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Supplementary Videos: 0

Reporting Checklist for Nature Neuroscience

This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. For more information, please read Reporting Life Sciences Research.

Please note that in the event of publication, it is mandatory that authors include all relevant methodological and statistical information in the manuscript.

Statistics reporting, by figure

- Please specify the following information for each panel reporting quantitative data, and where each item is reported (section, e.g. Results, & paragraph number).
- Each figure legend should ideally contain an exact sample size (n) for each experimental group/condition, where n is an exact number and not a range, a clear definition of how n is defined (for example x cells from x slices from x animals from x litters, collected over x days), a description of the statistical test used, the results of the tests, any descriptive statistics and clearly defined error bars if applicable.
- For any experiments using custom statistics, please indicate the test used and stats obtained for each experiment.
- Each figure legend should include a statement of how many times the experiment shown was replicated in the lab; the details of sample collection should be sufficiently clear so that the replicability of the experiment is obvious to the reader.
- For experiments reported in the text but not in the figures, please use the paragraph number instead of the figure number.

Note: Mean and standard deviation are not appropriate on small samples, and plotting independent data points is usually more informative. When technical replicates are reported, error and significance measures reflect the experimental variability and not the variability of the biological process; it is misleading not to state this clearly.

		TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
example	1a	one-way ANOVA	Fig. legend	9, 9, 10, 15	mice from at least 3 litters/group	Methods para 8	error bars are mean +/- SEM	Fig. legend	p = 0.044	Fig. legend	F(3, 36) = 2.97	Fig. legend
example	results, para 6	unpaired t-test	Results para 6	15	slices from 10 mice	Results para 6	error bars are mean +/- SEM	Results para 6	p = 0.0006	Results para 6	t(28) = 2.808	Results para 6

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		TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
+ -	3d(IBA1)	unpaired-t test	Fig. legend	Liposome study: (18, 18) PLX chow study: (16,11)	PBS (n=3, 18 sections) and CL (n=3, 18 sections); Iba1+ cells in control (n=4, 16 sections) and PLX chow groups (n=4, 11 sections)	Fig legend	Columns are mean ± SEM	Fig legend	p=0.0013 (Liposome) P<0.001 (PLX chow)	Fig legend	t(34)=3.506 (Liposome) t(25)=7.185(PLX chow)	
+ -	3d(AT8)	Unpaired-t test	Fig. legend	Liposome study: (16, 14) PLX chow study: (18,16)	AT8+ cells in PBS (n=3, 16 sections) and CL (n=3, 14 sections): AT8+ cells in control (n=4, 18 sections) and PLX chow groups (n=4, 16 sections)	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.017 (Liposome) p<0.0001 (PLX chow)	Fig. legend	t(28)=3.470 (Liposome) t(32)=4.605(PLX chow)	
+ -	3f(IBA1 and AT8)	Unpaired t-test	Fig. legend	IBA1 study: MEC:(23, 12) DG: (20,14) AT8 study: MEC (19, 11), DG (18, 14)	Iba1+ cells in the MEC in control (n=4, 23 sections) and PLX chow groups (n=3, 12 sections): Iba1+ cells in the DG in control (n=4, 20 sections) and PLX chow groups (n=3, 11 sections); AT8+ cells in control (n=4, 19 sections) and PLX chow groups (n=4, 14 sections): AT8+ cells in control (n=4, 18 sections) and PLX chow groups (n=4, 14 sections)	Fig. legend	Columns are mean ± SEM	Fig. legend	IBA1:p<0.0001(MEC) p<0.0001 (DG) AT8: p=0.033 (MEC) p<0.0001 (DG)	Fig. legend	IBA1: t(33)=7.647 (MEC), t(32)=10.35 (DG) AT8: t(28)=2.243 (MEC), t(30)=4.791	
+ -	4c	Two-way repeated measurement ANOVA	Fig. legend	A total of 61 fields from 61 slices (16 AAV-GFP, 10 AAV-GFP/tau, 16 AAV-GFP+PLX, and 19 AAV-GFP/tau +PLX)	16 AAV-GFP, 10 AAV-GFP/tau, 16 AAV-GFP+PLX, and 19 AAV-GFP/tau +PLX from 3 mice/ group	Fig. legend	Each dot represents mean ± SEM	Fig. legend	p=0.0003 for AAV-GFP +Control vs. AAV-GFP/tau +Control, p=0.0605 for AAV-GFP/tau +Control vs. AAV-GFP +PLX, p=0.0057 for AAV-GFP/tau +Control vs. AAV-GFP/tau +PLX	Fig. legend	F(14,364)=2.932 for AAV-GFP +Control vs. AAV-GFP/tau +Control, F(14,350)=1.668 for AAV-GFP/tau +Control vs. AAV-GFP +PLX, F(14,392)=2.263 for AAV-GFP/tau +Control vs. AAV-GFP/tau +PLX	
+ -	5f	One-way ANOVA	Fig. legend	3, 3,3,3,3	3 individual experiments	Fig. legend	Columns are mean ± SEM	Fig. legend	p<0.0001	Fig. legend	F(4,10)=253.3	
+ -	5h	One-way ANOVA	Fig. legend	12,9,9	+LPS+Tau (n=4, 12 sections), -LPS-Tau (n=3, 9 sections) and naked tau (n=3, 9 sections)	Fig. legend	Columns are mean ± SEM	Fig. legend	p<0.0001	Fig. legend	F(2,27)=36.08	

+ -	6c	Unpaired t-test	Fig. legend	261, 107	images from 20 pictures/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.0371	Fig. legend	t=2.092, df=366	
+ -	6d	One-way ANOVA	Fig. legend	3,3,3,3,3, 3	3 samples from two individual experiments	Fig. legend	Columns are mean ± SEM	Fig. legend	P<0.0001	Fig. legend	F(5,6)=539.3	
+ -	6e	One-way ANOVA	Fig. legend	3,3,3,3,3, 3	3 samples from two individual experiments	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.0078	Fig. legend	F(5,6)=9.632	
+ -	6g	One-way ANOVA	Fig. legend	3,3,3	3 samples from two individual experiments	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.0026	Fig. legend	F=12.34	
+ -	7c	Unpaired t-test	Fig. legend	3,3	3 individual experiments	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.0017	Fig. legend	t(4)=7.126	
+ -	7d	Unpaired t-test	Fig. legend	3,3	3 individual experiments	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.0060	Fig. legend	t(4)=5.325	
+ -	8c	Unpaired t-test	Fig. legend	MEC:(11, 10) Hp: (12,12)	MEC DMSO (11), MEC GW4869 (10), Hp DMSO (12), and Hp GW4869 (12) from 3 mice/group	Fig. legend	Columns re mean ± SEM	Fig. legend	p=0.8067(MEC) p=0.0013 (Hp)	Fig. legend	t(19)=0.2481(MEC) t(22)=3.698 (Hp)	
+ -	8d	Unpaired t-test	Fig. legend	3,3,3,3	3 mice/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.7512(MEC) p=0.0136 (Hp)	Fig. legend	t(4)=0.3397(MEC) t(4)=4.228 (Hp)	
+ -	S3b	One-way ANOVA	Fig. legend	17, 17, 22, 22	7dpi AAV-GFP (17), 7dpi AAV-Tau (17), 28dpi AAV-GFP (22) and 28dpi AAV-Tau (22) from 3 mice per group	Fig. legend	Columns are mean ± SEM	Fig. legend	p>0.9999 (7dpi), p=0.3231 (28dpi)	Fig. legend	F(32)=0.0, F(42)=0.9992	
+ -	S6a	Unpaired t-test	Fig. legend	3, 3	3 mice/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.8515	Fig. legend	t=0.1996, df=4	
+ -	S6b	Two-way ANOVA with multiple comparisons	Fig. legend	3, 3	3 mice/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p<0.0001	Fig. legend	F(1,20)=77.29, t(20)=2.987* (TNFA), 2.877* (IL1B), 5.422*** (IL6), 4.852*** (IL10), and 3.610** (TGFB1)	
+ -	S7d	One-way ANOVA	Fig. legend	3,3,3,3,3, 3	3 samples/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.0005 (MG), p=0.0005 (BV2)	Fig. legend	MG: F(2,6)=34.93, q(6)=11.82*** (MG no hTau vs. MG hTau), 5.781* (MG no hTau vs. MG hTau+CyD), and 6.039* (MG hTau vs. MG hTau +CyD). BV2: F(2,6)=34.94, q(6)=11.80*** (BV2 no hTau vs. BV2 hTau), 5.285* (BV2 no hTau vs. BV2 hTau+CyD), 6.517** (BV2 hTau vs. BV2 +CyD)	
+ -	S9a	Unpaired t-test	Fig. legend	3, 3	3 mice/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p=0.9295	Fig. legend	t(4)=0.09420	
+ -	S9b	Two-way ANOVA with multiple comparisons	Fig. legend	3, 3	3 mice/group	Fig. legend	Columns are mean ± SEM	Fig. legend	p<0.0001	Fig. legend	F(1,20)=28.89, t(20)=2.819 (TNFA), 1.535 (IL1B), 1.114 (IL6), 4.725*** (IL10), and 1.826 (TGFB1)	

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Representative figures

1. Are any representative images shown (including Western blots and immunohistochemistry/staining) in the paper?

   If so, what figure(s)?

   Fig1 a-e, Fig. 2 a-f, Fig3 a-c,e, Fig. 4a, Fig. 5 b-g, Fig. 6 a,f, Fig. 7a-d, Fig. 8a,b,d.

2. For each representative image, is there a clear statement of how many times this experiment was successfully repeated and a discussion of any limitations in repeatability?

   If so, where is this reported (section, paragraph #)?

   Yes, Figure legend of Fig. 1-8.

Statistics and general methods

1. Is there a justification of the sample size?

   If so, how was it justified?

   Where (section, paragraph #)?

   Even if no sample size calculation was performed, authors should report why the sample size is adequate to measure their effect size.

   Sample sizes are provided in the figure legend and/or the Methods section. No statistical methods were used to pre-determine sample sizes but our sample sizes are similar to those generally employed in the field. This is stated in the Statistics section of supplementary methods.

2. Are statistical tests justified as appropriate for every figure?

   Where (section, paragraph #)?

   Yes, it is in the respective figure legend.

   a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?

      Yes, the summary of statistical analysis was stated in the method section, and the method applied for each statistics was defined in the figure legend of each experiment.

   b. Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)?

      Where is this described (section, paragraph #)?

      The estimate of variance was determined by the standard deviation of each group, which was similar between groups for the statistical comparison, and the normality of a parametric test was examined for each experiment using D'Agostino-Peasron omnibus test (omnibus K2 test, Prism 6) for the sample size of 6 or higher. For a smaller sample size, the data distribution was assumed to be normal but this was not formally tested. This is described in the Statistics paragraph of the Method section.

   c. Is there any estimate of variance within each group of data?

      Is the variance similar between groups that are being statistically compared?

      Where is this described (section, paragraph #)?

      Yes, the estimate of variance was determined by the standard deviation of each group, which was similar between groups for the statistical comparison. This is stated in the Statistics section of the supplementary method(last paragraph).

   d. Are tests specified as one- or two-sided?

      It is specified wherever applicable.

   e. Are there adjustments for multiple comparisons?

      No adjustment is performed.

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3. Are criteria for excluding data points reported? Was this criterion established prior to data collection? Where is this described (section, paragraph #)?	Yes, some outliers are excluded after the omnibusK2 analysis.
4. Define the method of randomization used to assign subjects (or samples) to the experimental groups and to collect and process data. If no randomization was used, state so. Where does this appear (section, paragraph #)?	The ID of all the tested animals and tissue samples were de-identified for data collection (such as immunohistochemistry, image capturing, and Western blotting) and processing (such as statistical analysis) for testers, and the identity was disclosed at the completion of the experiment. The method of randomization is stated in the Experimental Procedure section of supplementary method (18th pragraph).
5. Is a statement of the extent to which investigator knew the group allocation during the experiment and in assessing outcome included? If no blinding was done, state so. Where (section, paragraph #)?	The investigator in charge of injection of AAV into mouse brain knows the identity of animals with the treatment, but the investigators/testers in charge of tissue collection, immunohistochemistry, Western blotting, and other procedures following euthanasia are blinded for the identity of the animals/ samples until the completion of the experiments and assessment of the outcomes. This is stated in the Experimental Procedure section of supplementary method (18th paragraph).
6. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included? Where (section, paragraph #)?	Yes, it is in the supplemental method part (1st paragraph).
7. Is the species of the animals used reported? Where (section, paragraph #)?	Yes, it is in the supplemental method part (1st and 2nd paragraph).
8. Is the strain of the animals (including background strains of KO/ transgenic animals used) reported? Where (section, paragraph #)?	Yes, it is in the supplemental method part (1st and 2nd paragraph).
9. Is the sex of the animals/subjects used reported? Where (section, paragraph #)?	No, our experimental design (acute protein propagation analysis in mouse brain) is not significantly affected by the gender difference.
10. Is the age of the animals/subjects reported? Where (section, paragraph #)?	Yes, it is in the supplemental method part (1st and 2nd paragraph)
11. For animals housed in a vivarium, is the light/dark cycle reported? Where (section, paragraph #)?	Yes, animals were housed in a standard light/dark cycle. This was stated in Animals section of the supplementary method (1st paragraph).
12. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported? Where (section, paragraph #)?	No, all the animals were housed individually to avoid postoperative complications.

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13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)?

    Where (section, paragraph #)?

N/A

14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported?

    Where (section, paragraph #)?

N/A

    a. If multiple behavioral tests were conducted in the same group of animals, is this reported?

       Where (section, paragraph #)?

N/A

15. If any animals/subjects were excluded from analysis, is this reported?

    Where (section, paragraph #)?

No animals were excluded from analysis.

    a. How were the criteria for exclusion defined?

       Where is this described (section, paragraph #)?

N/A

    b. Specify reasons for any discrepancy between the number of animals at the beginning and end of the study.

       Where is this described (section, paragraph #)?

N/A

Reagents

1. Have antibodies been validated for use in the system under study (assay and species)?

All of the commercially available antibodies were validated by the manufacturer. T22 rabbit polyclonal antibody was a custom product of Dr. Kayed's laboratory, and has been validated with citation.

    a. Is antibody catalog number given?

       Where does this appear (section, paragraph #)?

Yes, these information are in supplementary method section 5, 10, and 11th paragraph.

    b. Where were the validation data reported (citation, supplementary information, Antibodypedia)?

       Where does this appear (section, paragraph #)?

T22 rabbit polyclonal antibody is cited in "Lasagna-Reeves CA et al, Biochemistry. 2010; 49:10039-41".

2. If cell lines were used to reflect the properties of a particular tissue or disease state, is their source identified?

    Where (section, paragraph #)?

Yes. BV-2 murine microglia cell line was used on Supplementary Figure 7d. The source of BV-2 is listed in Supplemental Method under section "Tau Phagocytosis Assay" (p. 8, 1st paragraph)

    a. Were they recently authenticated?

       Where is this information reported (section, paragraph #)?

No, it was established in by Blasi E et al. in 1990 and has been utilized as a reference murine microglia cell line since then.

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Data deposition

Data deposition in a public repository is mandatory for:

a. Protein, DNA and RNA sequences
b. Macromolecular structures
c. Crystallographic data for small molecules
d. Microarray data

Deposition is strongly recommended for many other datasets for which structured public repositories exist; more details on our data policy are available here. We encourage the provision of other source data in supplementary information or in unstructured repositories such as Figshare and Dryad.

We encourage publication of Data Descriptors (see Scientific Data) to maximize data reuse.

1. Are accession codes for deposit dates provided?

   Where (section, paragraph #)?

N/A

Computer code/software

Any custom algorithm/software that is central to the methods must be supplied by the authors in a usable and readable form for readers at the time of publication. However, referees may ask for this information at any time during the review process.

1. Identify all custom software or scripts that were required to conduct the study and where in the procedures each was used.

N/A

2. If computer code was used to generate results that are central to the paper's conclusions, include a statement in the Methods section under "**Code availability**" to indicate whether and how the code can be accessed. Include version information as necessary and any restrictions on availability.

N/A

Human subjects

1. Which IRB approved the protocol?

   Where is this stated (section, paragraph #)?

N/A

2. Is demographic information on all subjects provided?

   Where (section, paragraph #)?

N/A

3. Is the number of human subjects, their age and sex clearly defined?

   Where (section, paragraph #)?

N/A

4. Are the inclusion and exclusion criteria (if any) clearly specified?

   Where (section, paragraph #)?

N/A

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5. How well were the groups matched?

   Where is this information described (section, paragraph #)?

N/A

6. Is a statement included confirming that informed consent was obtained from all subjects?

   Where (section, paragraph #)?

N/A

7. For publication of patient photos, is a statement included confirming that consent to publish was obtained?

   Where (section, paragraph #)?

N/A

fMRI studies

For papers reporting functional imaging (fMRI) results please ensure that these minimal reporting guidelines are met and that all this information is clearly provided in the methods:

1. Were any subjects scanned but then rejected for the analysis after the data was collected?

N/A

   a. If yes, is the number rejected and reasons for rejection described?

      Where (section, paragraph #)?

N/A

2. Is the number of blocks, trials or experimental units per session and/or subjects specified?

   Where (section, paragraph #)?

N/A

3. Is the length of each trial and interval between trials specified?

N/A

4. Is a blocked, event-related, or mixed design being used? If applicable, please specify the block length or how the event-related or mixed design was optimized.

N/A

5. Is the task design clearly described?

   Where (section, paragraph #)?

N/A

6. How was behavioral performance measured?

N/A

7. Is an ANOVA or factorial design being used?

N/A

8. For data acquisition, is a whole brain scan used?

   If not, state area of acquisition.

N/A

   a. How was this region determined?

N/A

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9. Is the field strength (in Tesla) of the MRI system stated?	N/A
a. Is the pulse sequence type (gradient/spin echo, EPI/spiral) stated?	N/A
b. Are the field-of-view, matrix size, slice thickness, and TE/TR/ flip angle clearly stated?	N/A
10. Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and pre-processing clearly stated?	N/A
11. Is the coordinate space for the anatomical/functional imaging data clearly defined as subject/native space or standardized stereotaxic space, e.g., original Talairach, MNI305, ICBM152, etc? Where (section, paragraph #)?	N/A
12. If there was data normalization/standardization to a specific space template, are the type of transformation (linear vs. nonlinear) used and image types being transformed clearly described? Where (section, paragraph #)?	N/A
13. How were anatomical locations determined, e.g., via an automated labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?	N/A
14. Were any additional regressors (behavioral covariates, motion etc) used?	N/A
15. Is the contrast construction clearly defined?	N/A
16. Is a mixed/random effects or fixed inference used?	N/A
a. If fixed effects inference used, is this justified?	N/A
17. Were repeated measures used (multiple measurements per subject)?	N/A
a. If so, are the method to account for within subject correlation and the assumptions made about variance clearly stated?	N/A
18. If the threshold used for inference and visualization in figures varies, is this clearly stated?	N/A
19. Are statistical inferences corrected for multiple comparisons?	N/A
a. If not, is this labeled as uncorrected?	N/A

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20. Are the results based on an ROI (region of interest) analysis? N/A

    a. If so, is the rationale clearly described? N/A

    b. How were the ROI's defined (functional vs anatomical localization)? N/A

21. Is there correction for multiple comparisons within each voxel? N/A

22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined? N/A

Additional comments

Additional Comments

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