusion of MCA

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EPV-145 | Endovascular treatment of cerebral venous thrombosis: A multicentric study

J. Alonso[1]; E. Cañada[1]; C. Ramos[1]; C. Gómez-Escalonilla[2]; A. de Felipe[3]; P. Calleja[4]; P. de la Riva[5]; C. Tejero[6]; L. Llull[7]; S. Trillo[1]
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EPV-146 | Absence of headache in clinical presentation of cerebral venous thrombosis – a single center study of 105 cases

M. Janković; T. Švabić Međedović; P. Stanarčević; I. Berisavac; V. Pađen; M. Mijajlović; M. Ercegovac; N. Kresojević; M. Kovačević; D. R. Jovanović
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EPV-147 | Secondary prevention of AF-related AIS: Deploying machine learning for robust validation and updating of CHA2DS2-VASc

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EPV-148 | The ivy sign in patients with moyamoya syndrome associated with atherosclerotic occlusion of the middle cerebral artery

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EPV-149 | Persistent primitive trigeminal artery associated with agenesis of common carotid artery

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EPV-150 | Histopathological analysis of thrombi obtained after mechanical thrombectomy. Project presentation

J. Romano[1]; J. Arnedo Fernández[2]; C. Chamorro Santos[3]; C. López Mesa[1]; Ó. Pérez Bustamante[3]; C. Moreno Franco[1]; R. Lorenzo López[1]; P. Jiménez Arco[1]; P. Casa Nova Leitao Moreira[1]; I. Pérez Ortega[1]; M. Fernandez Pérez[1]; J. Romero Fábrega[1]
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EPV-151 | Role and approach for assessment of nitric oxide bioavailability in cerebral small vessel disease

L. Dobrynina; K. Shamtieva; A. Shabalina
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EPV-152 | Reversal of vision metamorphopsia due to cerebrovascular pathology: A single-center case series

A. Karamyan[1]; H. Tsatryan[2]; A. Kunz[1]; S. Pikija[1]
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EPV-153 | Polypills and gender differences as tools to increase patients' compliance to secondary prevention of ischemic stroke

L. Martirosyan; S. Voskanyan; A. Papoyan; A. Madoyan; K. Kosyan; A. Ashugyan; K. Petrosyan
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EPV-154 | Impact of trimethylamine N-Oxide on stroke incidence and NOAF following STEMI: insights from gut microbiota metabolism

O. Knokneriene[1]; A. Aldujeli[2]; R. Unikas[2]; V. Tatarunas[2]; V. Skipskis[2]; A. Knokneris[3]
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EPV-155 | Impact of combined inflammatory markers on increased risk of mortality after ischemic stroke in young subjects

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EPV-156 | Comparison of troponin peak values between cerebral haemorrhages and untreated ischemic strokes

L. Mancinelli; G. Prandin; I. Scali; F. Palacino; E. Vincis; G. Furlanis; P. Caruso; M. Naccarato; P. Manganotti
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EPV-157 | Vasculitis with central nervous system involvement: A multicenter study

L. Santos[1]; I. Llera[1]; T. Montalvo[1]; J. Martínez[1]; J. Cebrian[1]; N. Barbero[1]; J. Fernández[1]; S. Pastor-Yvorra[2]
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EPV-158 | Moyamoya disease and syndrome: A European centre experience

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EPV-159 | High altitude-related factors may influence the stroke outcome: A pilot study from southern Armenia

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EPV-160 | Post-stroke neurogenic cardiac changes: A plea for extended cardiac monitoring

M. Manea[1]; I. Stoican[2]; I. Enache[2]; C. Ciulavu[2]; S. Tuta[1]; D. Dragos[3]
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EPV-161 | PAI mutation as a risk factor for large vessel occlusion – What is the best choice for treatment?

M. Cholakova
Nikolay Mihnev

EPV-162 | The role of inflammation in spontaneous cervicocephalic dissection: A comparative study and combined data analysis

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EPV-163 | Stroke in hypertensive patients: Differences between young and very elderly patients

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EPV-164 | Controversial endovascular approaches in childhood arterial ischemic stroke: A case report

M. Caccamo; D. Galotto; S. Grimaldi; N. Marrone; G. Milella; G. Falcicchio; A. Manni; S. Lamberti; M. Savarese; D. Mezzapesa; M. Petruzzellis; G. Defazio
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EPV-165 | Predictors of good 1-year outcome in stroke patients post successful recanalization with initial poor functional status

M. Gielczynski[1]; P. Wrona[2]; D. Wrobel[4]; T. Popiela[3]; G. Kapral[4]; J. Staniszewska[4]; M. Derechowska[4]; A. Slowik[2]
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EPV-166 | The role of the endothelium in the morphogenesis of changes blood vessels in cerebrovascular atherosclerosis

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EPV-167 | Thrombolysis in ischemic stroke due to cerebral small vessel disease: A case–control study

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EPV-168 | Neurofeedback in patients with early cerebral small vessel disease

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EPV-169 | Medical outcomes after ischemic stroke in an institutional cohort

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EPV-170 | Covert cerebrovascular disease in a stroke cohort

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EPV-171 | Young stroke patients: Modifiable risk factors and genetic scores

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EPV-172 | Impact of lower extremity physical function on quality-of-life post-stroke: Findings from the MOBITEC-stroke study

M. Ryan[1]; R. Rössler[1]; N. Rommers[2]; L. Iendra[3]; E. Peters[1]; R. Kressig[1]; A. Schmidt-Trucksaess[4]; S. Engelter[1]; T. Hinrichs[4]; N. Peters[1]
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EPV-173 | Timing of hemorrhagic stroke in Almería (Spain)

P. Olea-Rodríguez; M. Martínez Salmerón; J. Fernández Pérez; P. Sánchez Martínez; A. Arjona Padillo; M. Iglesias Espinosa
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EPV-174 | Vessel wall imaging in patients presenting with first ever stroke with intracranial atherosclerotic disease (ICAD)

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EPV-175 | Utility of antiaggregation for primary prevention in patients with leukoaraiosis on MRI: A historical cohort study

P. Garrido Jiménez; S. López Anguita; A. Lorenzo Montilla; J. Rodríguez Quinchanegua; F. Valenzuela Rojas; M. Olmedilla González
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EPV-176 | Ischemic stroke from cerebral arteritis treated with anti-retroviral therapy in newly diagnosed HIV infection

F. Pedroni; G. Cutillo; M. Vabanesi; E. Dotto; N. Anzalone; F. Simionato; R. Chieffo; G. Giacalone; M. Filippi; L. Roveri
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EPV-177 | Ischemic stroke in atrial fibrillation: Difference between oral anticoagulant treated and treatment-naive patients

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EPV-178 | Inflammation markers, clinical and radiological parameters in acute ischemic stroke: A new composite prognostic score

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EPV-179 | Prevalence of electrolyte imbalance in patients with acute stroke: A systematic review and meta-analysis

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EPV-180 | Abstract withdrawn

EPV-181 | MicroRNAs predictive of carotid stenosis severity

A. Raskurazhev; P. Kuznetsova; A. Shabalina; A. Mazur; V. Annushkin; M. Tanashyan
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EPV-182 | Cerebral venous thrombosis after lumbar puncture: About two cases

M. Mhiri; R. Guizani; R. Ben Dhia; N. Gouta; M. Frih-Ayed
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EPV-183 | Non abducens cranial nerves involvement in cerebral venous sinus thrombosis

R. Smaoui; K. Moalla; N. Bouattour; N. Farhat; S. Daoud; S. Sakka; M. Damak; C. Mhiri
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EPV-184 | Cerebral venous thrombosis and prothrombotic risk factors: A single-center experience from Tunisia

R. Smaoui; K. Moalla; S. Sakka; N. Bouattour; S. Daoud; N. Farhat; M. Damak; C. Mhiri
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EPV-185 | Stroke prevention in atrial fibrillation: Is chronic anticoagulant therapy over-prescribed?

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EPV-186 | The epidemiologic, clinical and etiological profile of young adult ischemic strokes in Morocco: About 57 cases

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EPV-187 | Could reversing direct oral anticoagulants change the outlook for hemorrhagic strokes?

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EPV-188 | Early elevation of troponin levels in acute stroke

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EPV-189 | Amaurosis fugax and ischemic stroke in a patient diagnosed with VEXAS syndrome

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EPV-190 | Association between anemia and cerebral venous thrombosis

R. Smaoui; K. Moalla; N. Bouattour; S. Sakka; S. Daoud; N. Farhat; M. Damak; C. Mhiri
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EPV-191 | Prolonged cardiac monitoring with textile wearable Holter technology in patients with ESUS stroke

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EPV-192 | Thrombophilia a significant cause of cerebral venous sinus thrombosis in East Africa: Retrospective review of 118 cases

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EPV-193 | Impact of the TICI3 versus TICI2b reperfusion score to predict long-term good outcome following mechanical thrombectomy

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EPV-194 | Internal carotid artery dissection due to Eagle-syndrome: Can the toothpick in your neck cause a stroke?

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EPV-195 | Factors associated with early versus late hemorrhagic transformation in acute ischemic stroke

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EPV-196 | Carotid web and atherosclerosis, double-trouble or double-face?

V. Tudisco[1]; L. Ferraù[1]; F. Giammello[2]; C. Dell'Aera[1]; M. Cotroneo[1]; A. Tessitore[3]; D. Vicari[3]; S. Vinci[3]; P. La Spina[1]; A. Toscano[1]
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EPV-197 | Improving written discharge communication in an acute stroke unit

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EPV-198 | Therapeutic approach to non-COVID-19 cardioembolic stroke in the first year of the pandemic

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EPV-199 | Evaluation of the quality of life and burden of caregivers of patients with stroke

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EPV-200 | Signal and biophysical models of diffusion MRI in assessing of cerebral small vessel disease progression

Z. Gadzhieva; L. Dobrynina; E. Kremneva; K. Shamtieva; A. Geints; A. Filatov; V. Trubitsyna; M. Krotenkova
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EPV-201 | Long-term perspectives of COVID-19 neurological consequences in young out-patients and in-patients

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EPV-202 | Clinical and neuropsychological characterization of mild cognitive impairment in primary psychiatric disorders

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EPV-203 | Suicide risk of patients with epilepsy and comorbid mental disorders

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EPV-204 | Efficacy of pharmacological interventions in fragile X syndrome: A network meta-analysis of randomised controlled trials

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EPV-205 | Genetic causes of rare paediatric diseases with complex neurological phenotypes in the South Kazakhstan region

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EPV-206 | Information, support and guidance provided by the Finnish Epilepsy Association

T. Koskinen; V. Mäkitalo; P. Salminen; P. Sorjonen; V. Tarkiainen; A. Mikkola
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EPV-207 | Executive functions and its correlation to language deficits

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EPV-208 | Neurocognitive and behavioral challenges in pediatric ASD and post-radiosurgery arteriovenous malformation

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EPV-209 | Abstract withdrawn

EPV-210 | Clinical and Electrophysiological characteristics of COVE in the light of current ILAE criteria

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EPV-211 | Role of neurophysiology in scan-negative myelopathy

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EPV-212 | PPP2R1A-related neurodevelopmental disorder: The first Korean case with a novel variant of PPP2R1A and literature review

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EPV-213 | Detailed mechanisms of neuronal hyperexcitability induced by hyperventilation in electroconvulsive therapy

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EPV-214 | Effect of concomitant medications on adverse event frequency, severity, and resolution in a cenobamate open-label trial

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EPV-215 | The assessment of subjective cognitive decline with major depressive disorder via montreal cognitive assessment (MoCA)

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EPV-216 | Hypoxia inducible factor 1 alpha (HIF-1A) – Biomarker of hypoxic cell suffering in children with status epilepticus

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EPV-217 | Neonatal seizures – Etiological, clinical and electroencephalographic aspects

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EPV-218 | International puzzle of needs & obstacles for the optimization of socio-cognitive assessment in neurocognitive disorders

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EPV-219 | Psychosocial vulnerability among patients living with Alzheimer's disease and frontotemporal dementia

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EPV-220 | "Doctor, I can't follow a movie if all of the actresses are blonde"

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EPV-221 | Brain health after COVID-19, pneumonia, myocardial infarction, and critical illness

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EPV-222 | Influence of preoperative nerve conduction studies on the outcome of carpal tunnel release surgery

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EPV-223 | The serum proteome of post-acute COVID-19 Syndrome: Implications for cognition and neurodegeneration

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EPV-224 | Examining cognitive intra-individual variability in adults with and without HIV-associated neurocognitive disorder

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EPV-225 | Clinical utility of surface EMG for evaluation the effect of orthodontic treatment in patients with malocclusion

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EPV-226 | Post-COVID-19 fatigue in the Moscow population: Prevalence and associated factors

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EPV-227 | Personality traits associated with suicidal ideation in patients with epilepsy

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EPV-228 | Exploring cognitive consequences: sNfL and sGFAP as biomarkers in post-COVID adults returning to work

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EPV-229 | Modern possibilities for early diagnosis of cerebral disorders in children and adolescents with type 1 diabetes mellitus

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EPV-230 | tDCS improves empathy scores without affecting telepathic abilities

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EPV-231 | EEG calculator. A new tool for daily use in electroencephalography

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EPV-232 | Measurement of olfactory impairment in Parkinson's disease patients and their relatives

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EPV-233 | Pneumocephalus and air embolism in COVID-19 interstizial pneumonia

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EPV-234 | Epilepsy, antiseizure medications, and their relationship with music understanding

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EPV-235 | The utility of EMG in the diagnosis of sciatica

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EPV-236 | Epilepsy diagnostic clinic: First-year retrospective analysis

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EPV-237 | COVID-19 vaccines and attributable risk of neurological disorders: A multicentre, case–control study (COVIVAX)

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EPV-238 | Gerstmann syndrome with acute/subacute and insidious onset: A systematic review with individual patient data analysis

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EPV-239 | Unveiling PURA-related Syndrome: A case study of a newborn with hypotonia

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EPV-240 | Cross-cultural adaptation of TEA-CIFunciona for assessing functioning in children with autism through parental reporting

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EPV-241 | Evaluation of facial synkinesis with applied blink reflex test

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EPV-242 | A single physical exercise imitating motor seizures increases the concentration of MMP-9 in the serum

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EPV-243 | Psychiatric features in aceruloplasminemia: A systematic review and meta-analysis

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EPV-244 | Psychotic disorders: Inaugural manifestations of multiple sclerosis

I. Ghorbel; H. Derbali; M. Messelmeni; M. Mednini; I. Bedoui; M. Mansour; J. Zaouali; R. Mrissa
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EPV-245 | Chronic inflammatory demyelinating polyneuropathy after COVID-19 vaccination

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EPV-246 | Diagnostic accuracy in non-lesional, drug-resistant focal epilepsy and its impact on clinical management

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EPV-247 | Amyloid angiopathy – beyond cerebral hemorrhage

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EPV-248 | Using historical data to derive reference limits – A validation of the E-norms approach

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EPV-249 | Association of family history of epilepsy with demographic and clinical characteristics of patients

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EPV-250 | Allergic reactions to antiseizure medications in epilepsy patients: Prevalence, patterns, and implications

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EPV-251 | Transcranial magnetic stimulation of the supplementary motor area in children with Tourette syndrome and chronic tics

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EPV-252 | Machine learning of cognitive trajectories in PD: Predicting STN-DBS impact with neuroimaging and clinical data

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EPV-253 | The health status of newborns in patients with multiple sclerosis on the background of natalizumab therapy

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EPV-254 | Value of neuroinflammatory dysfunction of the blood–brain barrier in the development of drug-resistant epilepsy

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EPV-255 | Features of physical activity in patients with epilepsy

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EPV-256 | Convulsive status epilepticus in an adult patient with Alexander disease: A case study

L. López Trashorras; A. Aldaz Burgoa; P. Abizanda Saro; N. Rodríguez Albacete; L. Franco Rubio; M. García Ruiz; J. Obregón Galán; P. Gutiérrez Bedia; A. Marcos Dolado; R. Ginestal López; E. López Valdés; P. Mayo Rodríguez
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EPV-257 | Generative language models in medical education: An observational study of ChatGPT performance in neurology questions

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EPV-258 | Awareness and practice of febrile convulsions first aid among parents of convulsing children

Babiker Bakri; R. Asim Mohammed; R. Mursi Hamid; M. Jaber Amin
Alzaiem Alazhari university Faculty of Medicine, Khartoum, Sudan

EPV-259 | Electroencephalographam in acute ischemic stroke as a prediction tool for poststroke epilepsy

M. Adouania; M. Ben Mahmoud; S. Fray; H. Jamoussi; N. Ben Ali; M. Fredj
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EPV-260 | Pregnenolone: A "Forgotten" marker and neurosteroid target in chronic fatigue

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EPV-261 | The level of anxiety in patients with vestibular dysfunction

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EPV-262 | Low frequency photoparoxysmal response in Creutzfeldt-Jakob Disease

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EPV-263 | Vanishing White Matter disease: Clinical heterogeneity by age of onset

M. Borrell-Pichot; T. Mederer-Fernandez; R. Sainz-Torres; G. Olmedo-Saura; M. Guasch-Jimenez; S. Martínez-Horta; J. Kulisevsky; J. Pérez-Pérez
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EPV-264 | Intracerebral hemorrhage (ICH) and epilepsy: A retrospective review

M. Hernandez Garcia; C. Hernandez Javier; G. González Toledo; D. García Alvarez; L. Iacampo Leiva; J. Rojo Aladro
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EPV-265 | Minor neurological anomalies in patients with first-episode psychosis

E. Abouda[1]; I. Betbout[1]; M. Mhiri[2]; A. Abess[2]; A. Ben Haouala[1]; L. Gasab[1]; A. Mechri[1]; A. Mhalla[1]
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EPV-266 | DHDDS mutation: A rare cause of hyperkinetic movement disorders and epileptic encephalopathy in a 13-year-old girl

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EPV-267 | Spatial navigation in primary age-related tauopathy and Limbic-predominant age-related TDP-43 encephalopathy

M. Laczó; Z. Svacova; H. Horakova; M. Vyhnalek; J. Hort; J. Laczó
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EPV-268 | Analytic visual information processing and cross modal illusions. Relevance for migraine research and therapy

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EPV-269 | Neuroimaging as a biomarker of comorbidities in children with cerebral palsy

M. Ben Hafsa[1]; H. Benrhouma[1]; T. Ben Younes[1]; M. Jamoussi[1]; A. Zioudi[1]; Z. Miladi[1]; H. Klaa[1]; I. Kraoua[1]; S. Nagi[2]; I. Ben Youssef-Turki[1]
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EPV-270 | MSL3 (Basilicata-Akhtar) syndrome: De-novo novel pathogenic variant of an ultra-rare genetic disorder

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EPV-271 | The burden of treatment-resistant schizophrenia: A neurological concern?

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EPV-272 | Dynamic study of neuropsychological complications arising as a result of the treatment of chronic lympholeukosis

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EPV-273 | The efficacy and safety of cannabidiol (CBD) in pediatric patients with Dravet syndrome: A systematic review

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EPV-274 | Peculiarities of cognitive and emotional changes in patients with primary hypothyroidism in the early stages

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EPV-275 | Impact of obesity on elective spine surgeries during COVID-19 pandemics

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EPV-276 | Introduction to QEMG Analytics: A new way to visualize and interpret EMG and Near Fiber EMG data

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EPV-277 | Minor/major malformations and neurodevelopmental outcomes in children prenatally exposed to LEV, LTG and CBZ monotherapy

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EPV-278 | Cognitive impairments – a symptom of post-COVID syndrome in the context of a global pandemic

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EPV-279 | Dyslexia: A word game to develop phonological awareness

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EPV-280 | Auditory verbal memory in children with autism spectrum disorders

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EPV-281 | Serial organization of movements in children with autism spectrum disorders and in children with speech dysontogenesis

E. Gorobets; R. Gamirova; Y. Volskaya; O. Ivanova
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EPV-282 | Is fear experienced under virtual reality? An electrophysiology study under virtual reality conditions

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EPV-283 | Postural control anomalies and gait dysfunction in Tourette's syndrome: A systematic review

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EPV-284 | B-cells cytokines activation in myelitis with predominant damage of lateral and posterior columns

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EPV-285 | Risk factors for sudden unexpected death in epilepsy

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EPV-286 | The analysis of circadian rhythm of heart rate variability in patients with epilepsy

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EPV-287 | Radiological features of carpal tunnel syndrome in the patients with hereditary transthyretin amyloidosis

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EPV-288 | The care of the aphasic patients: Experience from a stroke unit

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EPV-289 | The developing cavernous sinus thrombosis in patients who underwent COVID-19

S. Khudayarova; G. Rakhmatullayeva; S. Said-Akhmadova
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EPV-290 | Optimizing diagnostics and treatment for epileptic encephalopathy with continuous spike and wave during sleep

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EPV-291 | Unveiling neurophobia: Exploring factors among sudanese medical students and impact on neurology residency intentions

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EPV-292 | Electrophysiological changes in pediatric spinal muscular atrophy: Results from an observational study

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EPV-293 | Charles Bonnet syndrome as sequelae of occipital lobe infarct with hemorrhagic conversion: A case report

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EPV-294 | Specialized infrastructure in a tertiary hospital to administer disease modifying treatments in Alzheimer's disease

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EPV-295 | Late-onset valproate-induced encephalopathy: An untoward possible event

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EPV-296 | A rare case of megalencephaly-polymicrogyria-polydactyly-hydrocephaly syndrome with PIK3R2 mutation

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EPV-297 | Pediatric onset multiple sclerosis: A tertiary center experience

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EPV-298 | Repetitive transcranial magnetic stimulation in murine models of epilepsy: Methodological aspects and outcomes

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EPV-299 | Evoked potentials in the diagnosis of cognitive impairment syndromes after a cerebrovascular accident

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EPV-300 | Impact of post-COVID-19 syndrome on self-perceived impairment of working memory

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EPV-301 | Rheumatoid Arthritis triggered by Fremanezumab: The real-world side effects of the anti-CGRP migraine treatments

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EPV-302 | Searching for variants of the CACNA1A gene in migraine patients – Preliminary study

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EPV-303 | Leptomeningeal enhancement on brain MRI during an acute attack in a patient with familial hemiplegic migraine

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EPV-304 | Acute post traumatic idiopathic intracarnial hypertension-like syndrome associated with cerebral venous sinus stenosis

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EPV-305 | Characterization of the interictal burden: A global view of migraine

A. Sánchez Huertas; M. Lorenzo Diéguez; L. Portocarrero Sánchez; J. Diáz de Terán
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EPV-306 | Real world practice study: Eptinezumab in patients with failure of at least four previous preventive treatments

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EPV-307 | OnabotulinmtoxinA as a promising treatment for primary trochlear headache: A case series

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EPV-308 | Genetic insights into chronic migraine: New associations with polymorphisms in the genes ARG1, CES2, MOCS2 AND SLCO2B1

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EPV-309 | Efficacy and safety with cenobamate monotherapy conversion and dual therapy

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EPV-310 | Recurrent thunderclap headaches: Diverse presentations in a single patient

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EPV-311 | Assessment of response to botulinum toxin A in patients with trigeminal neuralgia: A case series study

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EPV-312 | Real-world effectiveness and safety of fremanezumab in migraine: 4th interim analysis of the Pan-European PEARL study

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EPV-313 | Real-world evidence of monoclonal use in refractory migraine patients on polytherapy in a headache center

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EPV-314 | Safety and tolerability of BHV-7000, a Novel Kv7 activator, in phase 1 single and multiple ascending dose studies

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EPV-315 | Using electroconvulsive therapy and vagal nerve stimulation to treat multi-resistant C-NORSE: A complex clinical case

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EPV-316 | Psychiatric comorbidities and quality of life of people with epilepsy in Costa Rica

C. Sequeira Quesada

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EPV-317 | Nerve blocks in emergency department for management of acute headaches: A systematic review and meta-analysis

C. Moura; R. Marcial; G. Nimer; J. Alves

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EPV-318 | Characterization of non-headache symptoms in migraine patients treated with anti-CGRP monoclonal antibodies

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EPV-319 | A comparison of greater occipital nerve block alone versus combined with trigger point injections in chronic migraine

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EPV-320 | Effectiveness and safety of cenobamate in patients with brain tumor-related epilepsy

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EPV-321 | Gender differences of migraine and tension-type headache in patients with medication-overuse headache

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EPV-322 | Clinical characteristics of sentinel headache before rupture of intracranial aneurysms

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EPV-323 | Efficacy of galcanezumab in PRRT2-associated familial hemiplegic migraine

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EPV-324 | Efficacy and safety of rimegepant for migraine prevention in subjects with medium or high frequency episodic migraine

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EPV-325 | Preventive migraine treatment optimization and shifts in headache frequency with eptinezumab: DELIVER post hoc analysis

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EPV-326 | The use of tocilizumab in new onset refractory status epilepticus: A promising therapeutic possibility

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EPV-327 | Abstract withdrawn

EPV-328 | Migraine epidemiology in Israel: A retrospective database study

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EPV-329 | Abstract withdrawn

EPV-330 | Exploring glymphatic involvement in idiopathic intracranial hypertension before and after treatment: A DTI-ALPS study

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EPV-331 | Cenobamate modulates EEG microstates enhancing epilepsy network in patients with drug-resistant temporal lobe epilepsy

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EPV-332 | Real-world effectiveness and tolerability of Lasmiditan: A prospective multicentric cohort study

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EPV-333 | Use of Cenobamate in real practice in patients with refractory epilepsy

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EPV-334 | Headaches and nonalcoholic fatty liver disease: How much is obstructive sleep apnea syndrome to blame?

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EPV-335 | The physiotherapy and rehabilitation approaches in chronic tension-type headache

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EPV-336 | Deep Brain Stimulation of the Ventral Tegmental Area (VTA) in refractory chronic cluster headache: Two case reports

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EPV-337 | Genetic testing in adolescents with epilepsy

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EPV-338 | The role of BDNF during cluster headache attack

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EPV-339 | Prognostic value of interictal EEG pattern in the control of generalized epilepsy

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EPV-340 | Mind the change: Possibility of de novo psychogenic nonepileptic seizures after epilepsy surgery

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EPV-341 | Flunarizine in migraine prophylaxis: The Turkish clinical experience

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EPV-342 | The role of gasser ganglion block and radiofrequency ablation in cluster headache

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EPV-343 | Mortality of status epilepticus in the intensive care unit from emergency institute from Chișinău

M. Vasilieva[1]; R. Racila[1]; C. Munteanu[2]; N. Gorincioi[3]; D. Ciolac[1]; I. Plesca[2]; V. Chiosa[2]; S. Groppa[2]

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EPV-344 | Super-refractory status epilepticus: Precipitating factors in a susceptible patient

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EPV-345 | Long-term efficacy and safety data about cenobamate use in focal epilepsy: A single centre real-world experience

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EPV-346 | Epilepsy risks for cognitive decline and their prevention

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EPV-347 | VNS and cenobamate: A therapeutic alliance for drug-resistant epilepsy?

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EPV-348 | Long-term perampanel effectiveness in generalized epilepsy as add-on therapy with 1 or 2 antiseizure medications

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EPV-349 | Factors associated with excessive daytime sleepiness in patients with focal epilepsy

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EPV-350 | An unexpected cause of epileptic seizures – Fahr's syndrome

H. Goldstein; L. Popa; S. Petrescu; H. Nicolae; V. Tiu; A. Daneasa; M. Popa; B. Azamfirei; L. Bica; S. Brita; C. Panea
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EPV-351 | Down syndrome and epilepsy

H. Abbashar; A. Hussein; A. Siddig; A. Abdelhaleem; A. Abbasher; M. Abbasher; S. Hamednalla; Z. Shihab; A. Algamal; A. Elamin; M. Abdulla; M. Mustafa
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EPV-352 | Pre-implantation scalp EEG can predict VNS efficacy in children

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EPV-353 | Genetic epilepsy and CDKL5 mutation: Case report

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EPV-354 | The effect of antiepileptic therapy on bone metabolism: Intermediate results

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EPV-355 | Impulsivity in episodic cluster headache

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EPV-356 | BHV-7000, a novel Kv7 potassium channel activator, demonstrates dose-dependent pharmacodynamic effects on EEG parameters

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EPV-357 | Migraine burden associated with triptan treatment satisfaction from the 2022 European National Health & Wellness Survey

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EPV-358 | Epilepsy in Alzheimer Disease; a late-stage complication or an integral part of Alzheimer Disease phenotype?

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EPV-359 | Validation of the self-assessment cognitive tool "Test Your Memory" (TYM) for people with epilepsy (PWE)

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EPV-360 | Drug resistance predictive utility of age of onset and cortical imaging abnormalities in epilepsy

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EPV-361 | Beneficial effect of Cenobamate in patients treated with vagus nerve stimulation for drug resistant epilepsy

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EPV-362 | The effect of GLP-1 agonists on idiopathic intracranial hypertension

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EPV-363 | Headache patients' characteristics and management at the emergency department

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EPV-364 | Ophthalmoplegic neuropathy, a rare cause of headache

L. Franco Rubio; P. Abizanda Saro; A. Aldaz Burgoa; L. López Trashorras; N. Rodríguez Albacete; P. Mayo; M. Malaret Segurado; J. Ortega Macho; A. Maruri Pérez; P. Gutiérrez Bedia; J. Obregón Galán
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EPV-365 | Lacrimal neuralgia: An unusual cranial neuralgia

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EPV-366 | Deep ear pain: A case report of nervus intermedius neuralgia

L. Franco Rubio; N. Rodríguez Albacete; L. López Trashorras; A. Aldaz Burgoa; P. Abizanda Saro; N. González García
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EPV-367 | Effectiveness of fremanezumab for the preventive treatment of migraine up to 12 months: PEARL Italian interim analysis

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EPV-368 | Treatment profile of adult patients diagnosed with Epilepsia Partialis Continua in a tertiary care hospital

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EPV-369 | Experience with cenobamate in drug-resistant patients in a general neurology practice of a secondary hospital

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EPV-370 | Status epilepticus as a presentation of inflammatory amyloid angiopathy. Clinical case

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EPV-371 | Recurrent syncope during migraine attacks

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EPV-372 | MRI defined structural etiology across lobar diagnoses in focal epilepsy

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EPV-373 | Seizure and non-seizure outcomes in generalized epilepsy patients: 24-month results from the CORE-VNS

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EPV-374 | "Double cortex syndrome" due to DCX gene mutation: A rare cause of distonic seizures

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EPV-375 | Neurological and ethical implications of rising botched executions in the U.S.

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EPV-376 | Unusual case of postictal cutaneous manifestation of generalized tonic–clonic seizure

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EPV-377 | Long-term patient retention rates with cenobamate in patients with different epilepsy aetiologies

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EPV-378 | Investigation of clinical characteristics and outcome of first-ever status epilepticus patients in a single center

N. Aydinli; B. Türk; M. Delil; S. Yeni; Ç. Özkara
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EPV-379 | Assessment of Toll-like receptor 4 (TLR4) biomarker in children with epilepsy

O. Constantin[1]; C. Calcii[2]; L. Feghiu[3]; E. Capestru[1]; I. Calistru[1]; S. Hadjiu[1]; S. Groppa[3]
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EPV-380 | Disrupted sleep architecture is associated with poor cognitive performance in adult patients with temporal lobe epilepsy

O. Tikhonova; A. Turchinets; F. Rider
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EPV-381 | VNS and cenobamate: A potential new run against Ultra-refractory focal lesional epilepsy?

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EPV-382 | One-year follow-up experience of epilepsy and electroencephalography in a rural center

Ö. Kizek
Gumushane State Hospital

EPV-383 | Efficacy of erenumab in patients with chronic migraine: A prospective single-center study

P. Garay Albízuri; D. Pérez Gil; B. Martínez García; A. Llanes Ferrer; G. García Alcántara; C. García Moreno; J. Masjuan; B. Zarza Sanz
Department of Neurology, Hospital Ramón y Cajal, Madrid

EPV-384 | Dealing with disclosure of risk for Parkinson's disease: A population-based pilot study

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EPV-385 | Efficacy of rimegepant for the acute treatment of migraine in women from China and South Korea

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EPV-386 | Sustained efficacy of rimegepant for the acute treatment of migraine in adults from China and South Korea

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EPV-387 | Clearing the shadows on CGRP antibodies and photophobia in migraine management

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EPV-388 | Efficacy of eptinezumab in patients with refractory chronic migraine: Is it worth it?

P. Dodu; D. Rodriguez Garcia; C. Algar Ramirez; V. Castro Sanchez
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EPV-389 | Mortality in people with epilepsy with alcohol withdrawal seizures

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EPV-390 | Electrophysiological examination of the "switch off lateralization" pattern

S. Özdemir; İ. İlgezdi Kaya; M. Özcan; A. Elmalı; N. Bebek
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EPV-391 | Two cases of focal onset seizures with amygdala enlargement

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EPV-392 | Socioeconomic disparities in clinical trials in attention deficit hyperactivity disorder and autism spectrum disorder

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EPV-393 | Evaluation of predictors of response to anti-CGRP monoclonal antibodies

V. Mendes Ferreira; G. Cabral; M. Serôdio; A. Caetano; M. Viana-Baptista
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EPV-394 | S-EEG guided thermocoagulation as a therapeutic option in drug-resistant epilepsy associated to ulegyria

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EPV-395 | Demographic description and analysis of difficulty in accessing advanced resources in a small population

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EPV-396 | Research of the effect of melatonin on cell viability and SLC7A11 in glioblastoma cell line

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EPV-397 | Non-convulsive-status-epilepticus related to leptomeningeal carcinomatosis mimicking a stroke: A first case-description

V. Laterza; L. Mumoli; A. Fratto; A. Colosimo; A. Clodomiro; E. Le Piane; R. Iannacchero; T. Tallarico; G. Frontera; A. Luccisano; D. Pirritano; M. Pantusa; D. Bosco

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EPV-398 | Causal errors in brain injury prognostication

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EPV-399 | The efficacy of GON and LON blockage for chronic migraine treatment in patients with multiple sclerosis

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EPV-400 | Headache profile of patients seen in neurology consultations at HASSAN II Hospital in Morocco

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EPV-401 | Rupture of an infected gastric artery aneurysm during treatment of Listeria monocytogenes meningitis

K. Inoue[1]; K. Yoshitaka[1]; A. Tamagake[1]; R. Ono[1]; A. Yasaka[1]; M. Otomo[1]; K. Tsukita[1]; G. Watanabe[1]; G. Yunome[2]; H. Rikimaru[3]; A. Sato[3]; Y. Suzuki[1]

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EPV-402 | Demographic and clinical characteristics of patients with Parkinson's disease in South Region of Kazakhstan

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EPV-403 | Association between Parkinson's disease and environment in south region of Kazakhstan

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EPV-404 | Functional mapping of cortical areas involved in affect discrimination using intracranial EEG

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EPV-405 | Respiratory failure (RF) in acquired motor neuron diseases (MND): Our experience with ventilatory support (VS)

G. González Toledo; A. Bartolomé Yumar; P. Helena; H. Maria José; L. Marcial; Ismael Naim; R. Jose
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EPV-406 | Post-partum onset of probable motor neuron disease in a young female

A. Ghiuta; M. Docan; E. Marin; B. Toron; L. Zurini; A. Arbune; A. Hanganu; A. Dulamea
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EPV-407 | Complex clinical conundrum: Tuberculous meningoencephalitis in a patient with concurrent HIV and SARS-CoV-2 infection

A. Resiga; A. Ribigan; M. Moldovan; I. Vasiliu; S. Stefan; F. Antochi
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EPV-408 | Capnocytophaga canimorsus meningoencephalitis secondary to a canine bite

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EPV-409 | Language as the working model of human mind

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EPV-410 | Gene mutation TBK1: A case report

A. Gómez González; C. Neurología; J. Pinel Ríos; M. Máñez Sierra; P. Carbonell Corvillo
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EPV-411 | Beyond movement: A comparative study between PD and ET using NMSQ

A. Fonseca; M. Lima; M. Seco; M. Calejo; P. Salgado
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EPV-412 | Neurological examination of patients with movement disorders via telemedicine: A systematic review

E. Angelopoulou; D. Kontaxopoulou; E. Stanitsa; S. Fragkiadaki; E. Smaragdaki; K. Vourou; C. Koros; J. Papatriantafyllou; L. Stefanis; S. Papageorgiou
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EPV-413 | Striatal dopamine transporter imaging correlates of neuropsychiatric symptoms in Progressive Supranuclear Palsy

A. Bougea; C. Koros; A. Simitsi; N. Papagiannakis; R. Antonelou; I. Pachi; C. Chrysovitsanou; Stefanis
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EPV-414 | Singin training in people with Parkinson's disease: A feasibility study

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EPV-415 | Assessment of autonomic dysfunction in Parkinson's disease: Electrophysiological insights and daily life implications

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EPV-416 | Integrative neurobiology of akathisia: Dissecting the role of basal ganglia and neurotransmitter systems

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EPV-417 | Amyotrophic lateral sclerosis: Blood brain barrier permeability and phagocytosis

D. Baranov; S. Kiryukhina; S. Labunskiy; V. Podsevatkin; N. Kolmykova
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EPV-418 | Continuous subcutaneous infusion with apomorphine or levodopa/carbidopa in Parkinson's disease: A systematic review

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EPV-419 | Deep brain stimulation in early stage Parkinson's disease: A systematic review and meta-analysis of randomized studies

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EPV-420 | Persisting cerebral vasculitis after bacterial meningitis. Report of two unusual cases

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EPV-421 | ADHD – A differential diagnosis for mild cognitive impairment in the adult

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EPV-422 | Possible H.parainfluenzae endocarditis with embolic stroke in a patient with patent foramen ovale – mimicking meningitis

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EPV-423 | Peripheral immune response pattern in a cohort of REM sleep behavior disorder patients

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EPV-424 | Anterior opercular syndrome in an immunocompetent elderly caused by herpes simplex encephalitis

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EPV-425 | A case of a stroke-like onset of ALS in a patient with TBK1 mutation

C. Meoni; C. Carlesi; F. Bianchi; L. Becattini; L. Fontanelli; B. Giovannini; G. Vadi; G. Siciliano
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EPV-426 | Down the rabbit hole

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EPV-427 | A case of HIV leucoencephalopathy during the COVID-19 pandemic

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EPV-428 | Deceptive mimicry: Neurobrucellosis masquerading as primary angiitis of the central nervous system

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EPV-429 | Intraventricular colistin in the treatment of healthcare-associated ventriculitis acinetobacter baumannii in an infant

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EPV-430 | Episodes of paroxysmal movements as an atypical presentation of a diffuse glioma

A. Garcia Maruenda; I. Martin Sobrino; M. Nieto Palomares; P. Gomez Ramirez; J. Cabello; R. Ibañez; J. Vaamonde Gamo
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EPV-431 | Headache rounds: A headache in an immunosuppressed individual

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EPV-432 | Clinically assessed walking capacity versus real-world walking performance in people with Parkinson's disease

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EPV-433 | Asymmetry of DAT SPECT imaging in Parkinson's Disease according to REM sleep behavior onset

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EPV-434 | Quantitative EEG in Parkinson's disease: When REM sleep behavior disorder onset really matters

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EPV-435 | Lower limb dystonia only during down the stairs: A rare task-specific dystonia

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EPV-436 | A case of SCA17 presentation in a young woman from Sri Lanka

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EPV-437 | Effectiveness and safety of using monoclonal antibodies against migraine in patients with a comorbid disorder

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EPV-438 | Possible non-pharmacological interventions for fatigue among Parkinson's disease patients

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EPV-439 | Are three times too many? Effect of repeated interruptions and restarts of erenumab treatment

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EPV-440 | The correlation between migraine and patent foramen ovale: An analysis in a group of patients at Berat Hospital, Albania

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EPV-441 | Visual snow syndrome in patients with migraine: Clinical features. Comparative analysis

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EPV-442 | Refinement of patient criteria in the selection process for STN-DBS in PD: An exploration of exclusionary factors

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EPV-443 | Abstract withdrawn

EPV-444 | Lyme neuroborreliosis: An unexpected cause of isolated abducens palsy

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EPV-445 | EBV complicating neuroborreliosis infection diagnosis in a female case with facial palsy

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EPV-446 | Stroke-mimicking hemiplegia as a presenting symptom of Listeria encephalitis in an immunocompromised patient

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EPV-447 | Clinical and neurophysiological follow-up of adult type III Spinal Muscular Atrophy patients treated with nusinersen

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EPV-448 | Prokineticin-2 is highly expressed in colonic mucosa of early Parkinson's disease patients

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EPV-449 | Daily and night functioning improvement in pharmacoresistant migraine patients treated with anti CGRP/R mAbs

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EPV-450 | Unravelling the complexity: A rare case of multiple sclerosis and amyotrophic lateral sclerosis and a literature review

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EPV-451 | Challenge in diagnosing spinal muscular atrophy with childhood onset

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EPV-452 | Rimegepant effectiveness and tolerability as acute migraine treatment (GAINER): A real-world multicentric Italian study

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EPV-453 | Follow-up of Nusinersen treatment in pregnancy and related considerations

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EPV-454 | Effects of the testosterone and estradiol hormones on the clinical course of cluster headache

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EPV-455 | Median nerve ultrasonography in Parkinson's disease: A systematic review and meta-analysis

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EPV-456 | Dramatic improvement of cerebral toxoplasmosis: An illustrative case from Mozambique

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EPV-457 | Cerebral toxoplasmosis presenting with confusion and headache: A case of study

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EPV-458 | Myeloradiculitis revealing an infection with the hepatitis B virus

I. Ghorbel; H. Derbali; I. Bedoui; M. Mednini; M. Messelmeni; M. Mansour; J. Zaouali; R. Mrissa
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EPV-459 | Observational pilot study on the efficacy of anti CGRP antibodies on quality of sleep and depression

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EPV-460 | Focal status epilepticus secondary to convexity subarachnoid hemorrhage due to infective endocarditis

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EPV-461 | Nummular headache: Demographics and clinical response in a case series

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EPV-462 | FaceLessInjection ParadigmStudy (FLIPAS) with onabotulinum toxin type A for chronic migraine

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EPV-463 | A rare location; Report of a case of tuberculoma in the cavernous sinus

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EPV-464 | Meningoradiculitis with involvement of the seventh nerve during Mediterranean spotted fever: A case report

F. Kchaou; K. Moalla; H. Hadj Kacem; N. Farhat; N. bouaatour; M. Damak; S. Sakka; C. Mhiri
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EPV-465 | Hemorrhagic reversible cerebral vasoconstriction syndrome caused by adrenaline and corticoids after an allergic reaction

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EPV-466 | Granulation amebic encephalitis: Diagnostic and therapeutic challenges through a case report from Morocco

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EPV-467 | Computed tomography predictors of post-stroke aphasia recovery in the acute period of ischemic stroke

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EPV-468 | Presentation of a multiphasic HaNDL syndrome patient, case present report and literature review

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EPV-469 | Exploring the relationship between fatigue and disease severity: Insights from ALS-FRS-r in ALS population

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EPV-470 | Anti-CGRP monoclonal antibodies reduce workplace disability

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EPV-471 | Cauda Equina syndrome due to varicella zoster virus infection: In relation to two clinical cases

L. López Trashorras; L. Franco Rubio; P. Abizanda Saro; A. Aldaz Burgoa; N. Rodríguez Albacete; M. García Ruiz; M. Lara González; E. López Valdés; A. Marcos Dolado; R. Ginestal López; A. Fernández Revuelta
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EPV-472 | The relationship of food components with the number of days with headache per month by patients with migraine

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EPV-473 | Treatment of hypnic headache: A single centre experience

M. Abu-Lafi; A. Avi Ashkenazi
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EPV-474 | Differences in neural activations between active and passive numerical symbol processing in large-scale brain networks

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EPV-475 | Rimegepant for acute migraine treatment across BMI categories: Pooled analysis of 4 phase 3 randomised clinical trials

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EPV-476 | Impact of personal traits on language preference by bilinguals

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EPV-477 | Orthonasal olfactory blockage determines the neural reorganization in the brain: First minutes

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EPV-478 | Central mechanisms of neural reorganization under short-term olfactory deprivation

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EPV-479 | Failure in migraine treatment with monoclonal antibodies after a positive initial response

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EPV-480 | Gender differences in idiopathic intracranial hypertension

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EPV-481 | Analysis of a series of cases of neuroborreliosis in Northern Spain

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EPV-482 | Efficacy of eptinezumab in patients with migraine reporting psychiatric comorbidities

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EPV-483 | Psychiatric comorbidities and dizziness in migraine

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EPV-484 | Unusual cause of secondary headache. A case report and literature review

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EPV-485 | Phylogenetic elucidation and philosophical inquiry into the Claustrum's implications in mammalian consciousness

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EPV-486 | A concept of viral etiogenesis of amyotrophic lateral sclerosis (ALS) in historical development

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EPV-487 | Amyotrophic lateral sclerosis – The most recent advances in understanding of pathogenesis and treatment (2023)

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EPV-488 | The effect of the psychiatric co-morbidities of migraine on medical university students: A cross-sectional study

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EPV-489 | Surviving the abyss: The diagnostic challenge of a case of herpetic encephalitis

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EPV-490 | Imaging and laboratory characteristics of case series diagnosed with probable sporadic Creutzfeldt-Jakob disease

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EPV-491 | Severe encephalitis after surgical resection of a posterior fossa hemangioblastoma

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EPV-492 | Case Report: A rare case of Neurosyphilis presenting with seizures and psychotic symptoms

S. Dirkeç; S. Üstün Özek; E. Ünal; C. Örken
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EPV-493 | Prospective study on the main side effects of the different antibodies against CGRP used in the prevention of migraine

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EPV-494 | Treacherous Lyme disease presented as a progressive lumbosacral plexopathy

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EPV-495 | Short-term psychodynamic psychotherapy as chronic migraine preventive therapy: Responders and predictive factors

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EPV-496 | The contribution of ACC to task regulation: A prospective study in patients with frontal lobe stroke

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EPV-497 | FIG4-associated disease: An aggressive amyotrophic lateral sclerosis phenotype

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EPV-498 | Clinical presentation of polyradiculoneuropathy revealing a neurological tuberculosis infection

Y. Zakaria; S. Benlamkadam; N. Kissani; M. Chraa
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EPV-499 | Headache and papilledema in IIH: An early integrated multidisciplinary management favors better outcome

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EPV-500 | Varicella zoster reactivation presented as pseudotumor cerebri in a young immunocompetent patient: A case report

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EPV-501 | A diagnostic model for Parkinson's disease based on anoikis-related genes

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EPV-502 | Efficacy and safety of efgartigimod in acute phase of neuromyelitis optica spectrum disorders: A case report

Z. Li[1]; Q. Xu[2]; J. Huang[3]; Q. Zhu[4]; X. Yang[1]; M. Zhang[1]; S. Zhang[1]; S. Huang[1]; G. Yu[1]; P. Zheng[1]; X. Qin[1]; J. Feng[1]
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EPV-503 | Wilson's disease: Clinical presentations and treatment outcomes

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EPV-504 | The whistle-smile reflex in Parkinson's disease

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EPV-505 | Dysphagia in synucleinopathies: Preliminary data of a retrospective study

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EPV-506 | Infoflex impact: Accelerating MS care through digital innovation

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Torbay and South Devon NHS Foundation Trust

EPV-507 | A decade with Duodopa®: Boon or bane?

A. Rodríguez-Vallejo; D. Alonso-Modino; J. De León-Machín; J. Lorenzo-Brito; E. Rojas-Pérez
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EPV-508 | Altered domain-specific striatal functional connectivity in patients with Parkinson's disease with urinary dysfunction

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EPV-509 | Sphingosine-1-phosphate receptor modulators induced lymphopenia – selectivity matters?

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EPV-510 | Central nervous system demyelination related to ustekinumab treatment

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EPV-511 | Kinematic signature of rigidity during passive upper limb mobilization in patients with Parkinson's disease

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EPV-512 | Online education yields significant gains in physicians' knowledge of biosimilars for multiple sclerosis

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EPV-513 | Tongue tremor as the main finding on neurological examination

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EPV-514 | Evaluation of non motor symptoms in GBA Parkinson patients in Albania

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EPV-515 | Clinical and neuroimaging features of a series of patients with diabetic striatopathy

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EPV-516 | Epidemiological aspects of Parkinson's disease in a population of southern Algeria. Dr. Bellagh Houria

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EPV-517 | Subnetwork effects of subthalamic deep brain stimulation during voluntary spiral drawing in Parkinson's disease

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EPV-518 | Siponimod from fingolimod direct switch in patients transitioning in secondary progressive multiple sclerosis

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EPV-519 | Comorbidity in multiple sclerosis: An Albanian population-based study on disease demographics

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EPV-520 | Impact assessment of rTMS with stabilometric training on neurocognitive function in progressive multiple sclerosis

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EPV-521 | Cognitive impairment and pulvinar volume alterations in MS patients

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EPV-522 | Is tremor in blepharospasm a manifestation of dystonia or a separate disease?

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EPV-523 | Writer's cramp: Our experience in North Tenerife

C. Hernández Javier; M. Hernández García; M. Fernández Sanfiel; M. Crespo Rodríguez; M. Lobato González; A. Bartolmé Yumar; I. Owrang Calvo; S. Del Águila Romero; M. Millet Oval1; J. Rojo Aladro
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EPV-524 | Acute disseminated encephalomyelitis associated with whipple disease

C. Coclitu; C. Chambon; M. Vaillant; O. Casez
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EPV-525 | Acquired demyelinating syndromes-Anti MOG antibodies associated with presence of CSF OCB-case series

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EPV-526 | Prevalence non-motor symptoms in adult Northern Thai patients with primary focal or segmental dystonia

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EPV-527 | Gene expression of inflammatory markers in multiple sclerosis disease modifying therapies

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EPV-528 | Risk factors for disease progression in patients with multiple sclerosis

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EPV-529 | Exploring the spectrum of saccadic intrusions in essential tremor

C. Terravecchia[1]; G. Mostile[1]; A. Rufa[2]; R. Terranova[1]; C. Chisari[1]; A. Salerno[1]; A. Luca[1]; G. Donzuso[1]; C. Cicero[1]; M. Zappia[1]; A. Nicoletti[1]
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EPV-530 | Nutritional status and mediterranean diet adherence in paediatric multiple sclerosis

C. Di Monaco[1]; A. Carotenuto[1]; E. Scarpato[2]; M. Serra[2]; A. Esposito[1]; M. Moccia[1]; A. Staiano[1]; V. Brescia Morra[1]; C. Mandato[3]; R. Lanzillo[1]
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EPV-531 | Atypical progression of motor symptoms in facio-scapulo-humeral dystrophy: Clinical worsening or overlap?

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EPV-532 | Transcranial alternating current stimulation of the cerebellum in cervical dystonia

D. Costa[1]; D. Birreci[1]; M. Passaretti[1]; A. Cannavacciuolo[1]; D. Colella[1]; L. Angelini[1]; G. Paparella[1]; A. Guerra[2]; A. Berardelli[1]; M. Bologna[1]
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EPV-533 | Comparative study of alpha-fetoprotein in Parkinson's disease and vascular parkinsonism

D. Akramova; G. Rakhimbaeva; T. Bobomuratov; B. Ibodov
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EPV-534 | A case of neuromyelitis optica spectrum disorder with paroxysmal dyskinesia

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EPV-535 | Lingual dystonia induced by speaking: Case series and literature review

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EPV-536 | RBD unmasked: LRRK2 and the prodromal path to Parkinson's disease

S. Datta; N. Ghosh; B. Chakraborty; M. Acharya
Indian Institute of Technology

EPV-537 | Dimethyl fumarate in relapsing–remitting multiple sclerosis: A study on patient satisfaction and treatment efficacy

D. Cetinkaya Tezer; I. Gungor Dogan; E. Uludasdemir; M. Turkkol; S. Demir
University of Health Science, Sehit Prof. Dr. Ilhan Varank Sancaktepe Training and Research Hospital, Department of Neurology

EPV-538 | How can I assess my patients with Parkinson's disease during a busy clinic day?

E. Madrigal[1]; J. Miranda[1]; G. Gámez-Leyva[1]; A. García[2]; S. Calvo[2]; L. Simon[2]; J. Rivadeneyra[2]; P. Martínez[3]; P. Mir[3]; D. Santos[4]; E. Cubo[1]
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EPV-539 | A man with dystonia and novel sequence variant in KMT2B

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EPV-540 | Expert report: Evaluation of efficacy and efficiency between safinamide and rasagiline

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EPV-541 | Cognition in patients with spinocerebellar ataxia type 1 and type 2

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EPV-542 | Uncovering the impact of deep brain stimulation on blood-based biomarkers in Parkinson's disease

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EPV-543 | Interindividual differences in the impact of adjusting the DBS frequency on upper limb bradykinesia

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EPV-544 | Dysautonomia and cognitive impairment as clinical predictors of disease progression in patients with Parkinson's disease

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EPV-545 | Cerebellar changes on MR spectroscopy in hereditary spastic paraparesis

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EPV-546 | Prevalence of deep brain stimulation in Parkinson's disease in Bologna: A population-based study

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EPV-547 | Efficacy of multidisciplinary intensive rehabilitation treatment in Parkinson's disease

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EPV-548 | Early cognitive impairment markers in Parkinson's disease

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EPV-549 | The Dashboard Vitals of Parkinson's: International screening of sleep dysfunction in the clinic

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EPV-550 | Abstract withdrawn

EPV-551 | Use of nutritional supplements and methods of complementary medicine among Parkinson's Disease patients in Lithuania

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EPV-552 | Abstract withdrawn

EPV-553 | Movement disorders in Antiphospholipid Syndrome: A case series of secondary chorea

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EPV-554 | The use of wearable sensor to detect symptomatic yet untreated early morning off periods in Parkinson's disease

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EPV-555 | Decoding slow orthostatic tremor (OT): Electrophysiology insights and a case report

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EPV-556 | Exploring Mediterranean Diet adherence in patients with Parkinson Disease and Glucocerebrosidase mutations

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EPV-557 | Clinical and genetical characteristics of Parkinson's disease patients with substantia nigra hyperechogenicity

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EPV-558 | Opicapone real-world experience in early motor fluctuations: 3-months analysis of the REONPARK study

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EPV-559 | Mutation of the ATP5F1A gene – rare case report of patient

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EPV-560 | Do cerebrovascular risk factors impact the clinical expression of idiopathic isolated adult-onset dystonia?

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EPV-561 | The impact of a 10-week intervention programme on static performance in Parkinson's disease patients

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EPV-562 | The relationship between axial posture and lower urinary tract symptoms in patients with Parkinson disease

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EPV-563 | The efficacy of stem cell therapy in patients with Parkinson's disease; A systematic review and meat-analysis

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EPV-564 | Analysis of gait parameters in Parkinson's disease and healthy individuals

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EPV-565 | Results from omega 3–6 fatty acids treatment in neurodegeneration with brain iron accumulation associated with C19orf12

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EPV-566 | Movement disorders in HIV patients: A critical challenge in developing countries

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EPV-567 | Optic neuropathy and ageusia in patient with Wilson's disease during penicillamine therapy

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EPV-568 | DNMT 1 mutation manifests as a progressive supranuclear palsy phenotype

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EPV-569 | Intestinal gel therapy for non-motor symptoms in advanced Parkinson's disease: Real-world benefits – A case study

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EPV-570 | Healthcare-centered perspective to Parkinson's disease stages

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EPV-571 | Effects of exercises programs on gastrointestinal symptoms in patients with restless legs syndrome

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EPV-572 | Safinamide vs. opicapone in fluctuating patients with Parkinson's disease in real clinical practice

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EPV-573 | Relation between subthalamic stimulation intensity and hand bradykinesia kinematics in Parkinson's disease

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EPV-574 | Is there a relation between bradykinesia and cognitive impairment in essential tremor?

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EPV-575 | The impact of non-motor symptoms on the quality of life people with Parkinson's disease of different motor subtypes

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EPV-576 | Clinical features of drug-induced paroxysmal dyskinesias

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EPV-577 | Dystonia and women: Impact on life satisfaction and psychosocial factors

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EPV-578 | Off-label levodopa use in dystonic syndromes

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EPV-579 | Tobacco induced visual symptoms in heavy smokers – Can they be real?

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EPV-580 | Abstract withdrawn

EPV-581 | An interesting case of young onset parkinsonism due to PLA2G6 gene mutation related dystonia Parkinsonism

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EPV-582 | Neuromodulation hypothesis in normal pressure hydrocephalus

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EPV-583 | Reversible hemifacial spasm as a complication of diabetic ketoacidosis

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EPV-584 | Differences and association in WOQ-19 score between people with Parkinson's disease and caregivers

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EPV-585 | The Vall d'Hebron initiative for PD: Searching for biomarkers

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EPV-586 | A comparison between essential tremor and Parkinson's disease: An acoustic study

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EPV-587 | Survey of the knowledge, attitudes, and practices of neurologists regarding exercise in Parkinson's disease

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EPV-588 | Insomnia in Parkinson's disease and quality of life

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EPV-589 | A case of neuroleptic malignant syndrome: An important differential from autoimmune encephalitis

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EPV-590 | Quality of life in patients with neurodegenerative cerebellar ataxias

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EPV-591 | Exploring the dynamic advancements in Parkinson's disease patients through a 10-week intervention programme

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EPV-592 | Dystonic tremor in systemic lupus erythematous and antiphospholipid syndrome

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EPV-593 | Early onset cervical dystonia associated with mutation in CACNA1A gene

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EPV-594 | Assessing turn characteristics in advanced PD patients – A motion sensor study

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EPV-595 | Peculiarities of bioelectrical activity of the brain in patients with Wilson's disease

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EPV-596 | Effect of STN-DBS on speech in a patient with Parkinson's disease: Fine-tuning with short pulse width stimulation

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EPV-597 | The European Huntington's Disease Network (ehdn.org): A platform for diverse collaboration

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EPV-598 | Differences in the severity of non-motor symptoms between brain-first and body-first Parkinson's disease

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EPV-599 | Levels of changes in NO-system parameters in vascular Parkinsonism

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EPV-600 | Analysis of risk factors affecting the development of vascular parkinsonism by gender

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EPV-601 | Clinical application and evaluation of optic neuritis diagnostic criteria: A single center clinical experience

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EPV-602 | Early serious adverse events under alemtuzumab in multiple sclerosis. Should we continue with subsequent cycles?

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EPV-603 | Functional near infrared spectroscopy in early multiple sclerosis: A pilot study on cognitive performance

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EPV-604 | Cost-minimisation analysis of natalizumab biosimilar compared to reference natalizumab for multiple sclerosis

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EPV-605 | Peculiarities of primary comorbid headache in patients with progressive multiple sclerosis

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EPV-606 | Sleep quality in multiple sclerosis: A systematic review and meta-analysis

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EPV-607 | Clinical and radiological features in multiple sclerosis patients with coexisting familial mediterranean fever

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EPV-608 | Gait parameters/cognitive function correlation in a myotonic dystrophy type 1 cohort: A sensor-based gait analysis

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EPV-609 | Abstract withdrawn

EPV-610 | Prevalence, characteristics and impact of headache in patients with multiple sclerosis: A cross sectional study

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EPV-611 | Presentation and diffusion of BRAINTEASER: Bringing Artificial INTelligencE home for a better cAre of ALS and MS.

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EPV-612 | Multicentric descriptive study of MOG associated disease patients in Peru

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EPV-613 | Francophone expert consensus on smouldering MS: Physiopathology, measures, and unmet needs

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EPV-614 | Identifying early predictors of long-term disability in multiple sclerosis: A decade of follow-up

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EPV-615 | Multiple Sclerosis (MS) and Amyotrophic Lateral Sclerosis (ALS): Advancing clinical decision making through wearables

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EPV-616 | A puzzling case of abrupt and atypical onset of multiple sclerosis

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EPV-617 | Psoriasis-multiple sclerosis association: Findings from an observational study

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EPV-618 | Evaluating the necessity of antiviral prophylaxis for hepatitis B reactivation in MS patients treated with ocrelizumab

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EPV-619 | Sexual disorders in patients with relapsing–remitting multiple sclerosis

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EPV-620 | Single center experience using siponimod in active SPMS

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EPV-621 | Evaluation of psychiatric characteristics in children of parents with multiple sclerosis

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EPV-622 | Evaluating the non-infectious elevation of acute-phase reactants in alemtuzumab treatment for multiple sclerosis

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EPV-623 | Advancing MOGAD diagnosis: Clinical experience with a sensitive cell-based flow cytometric assay

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EPV-624 | Long-term Cladribine treatment: Assessing additional treatment cycles

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EPV-625 | How should we manage stable patients treated with Cladribine after year four? A real-world experience in Rome

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EPV-626 | Sleep disorders and sleep disturbances in persons with multiple sclerosis

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EPV-627 | Serum levels of brain-derived neurotrophic factor and interleukin-6 in multiple sclerosis

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EPV-628 | Being highly sensitive person negatively impacts on cognitive and psychosocial fatigue in multiple sclerosis patients

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EPV-629 | Dietary patterns are associated with clinical disability in multiple sclerosis

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EPV-630 | Not just a childhood disease: A case report of Acute Disseminated Encephalomyelitis (ADEM) in an elderly patient

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EPV-631 | K-index as marker of inflammation is not related to cognitive impairment in naive multiple sclerosis patients

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EPV-632 | The impact of the economic and health crisis on people with multiple sclerosis and their access to treatment in Lebanon

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EPV-633 | Primary care physicians' greatest obstacles in detecting multiple sclerosis early

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EPV-634 | Correlation of cranial volume with cognitive scales in patients diagnosed with clinical isolated syndrome

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EPV-635 | Endotoxin is detectable in the cerebrospinal fluid of a subset of patients with multiple sclerosis

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EPV-636 | Apathy in early relapsing remitting multiple sclerosis

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EPV-637 | Self-reported fatigue in early relapsing remitting multiple sclerosis

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EPV-638 | Rare cases of infectious complications of anti-B-cell therapy for multiple sclerosis

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EPV-639 | Affective empathy is significantly increased in MS: An observational study of 300 patients

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EPV-640 | Double-negative neuromyelitis optica triggered by herpes zoster infection: Case report

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EPV-641 | Impact of COVID-19 pandemic on treatment decisions in MS: A prospective 4-year observational study in Poland

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EPV-642 | Enhancing disability measurement in multiple sclerosis: The promising role of the single leg stance test

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EPV-643 | Is there a relationship between retinal nerve fiber layer thickness, disability and cervical lesion load?

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EPV-644 | Tremor in multiple sclerosis

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EPV-645 | Resilience of patients with multiple sclerosis in the conditions of war in Ukraine

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EPV-646 | Brain-derived neurotrophic factor and progression in multiple sclerosis

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EPV-647 | The possibilities of using siponimod for patients with multiple sclerosis and older than 65 years

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EPV-648 | Evaluation of the effectiveness of therapy using biomarkers in patients with multiple sclerosis receiving interferons

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EPV-649 | Treatment satisfaction is associated with various PROMs in patients with relapsing–remitting multiple sclerosis

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EPV-650 | Trajectories of cognitive performance and PROMs in treatment-naïve and switching MS patients: A real-world study

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EPV-651 | Long-term alemtuzumab use: Real-world insights

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EPV-652 | The current landscape of global multiple sclerosis research efforts

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EPV-653 | Family history of multiple sclerosis (FSM) among patients of the Center in Zabrze – a pilot study

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EPV-654 | Cladribine in a Portuguese centre: Unveiling predictive factors, discontinuation patterns and safety insights

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EPV-655 | Atypical onset multiple sclerosis: A systematic review

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EPV-656 | Correlation of cognition and fatigue with balance and accelerometer-measured physical activity in patients with RRMS

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EPV-657 | Etiopathogenic and therapeutic considerations in a multiple sclerosis case with acute toxic hepatitis

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EPV-658 | Flammer's syndrome symptoms in patients with multiple sclerosis

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EPV-659 | Modelling predictors of relapsing adult myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD)

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EPV-660 | Vitamin D supplementation practices among multiple sclerosis patients in Malta

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EPV-661 | Lhermitte's sign as a predictor of imaging and neurophysiological changes in the diagnosis of myelopathy

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EPV-662 | Real-world data about dimethyl fumarate use in RRMS – Experience from Montenegro

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EPV-663 | Satralizumab use in NMOSD patients – Experience from Montenegro

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EPV-664 | Comparison of ocrelizumab efficiency in naïve patients and those switched from first- and second-line treatments

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EPV-665 | Correlation between sleep quality and cognitive function in multiple sclerosis

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EPV-666 | Headaches in the prodromal period of multiple sclerosis

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EPV-667 | The role of selected neurodegeneration, inflammatory and signaling parameters in the pathogenesis of MS

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EPV-668 | Optic nerve diameter and orbital circulation as predictors of progression in multiple sclerosis: A comprehensive review

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EPV-669 | Does serum neurofilament light chain measurement influence therapeutic decision-making in multiple sclerosis?

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EPV-670 | Multiple sclerosis and legal capacity

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EPV-671 | Assessment of disease-modifying treatment retention among patients with multiple sclerosis in Morocco

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EPV-672 | Central vein sign – A helping tool in atypical presentations of multiple sclerosis

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EPV-673 | Demographic and clinical characteristics of pediatric-onset multiple sclerosis patients in Turkey

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EPV-674 | Relapsing remittent multiple sclerosis debut after IL-4 inhibitor initiation for atopic dermatitis – A case report

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EPV-675 | Late progressive multifocal leukoencephalopathy recurrence after natalizumab withdrawal despite immune recovery

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EPV-676 | Atypical onset of multiple sclerosis: The uncommon presentation of numb Chin syndrome

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EPV-677 | Analysis of MS patients treated with natalizumab or fingolimod – 5 year observational study

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EPV-678 | The evaluation of cognitive impairment in multiple sclerosis patients in a second-level hospital: If you want, you can

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EPV-679 | Role of new prognostic factors when making decisions in neuromyelitis optica spectrum disorder

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EPV-680 | Assessing neurologists' care-related regret and its impact in decision making in neuromyelitis optica spectrum disorder

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EPV-681 | Radiologically Isolated Syndrome (RIS): The role of serum neurofilament light chain measurement in therapeutic decisions

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EPV-682 | Correlating clinical features with radiomic profiles in multiple sclerosis: Insights from MRI analysis

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EPV-683 | Impact of initial symptomatology and relapse dynamics on the progression of multiple sclerosis: A longitudinal analysis

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EPV-684 | Evaluating disability milestones in multiple sclerosis: A longitudinal study of disease progression

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EPV-685 | Brain gadolinium deposition in patients with MS receiving Natalizumab for extended periods

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EPV-686 | Patient-reported outcomes for Glatzi® (Glatiramer Acetate 40 mg) in patients with relapsing–remitting multiple sclerosis

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EPV-687 | Factors related to willingness to childbearing in women with MS

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EPV-688 | Fatigue and pain in people with multiple sclerosis: Discriminator factor analysis

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EPV-689 | Prodromal headache in optic neuritis with anti-myelin oligodendrocyte glycoprotein antibodies

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EPV-690 | Two-year longitudinal monitoring of corticospinal tract integrity in relapsing remitting multiple sclerosis

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EPV-691 | Experience with cladribine in multiple sclerosis patients in Montenegro: A national cohort study

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EPV-692 | Experience with natalizumab in multiple sclerosis patients in Montenegro: A national cohort study

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EPV-693 | Efficacy and safety of two therapeutic strategies in a multiple sclerosis population of Afro-Caribbean descent

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EPV-694 | The effect of ocrelizumab on the risk and outcome of Covid-19 infection in patients with multiple sclerosis

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EPV-695 | Epidemiology, clinical course and characteristics of MS in the Fergana region

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EPV-696 | Long term management with cladribine tabs: What to expect? Real-world clinical outcomes for years 1 and 2 in Greece

V. Deligianni; E. Kouremenos; O. Sideri; I. Spanou; K. Kournis; N. Skarli; C. Toilos
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EPV-697 | Relationship between kappa light chain level and demyelinating lesion localization in SPMS

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EPV-698 | Evaluation of the impact of autonomic dysfunction on the quality of life in multiple sclerosis patients

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EPV-699 | Association between multiple sclerosis and epilepsy

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EPV-700 | Utility of routine MRI in patients with multiple sclerosis (pwMS) on disease modifying therapies (DMTs)

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EPV-701 | Long-term follow up of patients with late-onset Pompe disease, treated with Enzymatic Replacement Therapy

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EPV-702 | SQSTM1 Pro392Leu presenting as a corticobasal syndrome

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EPV-703 | Exploring genetics associated with Parkinson's disease in deep brain stimulation outcomes

A. Fernandes[1]; C. Soares[1]; J. Massano[1]; A. Oliveira[1]; R. Araújo[1]; C. Chamadoira[2]; M. Rito[2]; C. Reis[3]; C. Silveira[4]; J. Lima[5]; C. Sousa[5]; M. José Rosas[1]
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EPV-704 | Diagnostic uncertainty in neurology: How much eludes diagnosis

A. Aguilar Monge; C. Ortega Hiraldo; A. Gomez Gonzalez; M. Vicente Dominguez; V. Delgado Gil
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EPV-705 | Formulation and standardization of frontotemporal lobar degeneration database in North Macedonia

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EPV-706 | Lambert-Eaton myasthenic syndrome in a Sicilian cohort of patients: A clinico-neurophysiological and therapeutic study

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EPV-707 | A rare mutation in autossomic recessive spinocerebellar ataxia type 10

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EPV-708 | Gene therapy approach for metachromatic leukodystrophy using recombinant adeno-associated virus encoding human Arsa gene

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EPV-709 | Evaluation of behavioural problems in the VISION-DMD study of vamorolone vs prednisone in Duchenne muscular dystrophy

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EPV-710 | Usefulness and feasibility of a self-monitoring diary for management and follow-up of patients with myasthenia gravis

A. Nuredini[1]; F. Stragliati[1]; P. Anceschi[1]; S. Romano[1]; G. Libelli[1]; A. D'Orsi[1]; I. Allegri[2]; E. Chierici[2]; E. Saccani[2]
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EPV-711 | Cognitive impairment associated to bladder dysfunction and ataxia

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EPV-712 | Extending the spectrum: Elderly-onset vanishing white matter disease

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EPV-713 | Canvas and sleep disorders: A prospective cross-sectional study

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EPV-714 | Prevalence of diabetic neuropathy in type 2 diabetes patients and its impact on quality of life in Pakistan

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EPV-715 | Diagnostic challenges in diplopia, ophthalmoplegia and Parkinsonism: A case report associated with POLG mutation

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EPV-716 | Multiple sclerosis in Albania: A 20 year-old history

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EPV-717 | Rituximab in myastenia gravis: A single center experience

C. Erra; F. Tuccillo; D. Ricciardi; B. De Martino; A. Fasolino; F. Habetswallner
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EPV-718 | Use of goal attainment scaling to identify relevant central nervous system domains in myotonic dystrophy type 1

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EPV-719 | Sudden-onset adult-onset Alexander disease and the concept of GFAP toxicity

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EPV-720 | Impact of HLADRB1 alleles on clinical and neuroimaging profile in hellenic pediatric onset multiple sclerosis patients

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EPV-721 | Meningitis mortality: A retrospective and observational study on Brazilian epidemiology

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EPV-722 | Different posology due to synthetic protein allergy during eculizumab therapy in a patient with myasthenia gravis

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EPV-723 | Comprehensive analysis of functional neurological disorders over a decade: Insights from a cohort study

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EPV-724 | Ocular myasthenia gravis: Determining the predictive factors of secondary generalisation

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EPV-725 | L-dopa-responsive Parkinsonism and down-beat nystagmus as first manifestation of SCA27B. A new red flag?

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EPV-726 | Eculizumab in refractory generalized Myasthenia Gravis: A single center 1 year experience

D. Ricciardi; F. Tuccillo; C. Erra; A. Fasolino; B. De Martino; F. Habetswallner
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EPV-727 | Myasthenia gravis control: Evolution over eight years of follow-up and patient characteristics

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EPV-728 | Epilepsy in relation to a case of a new variant in DLG4-related synaptopathy

D. Rodriguez Garcia; C. Algar; R. Dodu; P. Cabezudo Garcia; P. Serrano Castro; G. Garcia Martin
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EPV-729 | Descriptive study of Guillain-Barre syndrome in the health area of the Guadalajara Hospital (Spain)

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EPV-730 | Unraveling Isaacs Syndrome: A rare case of acquired neuromyotonia

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EPV-731 | The role of TGFbeta-1 and VEGFA gene in the development of cerebrovascular disorders in obesity

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EPV-732 | CANVAS family in Turkey: A report of five cases in one family

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EPV-733 | The role of IL1beta C3953T gene polymorphism in post-infectious encephalopathy

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EPV-734 | Titin variants of uncertain significance and myopathy

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EPV-735 | Potential genetic markers of multiple sclerosis in multi-incident Libyan families

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EPV-736 | Prevalence of psychiatric disorders in a neurofibromatosis 1 adult cohort

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EPV-737 | A case of lissencephaly-9 caused by a novel mutation in the MACF1 gene

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EPV-738 | CHCHD2 and DNAJC6 double gene mutation in an Italian patient with early-onset Alzheimer's disease

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EPV-739 | Mitochondrial encephalopathy due to the novel compound heterozygous variants c.182C > T and c.446A > AG in NARS2

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EPV-740 | Secondary symptomatic dystonia with a genetic cause

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EPV-741 | Defining the demographic and clinical characteristics of sleepy patients with myotonic dystrophy type 1 (DM1)

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EPV-742 | Beyond ALS: A case of facial onset sensory and motor neuronopathy (FOSMN)

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EPV-743 | Eculizumab versus rituximab for refractory acetylcholine receptor-positive generalized myasthenia gravis

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EPV-744 | Insight into inter-individual phenotypic differences in Korean patients with 16p11.2 deletion

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EPV-745 | Significance of light kappa chains in patients with seronegative myasthenia gravis (MG)

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EPV-746 | Endovascular thrombectomy complications due to vascular frailty in a patient with ACTA2 mutation

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EPV-747 | Clinical and genetic features of CANVAS: A single centre cohort experience

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EPV-748 | "Eyes wide shut": The challenging diagnosis of botulism – a case report

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EPV-749 | Phenotype variations within a family with Col4A1 mutation

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EPV-750 | A comprehensive review of neurological adverse events linked to mRNA Covid-19 vaccines

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EPV-751 | Hemorrhagic transformation in ischemic stroke after intravenous thrombolysis

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EPV-752 | Who should undergo thymectomy in non-thymomatous Myasthenia Gravis? Results from the Swedish Myasthenia Gravis Register

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EPV-753 | Late onset progressive external ophthalmoplegia caused by recessive MYH2-related myopathy

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EPV-754 | A novel FHL1 variant associated with adult-onset myopathy in a Portuguese family

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EPV-755 | Frequency and characteristics of intravenous immunoglobulin-associated headache

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EPV-756 | Mitochondrial dysfunction in phosphaturic mesenchymal tumor-induced myopathy and various clinical presentations of PMT

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EPV-757 | Navigating the enigma: Idebenone efficacy discrepancy in DNAJC30-associated mitochondrial disease

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EPV-758 | Prediction of refractory myasthenia gravis based on response to treatment within the first year from diagnosis

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EPV-759 | Ends of the PNPLA6-spectrum: Report of 2 cases

L. Santos Sánchez de las Matas; C. Ordás Bandera; B. Álvarez Mariño; J. Martínez Ramos; Á. Bonelli Franco; D. Landaeta Chinchilla; I. Llera López; N. Barbero Bordallo; A. Querejeta Coma
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EPV-760 | Boucher-Neuhauser syndrome; A novel missense mutation in the PNPLA6 gene in two siblings

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EPV-761 | Mitochondrial disorders are associated with morphological neuromuscular junction defects

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EPV-762 | Metabolic defects as a potential therapeutic target in Type 1 Myotonic Dystrophy

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EPV-763 | Impending myasthenic crisis successfully treated with ravulizumab

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EPV-764 | Epilepsy phenotype in KCNK4-related neurodevelopmental syndrome: A novel case and literature review

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EPV-765 | External respiration parameters in neuromuscular (NMD) patients with repeat expansion diseases

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EPV-766 | Malignant catatonia or neuroleptic malignant syndrome: When in doubt, same approach?

M. Capra; C. Gómez López de San Román; M. Vargas Cobos; D. Cerdán Santacruz; L. Caballero Sánchez; A. Castrillo Sanz; A. Mendoza Rodríguez; I. Bermejo Casado
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EPV-767 | Dropped head: Myasthenia gravis or Parkinsonism? The role of neurophysiology

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EPV-768 | Evaluation of cognitive decline, depression and subclinical atherosclerosis in patients with atrial fibrillation

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EPV-769 | Coexistence of hereditary spastic paraplegia and sodium chanel myotonia in a family

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EPV-770 | Rituximab in acethylcholine receptor antibody-positive myasthenia gravis: A Slovenian single centre experience

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EPV-771 | Cancer frequency and type in myotonic dystrophy, FSHD, and OPMD

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EPV-772 | The impact of nusinersen in adult spinal muscular atrophy type III beyond the central nervous system

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EPV-773 | Vanishing white matter disease in adulthood

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EPV-774 | Generalized myasthenia gravis case series: Patients with myasthenia gravis switching from eculizumab to ravulizumab

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EPV-775 | Novel case of longitudinally complete spinal cord lesion with proposed "Ram" sign

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EPV-776 | The complex connection between myasthenia gravis and its association to depression

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EPV-777 | The modified Neurological Impairment Scale to measure neurologic severity and complexity in acute setting

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EPV-778 | Understanding epilepsy stigma: Rural and urban female patients in a developing nation

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EPV-779 | Management of presymptomatic juvenile patients with Late-Onset Pompe Disease

M. Porcino; O. Musumeci; I. Arena; C. Usbergo; C. Rodolico; A. Toscano
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EPV-780 | Use onasemnogene abeparvovec for treatment spinal muscular atrophy

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EPV-781 | Asymptomatic/paucisymptomatic creatine kinase elevation in the neuromuscular disorders outpatient setting

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EPV-782 | Immune checkpoint inhibitor – Induced neuromuscular adverse events: Clinical findings and management of two cases

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EPV-783 | Whole-exome-sequencing in cerebellar ataxia: Broadening the clinical and treatment spectrum

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EPV-784 | Efgartigimod in AChR-Ab positive myasthenia gravis: A 2-year experience

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EPV-785 | Neuromuscular immune-related adverse events of checkpoint inhibitors. A case series at a hospital in Argentina

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EPV-786 | Complete inhibition of the classical complement pathway with IM-101, a novel anti-C5 antibody, in a Phase I study

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EPV-787 | Ocular myasthenia gravis mimics

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EPV-788 | Autoimmune thrombocytopenia in a patient with generalised Myasthenia Gravis in treatment with Eculizumab: A case-report

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EPV-789 | Thymoma-associated autoimmune diseases responsive to efgartigimod: A case report

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EPV-790 | Facial diplegia as a prominent symptom in sporadic Inclusion Body Myositis

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EPV-791 | Expanding the phenotype of Filamin C-related myopathies

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EPV-792 | Cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS) presenting as asymmetrical neuropathic pain

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EPV-793 | Efficacy and safety of steroids for chronic subdural hematoma: A systematic review and meta-analysis

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EPV-794 | Clinical variability in desminopathies: Description of two families

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EPV-795 | Respiratory course in a population of patients with facioscapulohumeral dystrophy: A retrospective study

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EPV-796 | Quality of life in patients with different neuromuscular diseases from the same cultural background

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EPV-797 | The Swedish Myasthenia Gravis registry: A nationwide, population-based high coverage registry

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EPV-798 | Efgartigimod in immune-checkpoint inhibitor induced myasthenia gravis, myocarditis and myositis: A case report

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EPV-799 | 'Like mother like daughter' A rare late-onset ataxia case: Spinocerebellar ataxia type 36

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EPV-800 | Long-term hospital readmission after non traumatic subarachnoid hemorrhage in a population-based study

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EPV-801 | Theranostic CEST-enhanced thermoresponsive hydrogel drug delivery system for postsurgical treatment of glioblastoma

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EPV-802 | Myasthenia gravis and systemic lupus erythematosus, a rare but important association regarding diagnosis and treatment

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EPV-803 | Anti-IgLON5 disease: A challenging diagnosis

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EPV-804 | The unexpected clinical course of NMOSD

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EPV-805 | Antineuronal antibodies for CASPR2 identified in two elderly men undergoing dementia investigations

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EPV-806 | Anti-HMGCR Ab myopathy treated with IVIG infusions: A case series

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EPV-807 | CLOCC secondary to chronic treatment with metronidazole

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EPV-808 | Overlapping and distinguishing neuroimaging features of the CNS demyelinating disorders: MS, NMOSD, and MOGAD

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EPV-809 | Assessing the impact of early de-escalation in aggressive multiple sclerosis: Clinical outcomes and functional capacity

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EPV-810 | Dimethyl fumarate vs. teriflunomide: Comparing effects on physical and psychological parameters in MS treatment

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EPV-811 | Disease activity in NMOSD and MOGAD patients during SARS-CoV-2 vaccination

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EPV-812 | Toxic multifocal leukoencephalopathy associated with cocaine use: Differential diagnosis

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EPV-813 | Clinical and immunologic spectrum of GQ1b syndrome in a third-level centre

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EPV-814 | Increased central obesity correlates with physical activity and food processing in multiple sclerosis

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EPV-815 | Multiple sclerosis and headache: A possible link?

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EPV-816 | Limbic encephalitis in patient with Crohn's disease

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EPV-817 | Pseudotumoral lesion as onset in multiple sclerosis

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EPV-818 | Anti-LGI1 encephalitis as a possible paraneoplastic manifestation of Langerhans cell histiocytosis: A case report

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EPV-819 | Multifocal toxic leucoencephalopathy due to cocaine

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EPV-820 | A case of cerebral venous thrombosis in MOGAD: Causal or casual association?

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EPV-821 | Rare case of juvenile Lupus with neuromyelitis optica spectrum disorder presenting as area postrema syndrome

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EPV-822 | Progressive aphasia as presenting symptom of anti-NMDAR encephalitis (A-NMDAE) and pancreatic tumour: A case report

A. Garcia Maruenda; I. Martin Sobrino; P. Gomez Martinez; M. El Harmochi Daoud; A. Sánchez Gómez; A. Hernandez Gonzalez
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EPV-823 | Sensitivity and specificity of FL-CBA versus IFA for NMO-IgG detection in neuromyelitis optica patients

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EPV-824 | Anti-neurofascin186-related neuropathy mimics Miller-Fisher syndrome: A case report

E. Baroncelli[1]; M. Bellucci[1]; C. Castellano[1]; E. Mobilia[2]; A. Lechiara[2]; G. Pesce[2]; C. Cabona[3]; L. Roccatagliata[4]; A. Schenone[1]; L. Benedetti[3]
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EPV-825 | Changes on EEG before the development of epilepsy

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EPV-826 | Efficacy and safety of biologic agents in neuromyelitis optica spectrum disorder. A systematic review and meta-analysis

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EPV-827 | Seasonal variation in myasthenia gravis incidence

S. Falso[1]; P. Zara[2]; S. Marini[1]; M. Puci[3]; E. Sabatelli[4]; G. Sotgiu[2]; M. Marini[1]; G. Spagni[5]; A. Evoli[1]; P. Solla[2]; R. Iorio[4]; E. Sechi[2]
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EPV-828 | Orbital inflammatory syndrome: Case series and review of literature

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EPV-829 | Immunotherapy and stroke: A case report

M. García Huguet; R. Ferrer Tarrer; C. Vera Cáceres; I. Saurina; C. Martínez; J. Serena; J. Álvarez-Cienfuegos; M. Terceño Izaga; S. Bashir; Y. Silva Blas
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EPV-830 | Assessment of clinical prognosis in autoimmune encephalitis: Girona Score

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EPV-831 | Autoimmune encephalitis-like malignant brain tumor: Case report and systematic review of the literature

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EPV-832 | Dark white matter

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EPV-833 | A multicenter study in Western Sicily, Southern Italy of immune mediated syndromes associated to onconeural antibodies

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EPV-834 | Clinical and immunological characteristics of epileptic encephalopathy in early childhood

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EPV-835 | Sarcoidosis-associated progressive multifocal leukoencephalopathy treated with infliximab

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EPV-836 | MOG IgG subtyping in differential diagnosis of MOGAD and multiple sclerosis: A focused study

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EPV-837 | An unexpected turn: Vertigo as the only telltale symptom of cerebellar hemangioblastoma

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EPV-838 | Neurological toxicity associated with immune checkpoint inhibitors: A case series study

P. Hernández Vitorique; M. Mañez Sierra; J. Pinel Rios; M. Afkir Ortega; M. Vicente Domínguez; P. Carbonell Corvillo
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EPV-839 | Neuromyelitis optica spectrum in the elderly: About four cases

I. Ghorbel; H. Derbali; M. Mednini; D. Hadjkacem; M. Mansour; J. Zaouali; R. Mrissa
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EPV-840 | Immune checkpoint inhibitor-related neuromuscular toxicity: An observational monocentric study

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EPV-841 | NMDAR-Ab spectrum disorders: A new entity? An unusual case of recurring inflammatory transverse myelitis

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EPV-842 | Descriptive analysis of autoimmune encephalitis. A case series

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EPV-843 | Epidemiological, clinical, therapeutic and functional differences between adults and children in ADEM

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EPV-844 | Imaging pattern might be different in dementia patients of positive brain amyloid PET with depression

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EPV-845 | Motor symptoms in anti-Hu paraneoplastic syndrome

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EPV-846 | The importance of early immunotherapy in anti-LGI1 encephalitis: Case report and systematic review of the literature

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EPV-847 | Neurosyphilis mimicking limbic encephalitis – A case report

K. Teo; A. Jiang; Y. Goh; K. Yip; J. Boey; A. Hui
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EPV-848 | Prognostic risk factors and clinical characterization of Susac's syndrome

L. Fuchs[1]; I. Vigiser[2]; H. Kolb[2]; K. Regev[2]; D. Zur[3]; Z. Habot-Wilner[3]; Y. Oron[4]; V. Furer[5]; O. Elkayam[5]; N. Shimon[6]; M. Hellmann[7]; I. Lotan[7]; E. Auriel[7]; A. Wilf-Yarkoni[7]; A. Karni[2]
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EPV-849 | Immunophenotyping of lymphocytes in patients with multiple sclerosis who interrupted natalizumab therapy

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EPV-850 | MRI factors predictive of progression from clinically isolated syndrome (CIS) to multiple sclerosis (MS)

N. Lakri; Y. Koubci; H. Bouzenada
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EPV-851 | Therapeutic challenge: Anquilosant spondylitis and concomitant multiple sclerosis

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EPV-852 | Not every serpinginous lesion is an arteriovenous malformation

L. Caballero Sánchez; C. Gómez López de San Román; M. Capra Remedi; M. Vargas Cobos; D. Cerdán Santacruz; I. Bermejo Casado; A. Castrillo Sanz; A. Mendoza Rodríguez
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EPV-853 | Quantification of the pyramidal tract pathology in highly active multiple sclerosis using diffusion tensor MRI

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EPV-854 | Cerebral vascular lesions in moldovan Parkinson's cohort

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EPV-855 | A novel use and dramatic efficacy of ofatumumab for seronegative autoimmune encephalitis: A case report

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EPV-856 | Characterizing cross presenting dendritic cells in CNS border compartments using a murine model of multiple sclerosis

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EPV-857 | Cotard's Syndrome as manifestation of autoimmune encephalitis

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EPV-858 | Falcotentorial meningioma: Clinical manifestations and management approach. A case report

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EPV-859 | Recurrent facial palsy as the sole neurological manifestation in Behcet disease (BD)

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EPV-860 | Cerebral air embolism after an endoscopic procedure: An infrequent cause of ischaemic stroke

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EPV-861 | Central diabetes insipidus, optic neuropathy and cerebral venous thrombosis in a young male: A rare CNS mishmash

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EPV-862 | New strategies in the diagnosis of ischemic stroke in women in Dagestan

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EPV-863 | Case report: Repeated late-onset neutropenia after ofatumumab treatment in a patient with multiple sclerosis

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EPV-864 | Combined central and peripheral demyelination: A small case series

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EPV-865 | Polymorphisms/gene variations in hemostasis-related genes in patients with ischemic stroke

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EPV-866 | Posterior circulation stroke (PCS) mimics. When the Head CT misleads the diagnosis

M. Hernandez Garcia; C. Hernandez Javier; D. García Alvarez; M. Lobato Gonzalez; A. Bartolome Yumar; J. Rojo Aladro
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EPV-867 | Hypomyelinating leukodystrophy with TUBB4A mutation and concominant mutation in the Spast gene, a case report

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EPV-868 | Transcranial brain sonography characteristics of neurosarcoidosis

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EPV-869 | Central and peripheral neurological involvement in MPO-ANCA-associated vasculitis: A diagnostic case report

M. Vicente Domínguez; C. Ortega Hidalgo; P. Hernández Vitorique; F. Pinel Rios; P. Carbonell Corvillo
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EPV-870 | A young woman with neuromyotonia, NMOSD, MG and SLE: Looking for tolerance

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EPV-871 | SNCA expression in synucleinopathies

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EPV-872 | Norepinephrine inhibits monocyte-induced Th17-/Th1-immune response in multiple sclerosis

M. Melnikov; O. Belousova; A. Lopatina
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EPV-873 | Imaging predictive factors of outcome after intravenous thrombolysis in acute ischemic stroke

E. Smaoui; K. Moalla; N. Farhat; S. Sakka; S. Daoud; N. Bouattour; M. Damak; C. Mhiri
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EPV-874 | Is COVID-19 mRNA vaccination related with autoimmune thrombotic thrombocytopenia with cerebral sinus thrombosis?

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EPV-875 | Advanced age guillain Barre syndrome case

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EPV-876 | Thalamic asymmetry in multiple sclerosis

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EPV-877 | Decades lost: Metachromatic leukodystrophy masquerading as a psychiatric disorder

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EPV-878 | Hypertrophic pachymeningitis (HP): A diagnostic and therapeutic challenge. Two cases reports

P. Gómez Ramírez; I. Martín Sobrino; M. Nieto Palomares; A. García Maruenda; M. El Harmochi Daoud; A. Sánchez Gómez; L. Quirós Illán; A. Mateos Romero; P. Otero Fernández; A. Hernández González; M. Del Real Francia
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EPV-879 | A MRI-based radiomics-clinical machine learning model for predicting radiation-induced temporal lobe injury

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EPV-880 | HHV-6 associated transverse myelitis: A case report and literature review

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EPV-881 | Myasthenia gravis and acute immune-mediated polyneuropathy. Simultaneous onset and diagnosis

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EPV-882 | Association of serum albumin levels with outcome in intravenous immunoglobulin–treated Guillain-Barre syndrome

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EPV-883 | Off-label rituximab use for neurological indications; observational data to assist with prescribing decisions

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EPV-884 | Neuroimaging and management controversials of Spontaneous Intracranial Hypotension (SIH): Description of 4 cases

P. Mahiques Ochoa; M. Warken Miralles; P. Ros Arlanzón; L. Ruiz-Escribano Menchén

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EPV-885 | Limbic encephalitis with anti Ma2 antibodies, associated with immunotherapy in renal cancer

P. Pinzón Benavides; A. Jimeno Hermoso; M. Martínez Palicio; D. Alonso Vallina; A. Cordero Novo; P. Rozas Fernández

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EPV-886 | Neuroimaging to enhance neurological diagnosis in Uzbekistan

A. Radjapov; Y. Madjidova; N. Xusenova; A. Bijanova; A. Ernazarov

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EPV-887 | Cognitive teleRehabilitation in patients with Encephalitis of AutoIMmune etiology: CoRe-AIM study

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EPV-888 | Refractory anti-nmdar encephalitis: Paradigm shift required in the treatment

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EPV-889 | Vocal cord palsy in late adulthood as a sign of recessive spinocerebellar ataxia type 10

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EPV-890 | Immune-checkpoint inhibitor-associated encephalitis: Case series in a tertiary hospital

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EPV-891 | Neurological and neuropsychological correlates of Klippel-Feil syndrome

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EPV-892 | Commercial volumetric and lesion segmentation MRI tools in Multiple Sclerosis (MS)

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EPV-893 | The significance of immunohistochemical expression of mesothelin in meningiomas

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EPV-894 | Clinical-genetic phenotype in Bulgarian patients with ALS and mutation in NEK1 gene

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EPV-895 | Temporal lobe glioblastoma: An uncommon mimic of autoimmune limbic encephalitis

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EPV-896 | ERLIN 2 mutations in an Italian series of patients: Phenotypic and genetic variability

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EPV-897 | Neuroimaging profile in a cohort of Brazilian cadasil patients

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EPV-898 | Auditory neuropathy and optic atrophy, linked with FDXR gene mutations

V. Fonseca; M. Saianda Duarte; J. Correia; A. Arraiolos; T. Lampreia; J. Vale
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EPV-899 | Structural changes of the brain in patients with Wilson's disease according to MR tomography and MR spectroscopy

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EPV-900 | Early-onset amyloid angiopathy

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EPV-901 | Isolated recurrent sixth nerve palsy: Could it be a presentation of microscopic polyangiitis?

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EPV-902 | Clinical effects of virtual reality training and tDCS for upper limb function in paediatric brain injury: A RCT protocol

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EPV-903 | Jaw drop in leptomeningeal metastasis

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EPV-904 | Effect of transcranial magnetic stimulation on functional outcome of patients with incomplete spinal cord injury

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EPV-905 | Papilledema and other neurological signs due to an atypical cause. A case report

A. Lagüela; V. Anciones; A. Rebollo; V. Fernández; L. Fernández; C. Valido; M. Martínez; Á. López; M. Freijo; A. Rodríguez-Antigüedad; A. Durán; J. Losada
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EPV-906 | Magnetic resonance imaging correlates of challenging gait condition in multiple sclerosis

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EPV-907 | Combination of different NIBS treatments for upper limb recovery in stroke. A systematic review

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EPV-908 | Limited effect of the rehabilitation training on post-injury spinal cord recovery

T. Ageeva; E. Davletshin; D. Sabirov; A. Timofeeva; E. Plotnikova; A. Rizvanov; A. Yakubova; Y. Mukhamedshina
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EPV-909 | When it seems to be SMART and it is not. The dark side of radiotherapy

A. Oliveira; T. Jesus; P. Grilo; S. Costa; C. Barroso
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EPV-910 | Atypical debut of multifocal primary central nervous system lymphoma: A case report

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EPV-911 | Autoimmune-encephalitis mimics: Red flags on a case resulting a glioblastoma multiforme

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EPV-912 | Redefining the superficial peroneal nerve: Stimulation technique, normal values, and clinical significance

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EPV-913 | Development of rehabilitation potential and restoration of motor function in ischemic stroke

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EPV-914 | Hypothetical neurological impacts of exceeding auditory thresholds in transcranial magnetic stimulation

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EPV-915 | Adapting LIMOS for stroke patients: Validating a patient-reported measurement in brazilian outpatient rehabilitation

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EPV-916 | The characterization of selected brain injury factors and cytokines in the CSF among RRMS patients

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EPV-917 | Central nervous system vasculitis in inflammatory Bowel disease: A rare cause of stroke

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EPV-918 | The SECONDs index score to assess consciousness fluctuations in acute patients with severe brain injury

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EPV-919 | The impact of aerobic exercise on cognitive function in individuals with multiple sclerosis

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EPV-920 | Exploring the efficacy of art therapy for cognitive improvement in dementia: A systematic review

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EPV-921 | WEBINO syndrome (Wall-Eyed Bilateral Internuclear Ophthalmoplegia): A case report

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EPV-922 | Eosinophilic granulomatosis with polyangiitis mimicking chronic inflammatory demyelinating polyneuropathy: A case report

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EPV-923 | Nonsense-mediated decay (NMD) as a shared peripheral immune dysregulation process across neurological disease

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EPV-924 | Expanding the horizon of paraneoplastic disorders: New intracellular antibody for progressive cerebellar degeneration

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EPV-925 | Bilateral horizontal diplopia of rare etiology: Paraneoplastic syndrome due to Anti-Ri

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EPV-926 | Rehabilitation of young children with epilepsy: Opportunities and safety

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EPV-927 | Neurodevelopmental therapy for cerebral palsy: A systematic review of systematic reviews

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EPV-928 | Vasculitic sensory motor peripheral neuropathy (ANCA-associated vasculitis) in juvenile primary Sjögren's syndrome

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EPV-929 | Left–right reversal of vision metamorphopsia caused by cerebellar glioma: A case report

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EPV-930 | Features differentiated treatment for pain in adults with complex regional pain syndrome (CRPS)

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EPV-931 | Unveiling erdheim chester disease enigma: Case report and literature review

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EPV-932 | NeuroGPT; is it really an AI capable of diagnosing and treating patients in neurology? A view through 72 patients

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EPV-933 | Idiopathic intracranial hypertension following abortion complicated with acute anaemia – a case report

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EPV-934 | Phenotypic spectrum of a series of temporally and spatially close cases of Guillain-Barré syndrome

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EPV-935 | Acute neurological complications following taxane chemotherapy in gastric adenocarcinoma: A case report

G. Ruta; D. Totaro; T. Giannelli; A. Fallacara; A. Introna; G. Falcicchio; D. Paolicelli; G. Defazio
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EPV-936 | Relaxation effects of environment of "the Way of Tea" on the autonomic nervous system

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EPV-937 | The AUREUS project (Austrian Rehabilitation Exchange with Uzbekistan) in Uzbekistan

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EPV-938 | Prospective and quantitative evaluation of gait and stance in patients with acute vertigo and dizziness

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EPV-939 | Diabetes and anemia during aceruloplasminemia: Systematic review and meta-analysis

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EPV-940 | Alameda, an opportunity for at-home neurologic rehabilitation (NR)-interim data collection results

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EPV-941 | Changes of emotional and neurophysiological status in cardiac surgery patients after multitasking cognitive training

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EPV-942 | Repeating CSF flow cytometry as a diagnostic strategy: Meningeal lymphomatosis secondary to follicular lymphoma

J. Alcalá Torres[1]; M. González Arbizu[1]; G. Ramos Moreno[2]; I. Zamanillo Herreros[2]; C. Santos Martín[1]; C. Amarante Cuadrado[1]; A. Herrero San Martín[1]
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EPV-943 | An unusual clinical case of metastasis in spinal nerves roots

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EPV-944 | A case of intractable hiccups caused by hemangioblastoma of the fourth ventricle

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EPV-945 | The effectiveness of cognitive training using virtual reality for patients with initial cognitive impairment

K. Shamtieva; V. Dubas; A. Valeeva; V. Zelentsova; T. Peters
Medical Research and Educational Center of Moscow State University named after M.V. Lomonosov

EPV-946 | Comparison US evaluated muscle thickness and echogenicity between control and stroke patients with spasticity

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EPV-947 | Outcome measures in the rehabilitation of children with autism: A systematic review aligned with the CIF

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EPV-948 | Assessing neurological manifestations in mucopolysaccharidoses type-III: Outcomes from a scoping review

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EPV-949 | Exploring neurological symptoms in mucopolysaccharidoses type VI: A scoping review

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EPV-950 | Evaluating neurological symptoms in mucopolysaccharidoses type VII: Results from a scoping review

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EPV-951 | Otolaryngologic presentation of giant cell arteritis (GCA)

L. Caballero Sánchez; C. Gómez López de San Román; M. Capra; M. Vargas Cobos; D. Cerdán Santacruz; I. Bermejo Casado; A. Castrillo Sanz; A. Mendoza Rodríguez
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EPV-952 | Acute polyneuropathy (APN) as a debut of Sjogren's syndrome (SS): Two cases and a review

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EPV-953 | Tuberculous papillitis, the "great imitator" of ocular disease

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EPV-954 | Advanced perspectives for the diagnosis of Parkinson's and Alzheimer's disease through machine learning techniques

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EPV-955 | Association between neuropsychiatric SLE and a Positive HLA-B51 antigen – Coincidence or clinical correlation?

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EPV-956 | Central neurocytoma: Casuistry of a tertiary center

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EPV-957 | What is essential is invisible to the eye

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EPV-958 | Targeting subclinical motor and cognitive impairment in patients with early onset multiple sclerosis: RELIABLE study

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EPV-959 | Is it possible to challenge a neurologist brain with Artificial Intelligence?

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EPV-960 | Parkinsonism, dystonia and vertical gaze palsy: A case report of an anti Ma2 paraneoplastic syndrome

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EPV-961 | Botulinum toxin A therapy in patients with post-stroke spasticity

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EPV-962 | Focal seizures in non-ketotic hyperglycaemia

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EPV-963 | Designing and deploying an innovative stroke rehabilitation system via the ReInsult mobile app

M. Bakhramov; Y. Madjidova; B. Bakhriev; S. Jabborova; Z. Abdullayev
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EPV-964 | Electromagnetic treatment of patients with motor deficits after a stroke

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EPV-965 | Isolated seizure secondary to embolic ischemic stroke: Libman-Sacks endocarditis debut, in unknown autoimmune diseases

P. Gómez Ramírez; I. Martín Sobrino; M. Nieto Palomares; A. García Maruenda; M. El Harmochi Daoud; A. Sánchez Gómez; L. Quirós Illán; A. Hernández González
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EPV-966 | Establishing an integrated Neurorehabilitation service for children with long-term neurological condition

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EPV-967 | Secondary central nervous system vasculitis: A series of 21 patients

S. Sellami; N. Farhat; H. Haj Kacem; N. Bouattour; K. Moalla; S. Daoud; S. Sakka; M. Damak; C. Mhiri
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EPV-968 | Using artificial intelligence in diagnostics of neurological diseases

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EPV-969 | Examining neurological manifestations in Bardet-Biedl syndrome: Insights from a scoping review

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EPV-970 | Anti-Yo antibody-mediated paraneoplastic cerebellar degeneration syndrome with pathological neuroimaging

M. Martínez Palicio; P. Pinzón Benavidez; A. Cordero Novo; D. Alonso Vallín; P. Rozas Fernández; R. Suarez Moro; M. Sánchez-Suarez López; J. Granda Méndez; M. Álvarez Álvarez
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EPV-971 | Indian perspective of patients with peripheral neuropathies receiving Gabapentinoid – A cross-sectional study

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EPV-972 | Artificially induced Mismatch-Training (AIM) and its impact on effective motor learning

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EPV-973 | Neurological manifestations of thrombotic thrombocytopenic purpura (TTP): Diagnostic and therapeutic difficulties

M. Nieto Palomares; M. El Harmochi Daoud; I. Martín Sorbrino; A. García Maruenda; P. Gómez Ramírez; A. Sánchez Gómez; A. Hernández González; M. Del Real Francia
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EPV-974 | rTMS as part of complex neurorehabilitation affecting motor symptoms in patients with Parkinson's

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EPV-975 | Aseptic meningitis associated with hyperalgic radiculitis – difficulties in establishing the diagnosis

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EPV-976 | Role of anti-neural antibodies in paraneoplastic neurological syndromes: A cohort study

R. García Yu; G. Zmork Martínez; P. López-Grueiro Valcarce; A. García Leal; M. Fernández-Fournier Fernández; A. Tallón Barranco; L. Lacruz Ballester
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EPV-977 | Neurological complications of graft-versus-host disease

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EPV-978 | Intraparenchymal hematomas as a manifestation of posterior reversible encephalopathy syndrome: About a case

S. Saaf; Y. Mimouni; S. Lhassani; Z. El Yacoubi; M. El Azhari; M. Hakimi; J. Aasfara; A. Hazim; H. Ouhabi
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EPV-979 | Impairment based aphasia therapy: Impact on grammar in patients with post stroke non-fluent aphasia

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EPV-980 | Multiple cranial neuropathy in atypical Ramsay-Hunt syndrome mimicking vertebral artery dissection: A case report

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EPV-981 | A potential aggravating factor in reversible posterior leukoencephalopathy syndrome

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EPV-982 | Adopting telehealth solutions for multiple sclerosis (MS) patients: Utilization trends and readiness assessment

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EPV-983 | To study Ophthalmic artery hemodynamics in patients with Optic Neuritis vs Ischemic Optic Neuropathy vs controls

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EPV-984 | Safety and efficacy of ofatumumab during one-year treatment: A multicentre study

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EPV-985 | Sanskrit Vedic Chants intervention provides beneficial behavioral and biological changes in Autistic spectral disorders

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EPV-986 | Investigating the effect of anti-meningococcal vaccine in patients on Eculizumab therapy

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EPV-987 | Long-term EEG reveals distinct variability patterns in epilepsy after autoimmune encephalitis

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EPV-988 | Effect of ascites paracentesis on cognitive performance in patients with hepatic encephalopathy

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EPV-989 | The effectiveness of prosthetic and exoskeleton control through brain-computer interfaces in rehabilitation

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EPV-990 | Long-term effect of COVID on the brain: A systemic review and meta-analysis

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EPV-991 | Ophthalmoplegic migraine – A longitudinal interventional follow up study from Indian subcontinent

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EPV-992 | Steeplechase: Challenges in using published repository data

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EPV-993 | A rare case of pachymeningitis in the context of Lymphoplasmacyte-rich, grade 1 en plaque meningioma

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EPV-994 | VOC-ALS: A smartphone-based app for VOiCe analysis in amyotrophic lateral sclerosis (ALS) patients

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EPV-995 | Posterior reversible encephalopathy syndrome (PRES) a rare presentation of granulomatosis with polyangiitis

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EPV-996 | Development of a self-help digital intervention for functional cognitive disorder (Mementum)

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EPV-997 | Rehabilitation approach for treatment of children with ASD

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EPV-998 | Clinical global impression in assessing IVIg response in CIDP patients: Learnings from the PRISM study

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EPV-999 | Beyond the norm: Ischemic stroke in Behcet's disease about two cases

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EPV-1000 | A prospective study to screen for cochleo-vestibular disorders in individuals with multiple sclerosis

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EPV-1001 | Brief intervention as a general method to address prescription or non-prescription medication misuse

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EPV-1002 | Dermatomal contact heat evoked potentials in non-myelopathic degenerative cervical spinal cord compression

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EPV-1003 | Botulinum toxin A for neuropathic pain – A systematic review and meta-analysis

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EPV-1004 | Headache after surgical sealing of cerebrospinal fluid leaks in patients with spontaneous intracranial hypotension

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EPV-1005 | Education needs in palliative care and ACP of Italian residents in neurology: An online survey

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EPV-1006 | Reversible cerebral vasoconstriction syndrome: Diagnosis and treatment monitoring with transcranial ultrasound

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EPV-1007 | Surgical vs conservative management of chronic sciatica (> 3 months) due to lumbar disc herniation

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EPV-1008 | Cytotoxic lesion of corpus callosum due to thermogenic supplement

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EPV-1009 | Segmental spinal myoclonus: An unusual presentation of spinal dural arteriovenous fistula

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EPV-1010 | Fluctuating paraparesis due to spinal vascular micromalformation, a case report

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EPV-1011 | Objective pain assessment in lower back pain: Integrating clinical treatment and biochemical markers

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EPV-1012 | Potential involvement of the mechanosensitive channel Piezo1 in regulating axonal regeneration after spinal cord injury

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EPV-1013 | Longitudinally extensive transverse myelitis, thinking beyond

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EPV-1014 | Improving palliative care in Parkinson's Disease: A Case on subcutaneous apomorphine infusion for patient comfort

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EPV-1015 | Risk Factors affecting the therapeutic effect of botulinum toxin A on chronic migraine: A retrospective study

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EPV-1016 | Clinical deterioration secondary to corticosteroid: Uncovering spinal dural arteriovenous fistula, a great imitator

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EPV-1017 | Ultrahigh-dose methylcobalamin's impact on clinical outcomes in amyotrophic lateral sclerosis: Meta-analysis

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EPV-1018 | Clinical outcomes of patients with chronic immune-mediated neuropathies treated with subcutaneous immunoglobulin

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EPV-1019 | The electrophysiological evaluation of replacement therapy on small fiber neuropathy due to B12 deficiency

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EPV-1020 | Patient reported outcomes in a 2-week randomized trial of a central muscle relaxant in acute low back pain with sciatica

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EPV-1021 | Fibrocartilaginous embolism as a rare condition of acute paraplegia

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EPV-1022 | Lack of neuro-palliative services adversely affects motor neurone disease patients in Kenya: An illustrative case series

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EPV-1023 | Peripheral nervous system dysfunction in systemic autoimmunity: A clinical insight

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EPV-1024 | Psychological distress as a chronification factor for headache

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EPV-1025 | Effect of tofacitinib and adalimumab in patients with rheumatoid arthritis with signs of central sensitization

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EPV-1026 | Which are the factors affecting the topography of nitrous oxide-induced neurological complications?

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EPV-1027 | Head injury in the city of Helsinki: The HEAD Helsinki study – design, rationale and patient characteristics

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EPV-1028 | Mortality of head injury in the city of Helsinki: The HEAD Helsinki study

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EPV-1029 | Psychiatric morbidity and substance use in a large head injury cohort: The HEAD Helsinki study

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EPV-1030 | Blood–brain barrier impairment as pathological hallmark in a novel model of closed-head concussive brain injury in mice

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EPV-1031 | Mitigating sports-related traumatic brain injuries: A systematic review of communication and education strategies

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EPV-1032 | Facial quantitative sensory testing in patients with trigeminal neuralgia

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EPV-1033 | Post-operative infection in Unilateral Biportal Endoscopy (UBE): A systematic review and meta-analysis

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EPV-1034 | Tetraplegia reversed with a simple neck collar: A case of spontaneous spinal epidural haematoma

M. González Gómez; M. Hernández Ramírez; J. Villamor Rodríguez; F. Sánchez García; D. Barbero Jiménez; J. Celi Celi; M. Mas Serrano
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EPV-1035 | Variations in the atlantoaxial joint anatomy detected by computer tomography in control subjects

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EPV-1036 | Fatal posterior reversible encephalopathy syndrome associated with atypical presentation Guillain-Barré syndrome

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EPV-1037 | Noninvasive deep brain stimulation

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EPV-1038 | Polyradiculoneuropathy following bariatric surgery – A clinical insight and review

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EPV-1039 | Carotid Free-Floating Thrombus case series diagnosed by duplex ultrasonography: Treatment options and risk of recurrence

J. Álvarez-Cienfuegos; C. Vera Cáceres; R. Ferrer Tarrés; M. García Huguet; I. Saurina Navarro; C. Martínez Follana
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EPV-1040 | Cefepime-induced neurotoxicity: An underestimated cause of in-hospital complications

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EPV-1041 | Correlation between hyperechogenicity of substantia nigra and olfactory dysfunction in patients with Parkinson's disease

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EPV-1042 | Stylohyoid syndrome (Eagle's syndrome): A case report

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EPV-1043 | Isolated conus medullaris demyelinating lesion following anti-TNF-α therapy

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EPV-1044 | Pregnenolone deficiency in fibromyalgia syndrome (FMS) – A diagnostic marker and potential therapeutic target?

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EPV-1045 | Characteristics of sleep and REM sleep without atonia in a group of patients affected by PANS

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EPV-1046 | Electrodiagnostic testing and prognosis of Guillain Barré syndrome – A case series

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EPV-1047 | Evidence of partial response to Safinamide in chronic patients with Parkinson's disease-related pain

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EPV-1048 | Evidence for independent pathways of fatigue and pain in people with Parkinson's disease-related pain?

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EPV-1049 | Improving cost effectiveness of IVIG in immune mediate peripheral neuropathies in the Maltese Islands

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EPV-1050 | Laughing gas lament: The neurological impact of recreational nitrous oxide inhalation

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EPV-1051 | Clinical relevance of Neutrophil-to-Lymphocyte Ratio in Guillain-Barré Syndrome

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EPV-1052 | Sovateltide (IRL-1620) enhances motor function and reduces hyperalgesia in a rodent model of spinal cord injury

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EPV-1053 | An unusual case of Parsonage-Turner syndrome triggered by HEV presenting with bilateral diaphragmatic paralysis

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EPV-1054 | Charcot–Marie–tooth disease type 4H and white matter demyelinating lesions: A case report and literature review

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EPV-1055 | Guillain-Barre syndrome after first dose of Pfizer COVID-19 vaccine: Case-series from Lebanon

K. Zammar[2]; D. Lizzeik[2]; C. Ibrahim[2]; B. Mcheik[1]; A. Shatila[2]; M. Dassouki[2]; H. Al Khuder[2]; W. Ayoub[2]; E. Abi Fadel[2]; S. Iskandar[2]; T. El Hajj[1]

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EPV-1056 | Syringomyelia syringobulbia present as acute stroke

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EPV-1057 | Sensory neuropathies (SN): A reappraisal of the utility of upper limb sensory-motor amplitude ratios

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EPV-1058 | Uncovering the unseen: Asymptomatic late-onset diastematomyelia

M. Mednini[1]; H. Derbali[1]; I. Ghorbel[1]; M. Messelmani[1]; I. Bedoui[1]; M. Mansour[1]; J. Zaouali[1]; R. Mrissa[1]

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EPV-1059 | A case of Charcot–Marie–Tooth disease and focal segmental glomerulosclerosis with novel variant of INF2 gene

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EPV-1060 | Prescription profile of narrow therapeutic index medications used in pediatric neurology

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EPV-1061 | Clinical and genetic characteristics of hereditary motor-sensory neuropathy type VIC in the Republic of Sakha (Yakutia)

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EPV-1062 | A spinal dural arteriovenous fistula at the ER: Acute presentation of an uncommon cause of progressive myelopathy

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EPV-1063 | Systemic lupus erythematosus associated Guillain-Barré syndrome: A systematic review

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EPV-1064 | Diagnostic utility of nerve ultrasound on ulnar neuropathy at elbow with normal electrodiagnostic features

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EPV-1065 | Head injuries in Helsinki emergency hospitals – Effect of alcohol on mortality and severity of head injury

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EPV-1066 | Severe case of contrast-induced encephalopathy following a cerebral arteriography

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EPV-1067 | Results of using cone beam computed tomography in patients with persistent idiopathic facial pain

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EPV-1068 | Ultrasonography of the superficial temporal and axillary arteries in giant cell arteritis diagnosis

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EPV-1069 | Cerebellar vulnerability in lithium therapy: An integrative review and conceptual analysis

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EPV-1070 | Evaluating Clonazepam's efficacy in facial erythromelalgia: Neurogenic kindling and psychosomatic interplay

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EPV-1071 | Occurrence and risk factors of epilepsy in severe traumatic brain injury: A narrative review

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EPV-1072 | Assessment of cerebrovascular reactivity in the acute phase of cerebrovascular events

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EPV-1073 | Neuromuscular manifestations of thyroid dysfunction: Insights from a retrospective cohort study

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EPV-1074 | A rare variant of Guillain–Barré syndrome: Isolated facial diplegia

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EPV-1075 | Frequency and aetiologies of isolated peripheral type cranial neuropathy in the neurology inpatient clinic

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EPV-1076 | Microvascular decompression for hemifacial spasm in a single center

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EPV-1077 | Thoracic sulcal artery infarct presenting as Brown-Sequard syndrome

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EPV-1078 | Therapeutic plasma exchange in treating neuromuscular diseases

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EPV-1079 | Spinal dural arteriovenous fistula presenting as recurrent spinal cord ischemic-like events

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EPV-1080 | Evaluation of treatment efficacy and autonomic symptoms in patients with neuropathic pain, single-centre evaluation

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EPV-1081 | Communication, coordination and security for people with multiple sclerosis (COCOS-MS): A randomised clinical trial

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EPV-1082 | Evaluation of PAP treatment on Retinal Fiber Thickness And Visual Pathways Using OCT and VEP in the patients with OSAS

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EPV-1083 | Evaluation of retinal fiber thickness and visual pathways with OCT and VEP in different clinical stages of OSAS

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EPV-1084 | Polyneuropathy as a presenting symptom of Sjogren's disease: A case report

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ABSTRACT

Late-breaking Abstracts

Monday, July 01 2024

Late breaking news 1

OPR-116 | Auricular vagal nerve stimulation in patients with mild cognitive impairment due to Alzheimer's disease

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Background and Aims: The study was conducted on patients diagnosed with mild cognitive impairment (MCI) due to Alzheimer's disease (AD). Auricular transcutaneous vagal nerve stimulation (atVNS) was applied using the VGuard device, which was specifically designed to minimize stimulation side effects and was applied only during sleep, a period characterized by higher activity of the vagal nerve.

Methods: The study was a randomized, double-blind, placebo-controlled trial conducted in a group of 51 patients with AD, 35 patients in the treatment arm and 16 patients in the placebo arm. The study consisted of a 12 week treatment period, with an extension of an additional 12 week period for 20 patients. After the extension period, stimulation was terminated. 15 patients underwent cognitive evaluation after an additional 24 weeks.

Results: The study showed statistically significant cognitive improvement between placebo and active treatment arms with $p < 0.01$ in the ADAS-COG, as well as improvements in Mini Mental Status Examination (MMSE), Color Trial Test (CTT) and Verbal Memory Probing (VMP). Cognitive improvement observed in the 15 patients during the stimulation period returned to baseline values after 24 weeks of no treatment.

Conclusion: The results of this randomized, doubled-blind, placebo-controlled study demonstrate that atVNS using the Vguard device significantly improved cognition in patients with MCI due to AD and may represent an effective therapeutic approach in delaying the conversion of MCI into initial stages of AD.

Disclosure: The study was co-financed by the European Funds under Priority Axis I: Research, development, and commercialization of knowledge of the Regional Operational Programme of the Lodz Voivodeship Poland for the years 2014-2020. Project nr RPLD.01.02.02-10-0067/17-00.

OPR-117 | Opioids and dementia; nationwide Danish population-based study

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Background and Aims: Opioid use has been associated with short-term adverse effects on cognition, but long-term studies on opioid-associated risk of dementia are lacking. We assessed associations between cumulative non-cancer opioid use and risk of age-related all-cause dementia.

Methods: Using national Danish registries, we conducted a nationwide nested case–control study within a cohort of 1,872,854 individuals aged 60–75 years, without dementia, cancer, or opioid addiction followed from 2000–2020. By incidence-density-matching, each dementia case was matched to five controls. Use of opioids was evaluated from redeemed prescriptions translated into total standardized doses (TSD). Conditional logistic regression yielded adjusted incidence rate ratios (IRR).

Results: During follow-up, 93,638 individuals developed dementia. Opioid exposure up to 90 TSDs was not associated with increased dementia risk. Use of more than 90 TSDs was associated with an increased dementia risk occurring before age 90 years with indication of a dose–response pattern. IRR of dementia occurring at age 60–69 years was 1.28 (1.16–1.41) for 91–200 TSDs of opioid use. Corresponding IRRs for ages 70–79 years and 80–89 years at dementia diagnosis were 1.16 (1.10–1.21) and 1.09 (1.04–1.14), respectively. Associations persisted in individuals with specified chronic non-cancer pain diagnoses and with exclusive use of weak opioids.

Conclusion: Opioid use up to 90 TSDs did not show increased dementia risk. Exposure to more than 90 TSDs was associated with a slightly increased dementia risk, also with use of weak opioids only and among individuals with chronic non-cancer pain. Further studies are needed to determine if these findings represent causality between opioid use and dementia.

Disclosure: Nothing to disclose.

OPR-118 | **The diagnostic value of transcranial ultrasound in Swedish parkinsonism patients: A retrospective cohort study**

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Background and Aims: Although transcranial ultrasound (TU) assessing hyperchogenic substantia nigra (SN+) as biomarker for Parkinson's disease (PD) has been introduced elsewhere, the clinical relevance and validity in a Swedish population is still unknown.
Methods: From 2013 to 2017, 75 patients with parkinsonism have been examined by TU to be able describing the SN+ status in relation to PD, atypical parkinsonian disorders (APS) and essential tremor (ET) and aimed for a long follow-up (FU) to be sure about the correct final diagnosis.
Results: In 2024, we found a mean FU time of 95 months. The initial diagnosis was changed in 36 cases (47%). 4% ($n = 3$) had no transcranial bone window necessary for TU and were excluded. 41 of 56 true PD-patients and 2 of the 16 non-PD patients had the SN+ finding ($p < 0.001$). Sensitivity and accuracy were low (73% and 76%, respectively) whereas specificity and the positive predictive value were higher (87.5 and 95.3%, respectively). The study's limitations were small sample size, single center data, retrospective design, no interrater comparison due to only one sole sonographer, unknown reliability and a cut-off value only validated for discrimination between PD and healthy controls.

Table 1

Baseline characteristics

Variable	All (n=75)
	Demographics
Age, mean	66 (range 43-88)
Women/men, no.	29/46
	Time variables
FU duration, months	95
Symptomduration prior visit, months	18
Time from 1st visit to TU examination, months	8
	Medical
Change of diagnosis during FU, no. (%)	36 (47)
PET and/or SPECT, no.	27
Died during FU, no.	23
Dementia during FU, no.	19

Baseline characteristics of study population.

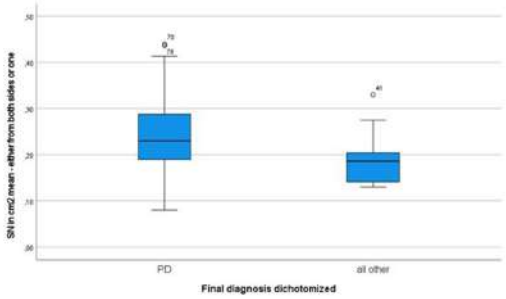
Table 2: Hyperechogenicity of Substantia Nigra vs. Final Diagnosis

	PD (no.)	Non-PD (no.)	All (no.)	p
SN+	41	2	43	*<0.001*
Normal SN	15	14	29	*<0.001*
	56	16	72	*<0.001*

Numbers of patients with positive/negative test results in the study population (cross tabulation).

Conclusion: We conclude TU possibly being a valuable add-on tool in PD diagnostics in our patient population because SN+ has a high probability to support a diagnosis already in the early stage of disease. TU seems not being suitable as single first-line diagnostics due to unsatisfactory sensitivity and accuracy. More studies are needed, especially on TU reproducibility and head-to-head studies comparing TU and PET/SPECT.

Figure 1: Boxplots of mean SN-size (cm^2) vs. final diagnosis (p 0.05)



Size of Substantia Nigra in PD- and non-PD patients.

Disclosure: Thanks to The Husbands Stoltz Foundation, Malmö and The Elsa Schmidt Foundation, Lund for research grants and special thanks to Our experienced PD nurse Eva Berg The participating patients.

OPR-119 | Long-term findings of N-acetyl-L-leucine for Niemann-Pick disease type C

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Background and Aims: The IB1001-301 clinical trial was a Phase II, double-blind, randomized, placebo-controlled trial comparing N-acetyl-L-leucine (NALL) with placebo for the treatment of neurological signs and symptoms in Niemann-Pick disease type C (NPC) after 12 weeks. The primary Scale for the Assessment and Rating of Ataxia (SARA) endpoint was reduced −1.97 points with NALL and −0.60 with placebo ($p < 0.001$). Extended follow-up data were obtained in an open-label Extension Phase (EP) to evaluate the long-term, neuroprotective effects of NALL for NPC.

Methods: Patients received treatment with orally administered NALL 2–3 times per day. The primary endpoint was the modified 5-domain NPC Clinical Severity Scale (5-Domain NPC-CSS) (range 0–25 points; lower score representing better neurological status). Comparisons were made to the expected annual trajectory of disease decline established in published natural history studies. Exploratory endpoints included the 17-domain NPC-CSS (excluding hearing) and SARA.

Results: 54 patients aged 5–67 years were treated in the EP. After 12 months, the mean (±SD) change from baseline on the 5-domain NPC-CSS was −0.115 (±2.60) and 1.5 ± 3.1 in the historical cohort (mean difference 1.56; 95% Confidence Interval, 0.31–2.92; $p < 0.017$), a 108% reduction in annual disease progression. The result of the 17-domain NPC-CSS was supportive of the primary analysis and the improvements in neurological status demonstrated in the Parent Study's primary SARA endpoint were sustained over the long-term follow-up.

Conclusion: In NPC, treatment with NALL after 1 year was associated with a statistically and clinically significant reduction in disease progression and consistent with a neuroprotective, disease-modifying effect.

Disclosure: Tatiana Bremova-Ertl received speaker's honoraria and consultancy fees from Actelion, Sanofi-Genzyme and Zevra as well as blinded video-rater fees from Intrabio.

OPR-120 | Alterations in BDNF and plasmin-related proteins are associated with regional brain atrophy in alpha-synucleinopathies

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Background and Aims: Plasmin is serine protease acting in tissue and synaptic remodeling, inflammation regulation and modulation of neurotrophic factors, and is regulated by activating tissue plasminogen activator (tPA), and by inhibiting plasminogen activator inhibitor-1 (PAI-1). Brain derived neurotrophic factor (BDNF) is abundant neurotrophin. Their levels and associations with regional brain atrophy in alpha-synucleinopathies (PD, DLB and MSA) are unclear.

Methods: Serum levels of tPA, PAI-1, BDNF and their ratios were investigated in 34 DLB, 12 MSA and 11 PD patients compared to 11 cognitively unimpaired controls, evaluated including brain MRI. Protein serum concentrations were quantified using ELISA and compared across the groups. Regional brain atrophy was measured using automated algorithm FreeSurfer v7.0 and associations with protein serum levels were assessed using false discovery rate.

Results: Adjusting for age, we showed dysregulated plasmin synthesis by differences in PAI-1 among groups ($p < 0.001$): PD ($p = 0.027$) and especially MSA ($p < 0.001$) patients showed higher levels of PAI-1 vs controls. PAI-1 differed in DLB vs MSA ($p = 0.008$). BDNF levels were higher in DLB ($p < 0.001$), PD ($p < 0.001$) and MSA ($p = 0.012$) vs controls, and PAI-1/BDNF ratio differed in MSA vs DLB ($p = 0.008$). PAI-1 and PAI-1/BDNF ratio levels were inversely associated with regional brain atrophy in several brain regions including cholinergic basal forebrain nuclei volume, posterior cingulate, retrosplenial, parahippocampal cortical thickness and nucleus accumbens, hippocampal, basal ganglia and brainstem volumes ($p < 0.05$).

Conclusion: Plasmin system and BDNF are altered in alpha-synucleinopathies. Increased BDNF levels may suggest compensatory mechanism. Plasmin system and BDNF may be explored as a therapeutic targets in these neurodegenerations.

Disclosure: Nothing to disclose.

Late breaking news 2

OPR-121 | Single-cell analysis of anti-BCMA CAR T cell therapy in patients with central nervous system autoimmunity

C. Qin[1]; M. Zhang[1]; L. Zhou[1]; M. Dong[1]; W. Wang[2]; S. Cai[2]; C. Li[3]; D. Wang[3]; B. Bu[1]; D. Tian[1]; W. Wang[1]

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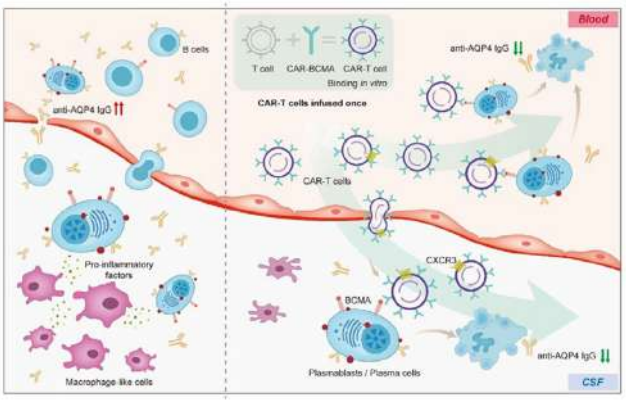
Background and Aims: Chimeric antigen receptor (CAR) T cell immunotherapy for the treatment of neurological autoimmune diseases is promising, but CAR T cell kinetics and immune alterations following treatment are poorly understood.

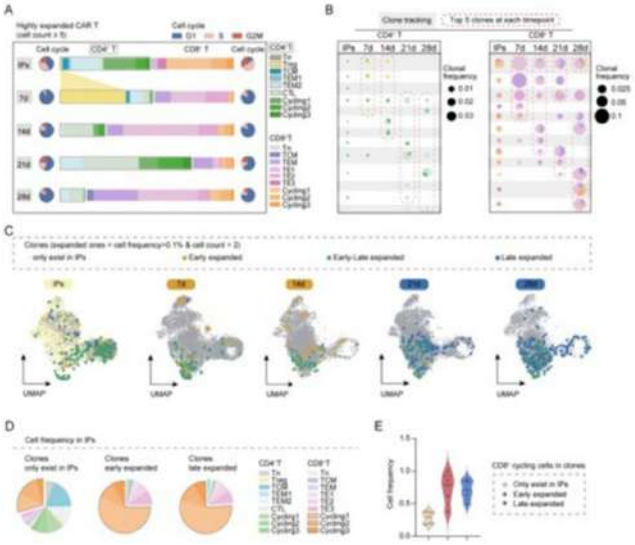
Methods: We performed single-cell multi-omics sequencing of paired cerebrospinal fluid (CSF) and blood samples from patients with neuromyelitis optica spectrum disorder (NMOSD) treated with anti-B cell maturation antigen (BCMA) CAR T cells.

Results: Proliferating cytotoxic-like CD8+ CAR T cell clones were identified as the main effectors in autoimmunity. Anti-BCMA CAR T cells with enhanced features of chemotaxis efficiently crossed the blood–CSF barrier, eliminated plasmablasts and plasma cells in the CSF, and suppressed neuroinflammation. The CD44-expressing early memory phenotype in infusion products was potentially associated with CAR T cell persistence in autoimmunity. Moreover, CAR T cells from NMOSD patients displayed distinctive features of suppressed cytotoxicity compared with those from hematological malignancies.

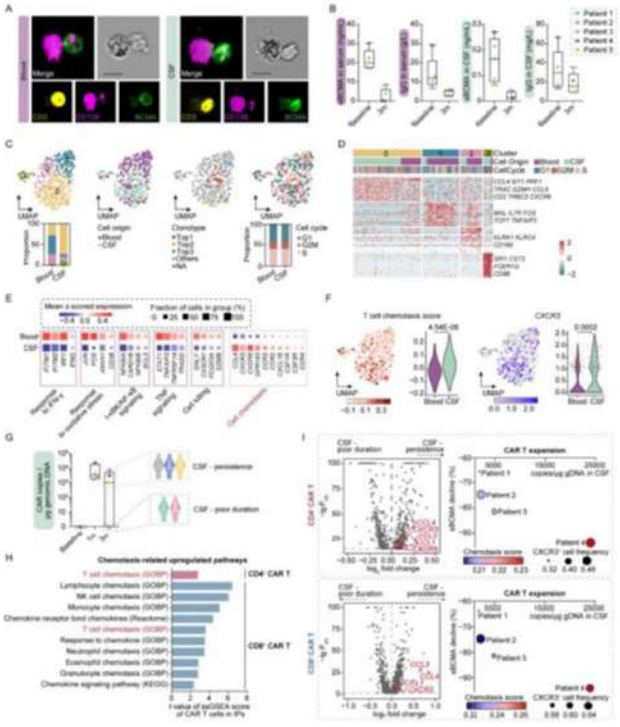
Conclusion: These data provide mechanistic insights into CAR T cell function in patients with neurological autoimmune disease.



CAR T cells reversed immune dysfunction in the CSF of NMOSD patients.



Clonal kinetics of CAR T cells in patients with NMOSD.



Properties associated with CAR T cell infiltration into CSF.

Disclosure: Nothing to disclose.

OPR-122 | Prognostic scoring and goal-concordant care after severe acute brain injury: A mixed-method study

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Background and Aims: As patients after severe acute brain injury (SABI) typically lack decisional capacity, families and clinicians in the ICU share prognostic uncertainty and treatment decisions. Our study aims to compare the impact of prognostic scoring on decisions from the patients, families and ICU clinicians' perspectives.
Methods: Families, physicians and nurses responded to a survey on treatment decisions for SABI patients in the ICU with a GCS < 12 after day 2. At 6 months, we assessed the patients and families' perspectives on goal-concordant care through a survey and semi-structured interviews.
Results: We enrolled 110 patients, 71 relatives and 205 clinicians. At enrollment, 65% of families reported discussion on prognosis with clinicians and 48% on patient's presumed wishes. Regarding goal-concordance care, 66% of families and clinicians were aligned in their estimates. They felt that prognostic scores and their personal estimates would have a major influence on their decisions in 46% and 55% respectively. The use of hypothetical prognostic scoring (patient's risk of dependency of 50% vs 90%) significantly increases presumed decisions to withdraw LST (29 vs 44%). In addition, 52% said they would strongly regret prolonging LST if they knew the patient could survive with severe and irreversible deficits, while 40% feared withdraw LST even if the chances of recovery were extremely low.
Conclusion: A substantial proportion of families consider that prognostic scores and their own assessment of the patient's chances of recovery significantly influence their decisions. Early discussion on prognostic estimates and goals-of-care may improve decisions concordant with the patients' wishes.
Disclosure: Nothing to disclose.

OPR-123 | Outcomes of cancer-related strokes according to antithrombotic drug used for secondary prevention

M. Kielkopf[1]; S. Venzin[1]; J. Göcmen[1]; F. Steinauer[1]; M. Branca[2]; A. Boronylo[1]; G. Martina[1]; J. Kaesmacher[3]; A. Mujanovic[3]; T. Meinel[1]; D. Seiffge[1]; P. Bücke[1]; M. Heldner[1]; A. Liberman[4]; U. Fischer[1]; M. Arnold[1]; T. Pabst[5]; M. Berger[5]; S. Jung[1]; A. Scutelnic[1]; B. Navi[4]; M. Beyeler[6]
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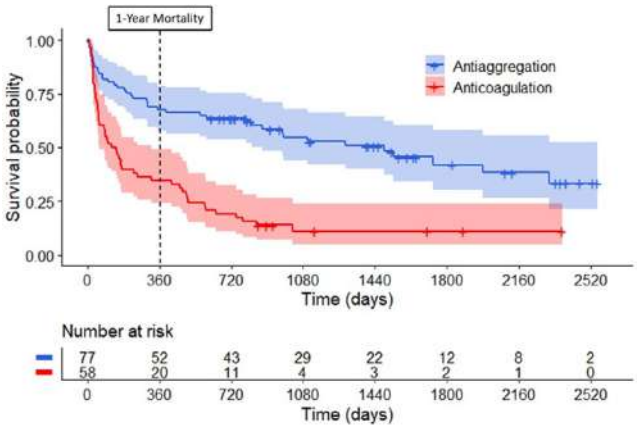
Background and Aims: Acute ischemic stroke (AIS) patients with active cancer are common (≈10% of all AIS) and are at high risk of AIS recurrence and death. Although anticoagulation is often preferred because of the presumed paraneoplastic coagulopathy, the optimal antithrombotic strategy in this population remains undefined. This study aimed to assess the association between anticoagulation versus antiaggregation as secondary prevention in AIS patients with active cancer.
Methods: AIS patients with active cancer were identified in the consecutives AIS patients treated at our comprehensive stroke center between January 2015 and December 2020. The association between anticoagulation versus antiaggregation and mortality in follow-up was assessed and cerebrovascular events in the follow-up were reported.
Results: Of 5012 AIS patients, 135 patients with active cancer were included. The mortality rate at one year was higher in the anticoagulation group ($n = 58$, 66%) than in the antiaggregation group ($n = 77$, 33%). In the adjusted analysis the use of anticoagulation compared to antiaggregation was not associated with lower mortality neither at one year (adjusted hazard ratio [aHR] 0.76; 95% CI 0.36–1.63) nor in the long-term (aHR 1.29; 95%-CI 0.63–2.47). The number of recurrent AIS cases in the long-term follow-up was similar in the anticoagulation group (8.6%) and the antiaggregation group (7.8%; $p = 1.00$).



Long-term survival curves for AIS patients with cancer treated with antiaggregation and anticoagulation as secondary prevention Compared to patients treated with antiaggregation (in blue), patients with anticoagulation (in red) demonstrated higher mortal.

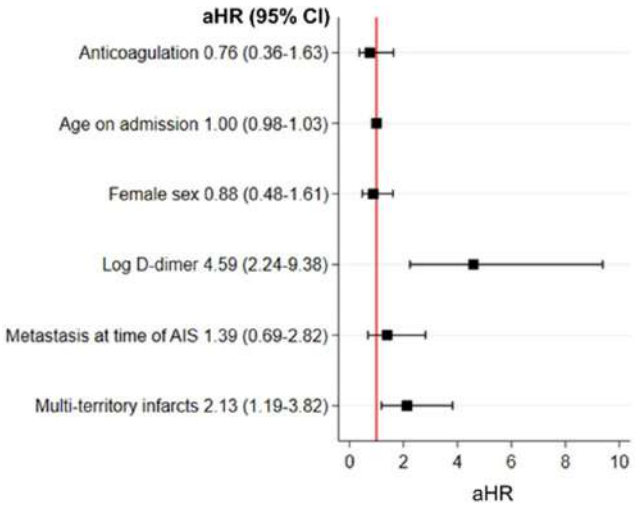


FIGURE 2 Association between one year mortality after AIS and antithrombotic drug prescribed as secondary prevention at discharge and other co-variables. In the adjusted analysis, the primary outcome (mortality at one year after AIS) was not associated.

Conclusion: AIS patients with active cancer treated with anticoagulation showed more signs of paraneoplastic coagulopathy and metastatic cancer. This indication bias resulted in a higher mortality rate in patients with anticoagulation in the unadjusted model. After adjustment, however, there was no difference in outcomes between the two groups.

Disclosure: Dr. Beyeler reports research support from the Department of Neurology, University Hospital, Switzerland.

OPR-124 | **Predicting outcome and improvement after first-line treatment of anti-NMDAR encephalitis at diagnosis: The NEOS2 scores**

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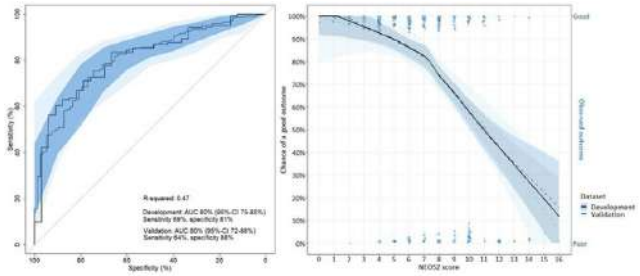
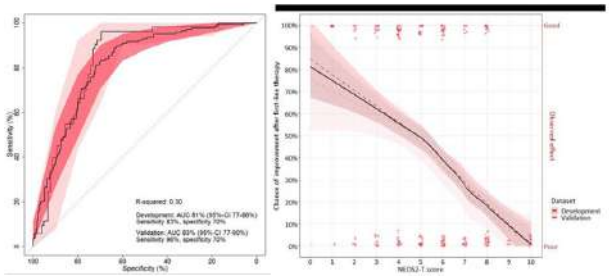
Background and Aims: Anti-NMDAR encephalitis (anti-NMDARE) is a treatable condition, although often resulting in long-term disability. The available 'anti-NMDAR Encephalitis One-Year Functional Status' (NEOS) score predicts independence after one year, considering the effect of first-line treatment only after four weeks. We developed a model predicting outcome already before treatment initiation (NEOS2), and who is likely to improve after first-line treatment.

Methods: International cohorts (France, Germany, the Netherlands, Spain and Japan) were combined to develop (70%) and validate (30%) multivariable models to predict (1) improvement after first-line treatment (NEOS2-T), (2) one-year functional status (NEOS2) and (3) return-to-school/work (NEOS2-W), incorporating variables available at diagnosis. We performed logistic-regression analyses and simplified the models for applicability in clinical practice.

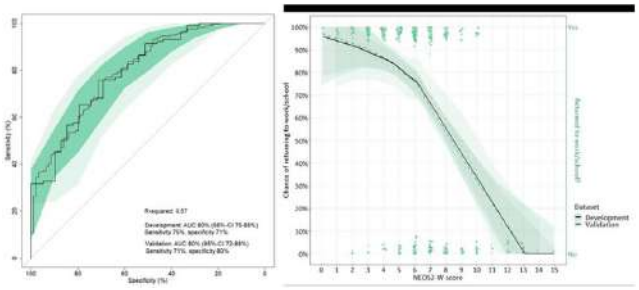
Results: We have included 712 patients (79% female, average age 23 years; 80% independent after one year, 74% resumed school/work). We could predict outcome already at diagnosis, with similar accuracy (AUC 80%) as the original NEOS score. We could predict improvement following first-line immunotherapy with the same variables (AUC 81–83%), identifying patients that could benefit from early intensified treatment, potentially improving outcomes. The NEOS2-T and NEOS2-score accurately identify patients with a high (~80%) likelihood of improving after first-line treatment and a good outcome (~100%), versus patients with high risk of first-line failure (~100%) and a poor outcome (80–90%; Figures 1B and 2B). Resuming school/work was a very long-term outcome-measure (3 years), and could be predicted with the same variables and accuracy.



A: ROC of the model for one-year functional outcome, showing very good accuracy and specificity, and good sensitivity. B: The NEOS2 score classifies (at diagnosis) patients with an almost 100% chance of a good outcome vs high risk (~90%) of a poor outcome.



A: ROC of the model for improvement after first-line treatment, showing very good accuracy, specificity and sensitivity. B: The NEOS2-T score classifies patients with ~80% chance of improvement with first-line therapy vs those with almost definite failure.



A: ROC of the model for resuming school/work, showing very good accuracy, specificity and sensitivity. B: The NEOS2-W score classifies patient almost definitely resuming school/work vs those who are very unlikely.

Conclusion: The easily applicable NEOS2 score accurately predicts (long-term) outcome and identifies anti-NMDARE patients who may benefit from early intensified treatment.

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