

INFORMAZIONI PERSONALI

FEDERICO BRANDALISE

D.O.B.

13.04.1986

Indirizzo

Università degli studi di Milano, Dipartimento di Bioscienze (DBS), Via Giovanni Celoria, 26, 20133 Milano MI

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EDUCATION

06/2013 – 12/2016 (PhD 29/08/2016 – PhD advisors: Fritjof Helmchen and Urs Gerber)

PhD in neuroscienze

University of Zurich - Brain Research Institute. Winterthurerstrasse 190, 8057 Zürich (CH)

Titolo della tesi: The Dendritic NMDA Spike as a Fundamental Mechanism Initiating Associative Plasticity in the CA3 Region of the Hippocampus

5/10/2009 – 26/06/2013

Master Degree in Neurobiology

University of Pavia, Via Forlanini 6, 27100, Pavia (IT)

Titolo della tesi: Synaptic cross-talk between granule cells and Golgi cells through GABA_B mediated modulation of GABA_A-dependent neurotransmission in the cerebellum.

1/10/2005 – 22/09/2008

Laurea Triennale in Biologia Umana e Scienze Biomediche

University of Pavia, Via Forlanini 6, 27100, Pavia (IT)

Thesis title: The NR2A subunit of the N-methyl D-aspartate receptor is required for potentiation at the cerebellar mossy fiber to granule cell synapse and vestibulo-cerebellar motor learning.

STORIA DEL LAVORO E RESPONSABILITÀ ISTITUZIONALI

10/2021 – ongoing

RTDB

University of Milan, Department of Bioscience

10/2018 – 09/2021

Post-Doctoral Fellowship

University of Geneva, Department of Fundamental Neuroscience (NEUFO) {Anthony Holtmaat lab}

Project Title: POM learning-related modulation of active S1 cortical dendrites during a texture-discrimination task.

Skills: Intracranial injections of viral constructs, cranial windows for brain *in-vivo* imaging, 2P-calcium imaging.

01/2017 – 09/2018

Post-Doctoral Fellowship

University of Texas at Austin - Center for Learning and Memory. 100 East 24th St., 78712 Austin (TX) {Daniel Johnston lab}

Project Title: Dynamics and Plasticity of Dendritic Signaling in the Prefrontal Cortex of a Fragile X Syndrome Mouse Model

Skills: Dendritic patch clamp recordings in mPFC and hippocampus. Single channel recordings. Behavioral investigation of delayed eye-blink conditioning paradigm.

06/2013 – 08/2016

Dottorato in Neuroscienze

University of Zurich, Brain Research Institute, Laboratory of Electrophysiology. Winterthurerstrasse 190, 8057 Zürich (CH) {Urs Gerber lab and Fritjof Helmchen lab}

Scopo del progetto: comprendere i circuiti coinvolti nell'elaborazione degli input sinaptici nell'ippocampo utilizzando un approccio elettrofisiologico e di imaging. In particolare, ho esaminato l'integrazione di diversi input su cellule piramidali CA3 e come questi input convergono per generare spike dendritici

Skills: Registrazione patch clamp da neuroni in colture organotipiche e sezioni acute di ippocampo, cervelletto e amigdala. Doppia registrazione da soma e dendrite della stessa cellula piramidale CA3. Patch clamp perforato. Imaging del calcio. Imaging di calcio a due fotoni.

12/2010 - 05/2013

Tesi di Laurea Magistrale in Neurobiologia

University of Pavia, Laboratory of Electrophysiology. Via Forlanini 6, 27100 Pavia (IT) {Prof. Paola Rossi and Prof. Egidio D'Angelo}

Scopo del progetto: indagando le proprietà neuronali e sinaptiche coinvolte nell'apprendimento cerebellare, con particolare attenzione alla plasticità sinaptica a livello delle cellule dei granuli e delle cellule del Golgi. Ho studiato lo sviluppo di cellule granulari cerebellari dallo strato granulare esterno (EGL) allo strato granulare interno (IGL) in topi wild-type e weaver (modello animale di atassia).

Skills: Registrazione patch clamp di cellule granulari cerebellari in sezioni acute. Patch clamp in colture di cellule staminali.

06/2013 - 10/2014

Collaborazioni elettrofisiologiche e di comportamento animale:

Miconet srl (start-up) - University of Pavia (Prof. Paola Rossi).

Scopo del progetto: studiare gli effetti degli estratti naturali del fungo *Hericium erinaceus* sull'attività e sul comportamento neuronale del topo.

Skills: Elettrofisiologia (patch clamp in fettine acute di ippocampo e corteccia entorinale, registrazione della trasmissione sinaptica spontanea ed evocata). Test comportamentali (labirinto a Y, labirinto radiale, labirinto acquatico, test emergente, campo aperto). Biologia molecolare (real-time PCR, end-point PCR).

APPROVED RESEARCH PROJECTS

Dynamics and Plasticity of Synaptic Signaling at Identified Synapses in Hippocampus (Prof. Urs Gerber – Swiss National Science Foundation) 01.10.2012 - 30.09.2015 (staff member)

Dynamics and Plasticity of Dendritic Signaling in Hippocampal CA3 Pyramidal Cells (Prof. Urs Gerber – Swiss National Science Foundation) 01.10.2015 - 30.09.2017 (staff member)

Dynamics and Plasticity of Dendritic Signaling in the Prefrontal Cortex of a Fragile X Syndrome Mouse Model (Dr. Federico Brandalise - Swiss National Science Foundation) 01.01.2017 - 30.06.2018 (responsible applicant)

Fragile X Mental Retardation Protein (FMRP) modulates the functional membrane expression of HCN channel via protein-protein interaction: characterization of a novel regulatory mechanism.
(Dr. Federico Brandalise - Swiss National Science Foundation) 01.07.2018 - 30.09.2018 (responsible applicant)

TEACHING ACTIVITIES

Teaching assistant “BIO 434: Electrophysiological Recording Techniques” - University of Zurich (years 2013; 2014; 2015)

Lesson entitled: “The application of non-stationary fluctuation analysis to determine single channel’s properties” as part of the Cell Biophysics course at “Università degli Studi di Milano” (A.Y. 2020/2021)

MEMBERSHIPS

Swiss Society for Neuroscience

Society for Neuroscience

PRICES, AWARDS, FELLOWSHIPS

SSN Travel grant 2014

SNF “Early Post Doc Mobility Fellowship 2016”

SNF “Advanced Post Doc Mobility Fellowship 2018”

1st Prize at the HIFO PhD competition 2015 (Zurich, 03/2015)

3rd Prize “Best Poster Award” at the EMBO Conference “Dendritic Anatomy, Molecules and

Function" (Crete, 06/2016)

SSN Travel grant 2017 (06/2017)

ZNZ Best PhD Dissertation Award 2017 (Zurich, 09/2017)

PERSONAL SKILLS

Language skills: Italian (native); English (highly proficient in spoken and written); German (good working knowledge); French (good working knowledge). Digital competences: Office, Corel Draw, Illustrator, Igor Pro, Prism, Clampfit, Clampex, Origin, ImageJ, HelioScan software, Matlab.

PRINCIPALI RISULTATI NELLA RICERCA

Mi sono interessato alla neurofisiologia come studente universitario, quando ho avuto l'opportunità di trascorrere due estati nel laboratorio del Prof. E. D'Angelo e del Prof. P. Rossi all'Università di Pavia. Ho poi completato il mio Master in questo laboratorio lavorando sulla fisiologia sinaptica cerebellare. Per il mio dottorato di ricerca, mi sono trasferito nel laboratorio del Prof. U. Gerber presso il Brain Research Institute dell'Università di Zurigo, dove ho studiato come la depolarizzazione sinaptica locale può modulare la forza sinaptica e, in determinate condizioni, indurre un picco NMDA. Nel nostro articolo, abbiamo osservato una forte correlazione tra la probabilità di evocare NMDA spikes e l'induzione di LTP. Questa idea è stata successivamente confermata in vivo (Gambino et al. 2014; Scheffield & Dombek 2015; Chicon & Gan 2015). Inoltre, ho ottenuto prove di compartimentazione dendrite-specifiche degli spike dendritici. Ho poi lavorato come post-doc nel laboratorio di Daniel Johnston dell'Università del Texas ad Austin, dove ho descritto per la prima volta una nuova interazione proteina-proteina modulata dai canali FMRP e HCN che causava una ridotta regolazione dell'integrazione dendritica sia nel ippocampo e nella corteccia prefrontale mediale. Nel laboratorio di Anthony Holtmaat, come mio secondo post-doc ho studiato come diversi input durante un task di discriminazione, convergono nello strato 2/3 nella corteccia del barile e innescano eventi sopralineari che sono possibilmente coinvolti nel potenziamento e nella memoria a lungo termine.

PUBBLICAZIONI IN RIVISTE SCIENTIFICHE

BACHELOR:

NR2A subunit of the N-methyl D-aspartate receptors are required for potentiation at the mossy fiber to granule cell synapse and vestibulo-cerebellar motor learning. Andreescu CE, Prestori F, **Brandalise F**, D'Errico A, De Jeu MT, Rossi P, Botta L, Kohr G, Perin P, D'Angelo E, De Zeeuw CI. *Neuroscience*. 2011 Mar 10;176:274-83. I.F. 3.327 <https://www.ncbi.nlm.nih.gov/pubmed/21185357>

MASTER:

Gene signatures associated with mouse postnatal hindbrain neural stem cells and medulloblastoma cancer stem cells identify novel molecular mediators and predict human medulloblastoma molecular classification. Corno D, Pala M, Cominelli M, Cipelletti B, Leto K, Croci L, Barili V, **Brandalise F**, Melzi R, Di Gregorio A, Sergi LS, Politi LS, Piemonti L, Bulfone A, Rossi P, Rossi F, Consalez GG, Poliani PL, Galli R. *Cancer Discov*. 2012 Jun;2(6):554-68. <https://www.ncbi.nlm.nih.gov/pubmed/22628409>

Golgi cell-mediated activation of postsynaptic GABA_B receptors induces disinhibition of the Golgi cell– granule cell synapse in rat cerebellum. **Brandalise F**, Gerber U and Rossi P. *PLoS One*. 2012;7(8):e43417. doi: 10.1371/journal.pone.0043417. <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0043417>

PhD:

Mossy fiber-evoked subthreshold responses induce timing-dependent plasticity at hippocampal CA3 recurrent synapses.* **Brandalise F, Gerber U. *Proc Natl Acad Sci U S A*. 2014 Mar 18;111(11):4303-8. doi: 10.1073/pnas.1317667111 [Recommendation by Prof. Tomoki Fukai in F1000Prime]. <https://www.ncbi.nlm.nih.gov/pubmed/24550458>

Improving training condition assessment in endurance cyclists: effects of Ganoderma lucidum and ophiocordyceps sinensis dietary supplementation. Rossi P, Buonocore D, Altobelli E, **Brandalise F**, Cesaroni V, Iozzi D, Savino E, Marzatico F. *Evid Based Complement Alternat Med*. 2014;2014:979613. doi: 10.1155/2014/979613.

<https://www.ncbi.nlm.nih.gov/pubmed/24799948>

Distinct molecular components for thalamic-and cortical-dependent plasticity in the lateral amygdala. Mirante O, **Brandalise F**, Bohacek J, Mansuy I. *Front Mol Neurosci.* 2014 Jul 3;7:62. doi: 10.3389/fnmol.2014.00062. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4080466/>

Fear is the mother of invention: anuran embryos exposed to predator cues alter life-history traits, post-hatching behaviour and neuronal activity patterns. Gazzola A*, **Brandalise F***, Rubolini D, Rossi P and Galeotti P*. *Journal of Experimental Biology* 218, no. 24(2015):3919-3930. *these authors contributed equally to this work. <https://www.ncbi.nlm.nih.gov/pubmed/26567349>

Inwardly rectifying potassium currents in cerebellar granule cells exhibit distinct ontogenetic expression in the hemispheres as compared to the vermis. **Brandalise F**, Lujan R, Leone R, Cesaroni V, Romano C, Gerber U and Rossi P. *European Journal of Neuroscience*, 43(11), 1460-1473. <https://www.ncbi.nlm.nih.gov/pubmed/26921581>

*Dietary supplementation of *Herichium erinaceus* increases mossy fiber-CA3 hippocampal neurotransmission and recognition memory in wild-type mice*
Federico Brandalise, Valentina Cesaroni, ... , Paola Rossi *Evidence-Based Complementary and Alternative Medicine*

Dendritic NMDA spikes are necessary for timing-dependent associative plasticity at synapses between hippocampal pyramidal cells.* **Brandalise F, Carta S, Helmchen F, Lisman J, Gerber U. *Nature Communications*, 7, 13480 <https://www.nature.com/articles/ncomms13480>

*Dietary Supplementation of Lion's Mane Medicinal Mushroom, *Herichium erinaceus* (Agaricomycetes), and Spatial Memory in Wild-Type Mice.* Paola Rossi, Valentina Cesaroni, **Federico Brandalise**, Alessandra Occhinegro, Daniela Ratto, Fabio Perrucci, Veralice Lanaia, Carolina Girometta, Germano Orrù, Elena Savino (2018). *International journal of medicinal mushrooms*, 20(5):485-494.

Conditioning by subthreshold synaptic input changes the intrinsic firing pattern of CA3 hippocampal neurons. Soldado-Magraner, S*, **Brandalise, F***, Honnuraiah, S., Pfeiffer, M., Moulinier, M., Gerber, U., & Douglas, R. (2019). *Journal of neurophysiology*, 123(1), 90-106. *these authors contributed equally to this work.

Squaring the Circle: A New Study of Inward and Outward-Rectifying Potassium Currents in U251 GBM Cells. Ratto, D., Ferrari, B., Roda, E., **Brandalise, F.**, Siciliani, S., De Luca, F., ... & Bottone, M. G. *Cellular and Molecular Neurobiology* (2019): 1-16.

Fragile X Mental Retardation Protein Bidirectionally Controls Dendritic Ih in a Cell Type-Specific Manner between Mouse Hippocampus and Prefrontal Cortex.* **Brandalise, F*, Brian E. Kalmbach*, Preeti M., Olivia T., D. Johnston, B. V. Zemelman, and D. H. Brager. *Journal of Neuroscience* 40, no. 27 (2020): 5327-5340.

Deeper and Deeper on the Role of BK and Kir4.1 Channels in Glioblastoma Invasiveness: A Novel Summative Mechanism? **Brandalise, F.**, Ratto, D., Leone, R., Olivero, F., Roda, E., Locatelli, C. A., ... & Rossi, P. (2020). *Frontiers in Neuroscience*, 14, 1237.

"A New Platinum-Based Prodrug Candidate for Chemotherapy and Its Synergistic Effect With Hadrontherapy: Novel Strategy to Treat Glioblastoma." Ferrari, B., Roda, E., Priori, E.C., De Luca, F., Facoetti, A., Ravera, M., Brandalise, F., Locatelli, C.A., Rossi, P. and Bottone, M.G., *Frontiers in Neuroscience* 15 (2021): 183.

Dendritic branch-constrained NMDA spikes drive synaptic plasticity in hippocampal CA3 pyramidal cells. **Brandalise, F.**, S. Carta, R. Leone, F. Helmchen, A. Holtmaat, and U. Gerber. *Neuroscience* (2021).

A subpopulation of cortical VIP-expressing interneurons with highly dynamic spines. Georgiou, C., Kehayas, V., Lee, K.S., Brandalise, F., Sahlender, D.A., Blanc, J., Knott, G. and Holtmaat, A. *Communications biology* 5(1), pp.1-15 (2022).

PRESENTAZIONI ORALI IN CONFERENZE

Invited speaker:

- “Evolution and the brain” – University of Pavia, 10/2013

- “Decoding the brain’s sense of place” – University of Zurich, 10/2014 https://www.youtube.com/watch?v=00_nsjv17Co&t=35s
- “The NMDA-spike as a fundamental mechanism in timing-dependent plasticity at hippocampal CA3 recurrent synapses” – GIESSBACH NEUROSCIENCE MEETING 03/2014
- “The NMDA-spike as a fundamental mechanism in timing-dependent plasticity at hippocampal CA3 recurrent synapses” - Gordon Research Conference: “Dendrites: Molecules, Structure & Function” 03/2015 – Ventura (CA).
- “Fragile X Mental Retardation Protein bidirectionally controls dendritic Ih in a cell-type specific manner between mouse hippocampus and prefrontal cortex” - University of Padova; invited lecture hosted by Prof. Daniela Pietrobon 11/2019
- “Dendritic integration of long-range inputs by barrel cortex pyramidal cells” SWISSKERS MEETING (Bern-CH) 01/2020
- Cell type and input selective non-linear dendritic responses in layer 2/3 pyramidal cells of the somatosensory cortex – GIESSBACH NEUROSCIENCE MEETING 09/2021

POSTERS IN CONFERENZE

Synaptic activation of GABA_B receptors in granule cells reduces GABA_A receptor-mediated responses at the Golgi cell–granule cell synapse in rat cerebellum.

8th IBRO World congress of Neuroscience – Florence.

Subthreshold mossy fiber input can trigger synaptic plasticity between CA3 pyramidal cells.

Neuroscience meeting 2011 – Washington DC.

Cerebellar granule cells exhibit distinct developmental expression of voltage-dependent channels in the hemispheres as compared to the vermis.

FENS meeting 2014 – Milan.

Distinct developmental expression of G-protein coupled inwardly rectifying potassium (GIRK) channels in cerebellar granule cells in the hemispheres as compared to the vermis

Neuroscience meeting 11/2014 – Washington DC.

The NMDA-spike as a fundamental mechanism in timing-dependent plasticity at hippocampal CA3 recurrent synapses

Gordon Research Conference: “Dendrites: Molecules, Structure & Function” 03/2015 – Ventura (CA).

The NMDA-spike as a fundamental mechanism in timing-dependent plasticity at hippocampal CA3 recurrent synapses

Neuroscience meeting 10/2015 – Chicago.

Dendritic spike generation at CA3 pyramidal cells triggers LTP at recurrent synapses

SSN Annual Meeting 01/2016 – Lausanne.

Dendritic NMDA spikes are necessary for timing-dependent associative plasticity at recurrent synapses of CA3 hippocampal pyramidal cells

EMBO Conference “Dendritic Anatomy, Molecules and Function”, Crete (06/2016)

From full-blow spikes to graded boosting NMDA dendritic supralinearities: what causes the switch?

Neuroscience meeting 2016 – San Diego (CA).

Cell-type specific regulation of ion channel function by fragile x mental retardation protein

Neuroscience meeting 2017 – Washington (DC).

FMRP bidirectionally controls differentially regulates dendritic HCN in a cell-type specific manner between in mouse hippocampus and prefrontal cortex

Swiss Neuroscience meeting 2019 – Geneva (CH).

FMRP regulation of dendritic HCN channels between in mouse hippocampus and prefrontal cortex

Synapse meeting 2019 – Lausanne (CH).

Input specific dendritic integration by barrel cortex supragranular pyramidal cells
Swiss Neuroscience meeting 2020 – Bern (CH).

CERTIFICATI E ABILITAZIONI PER SPERIMENTAZIONE ANIMALE

RESAL module 1: Introductory course in laboratory animal science. Education and training of Persons Conducting Animal Experiments (Ordinance governing Education in Keeping and Handling Animal in Switzerland (455.109.1), Septembre 2008,5th)

PUBBLICAZIONI

Highly dynamic spines on a cortical VIP interneuron subtype. C. GEORGIU , V.KEHAYAS, **F. BRANDALISE**, D. A. SAHLENDER, J. BLANC, G. KNOTT, A. HOLTMAAT [under review in Nature Communications].

MANUSCRITTI IN PREPARAZIONE

Loss of dendritic Na⁺ channels impairs dendritic spike generation in L5 PFC neurons in Fragile X syndrome
F. BRANDALISE*, B. KALMBACH*, JOHNSTON, D. H. BRAGER [in preparation].

***these authors contributed equally to this work.**

Dendritic integration of long-range inputs by barrel cortex pyramidal cells **Brandalise F***, Chereau R*, Pages S.* Holtmaat Anthony [in preparation]. ***these authors contributed equally to this work.**