nature portfolio

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Last updated by author(s): Apr 9, 2026

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	*Provide a description of all commercial, open source and custom code used to collect the data in this study, specifying the version used OR state that no software was used.*
Data analysis	*Provide a description of all commercial, open source and custom code used to analyse the data in this study, specifying the version used OR state that no software was used.*

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The single-cell RNAseq data generated in this study have been deposited in the GEO database under accession code GSE327886. Any other relevant data or information will be shared by the corresponding authors on reasonable request.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	*Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used.* *Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected.* *Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.*
Reporting on race, ethnicity, or other socially relevant groupings	*Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).* *Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)* *Please provide details about how you controlled for confounding variables in your analyses.*
Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	*Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No statistical methods were used to pre-determine sample sizes but our sample sizes are similar to those reported in previous publications (Baruch et al. 2016, Nat. Med.; Rosenzweig et al., 2019, Nat. Comm.; Dvir-Szternfeld et al., 2022, Nat. Aging).
Data exclusions	No data was excluded from analysis.
Replication	All the flow cytometry analyses are the result of two or three repetitions.
Randomization	Animals were asigned to sham or denervated groups randomly, as well as for anti-CCR2 treatment or TH-overepxression.
Blinding	The treatment of each animal was blinded to the person performing and analyzing the behavioral tests and the histological analysis.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

Antigen Fluorophore Clone Supplier Ref. No. Dilution
CD117 (cKit) PE 2B8
BioLegend 105808 1/200
CD11b PE M1/70 BioLegend 101207 1/500
CD11b FITC M1/70
BioLegend 101206 1/500
CD150 PE-Cy5 TC15-12F12.2 BioLegend 115912 1/200
CD44 APC IM7 BioLegend 103011 1/200
CD45 BV421 30-F11 BioLegend 103134 1/200
CD48 APC-Cy7 HM48-1 BioLegend 103432 1/200
Lineage Cocktail Biotin --- Miltenyi Biotec 130-092-613 1/20
Ly-6C PE-Dazzle HK1.4
BioLegend 128044 1/200
Ly-6G APC 1A8 BioLegend 127613 1/500
Ly-6A/E (Sca-1) PE-Cy7 D7 BioLegend 108114 1/200
Streptavidin FITC --- BioLegend 405202 1/200
TCRbeta APC-Cy7 H57-597 BioLegend 109220 1/200

Validation

For flow cytometry experiments, antibodies were used according to manufacturer's instructions and each antibody was further compared to an unstained sample or fluorescence-minus-one control.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

HEK293T: Human Embryonic Kidney cells, female.

Authentication

None of the cells were authenticated.

Mycoplasma contamination

Negative for mycoplasma.

Commonly misidentified lines
(See ICLAC register)

Name any commonly misidentified cell lines used in the study and provide a rationale for their use.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals

All experiments described here complied with the regulations formulated by the Institutional Animal Care and Use Committee (IACUC) of the Weizmann Institute of Science. Female and male mice were bred and maintained by the animal breeding center of the Weizmann Institute of Science. For all experiments, heterozygous 5xFAD transgenic mice (line Tg6799, The Jackson Laboratory) on a C57/BL6-SJL background and wild-type (WT) littermates were used. Genotyping was performed by PCR analysis of ear clip DNA, as previously described. Mice subjected to the various manipulations were mixed within cages.

Wild animals

n/a

Reporting on sex

Sex of the animals used in the study is reported in the figure legends.

Field-collected samples

n/a

Ethics oversight

All experiments detailed here were approved by the Institutional Animal Care and Use Committee (IACUC) of the Weizmann Institute of Science and by the Ethical Committee for Animal Testing at the University of Navarra.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	For immune profiling of brain immune cells by Flow Cytometry or scRNAseq, the brains were excised excluding the medulla, without dissecting meninges and choroid plexus, and manually chopped (0.5–1.0mm2 in size), before enzymatic dissociation using 0.4mg/ml Collagenase D, 2mM HEPES (BI Industries), 10µg/ml DNase (Sigma), and 2% FCS for 20 min at 37°C. For density gradient separation, the pellet was resuspended with 37% Percoll in PBS and centrifuged at 800g for 20min at 4°C with no brake; the supernatant was then discarded. Cells were suspended in ice-cold sorting buffer (PBS supplemented with 2 mM EDTA and 2% FCS) supplemented with anti-mouse CD16/32 (1:100, no. 101302, BioLegend) to block Fc receptors before labeling with fluorescent antibodies against cell-surface epitopes (Supplementary Table 1).
Instrument	CytoFlex S or FACS Aria II
Software	FlowJo v10
Cell population abundance	*Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.*
Gating strategy	Monocytes: CD45+ CD11b+ Ly6Chigh

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.