nature research

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Last updated by author(s): May 25, 2021

Reporting Summary

Nature Research 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 Research 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	Scanco Medical, IPL for custom ROI picker tool (http://www.scanco.ch/en/applications/biomedical.html) Zeiss microscopy software
Data analysis	https://matplotlib.org https://numpy.org pi2 software (version 3.0) (https://github.com/arttumiettinen/pi2) Python 3.6. http://www.openwalnut.org/ for 3D renderings 3D Slicer 4.10.2 (https://www.slicer.org), to register the whole-brain images to the Allen Brain Atlas

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 Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The raw data underlying all graphical figures is provided in individual Excel (comma separated value (".csv")) files via Figshare (https://doi.org/10.6084/m9.figshare.13483119). For each panel of every figure, a ".cvs" file is provided with the linked figure noted within both the file and the file name.

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	Power calculations based on the expected or biologically relevant difference between the groups should be made prior to the experiments. In principle, more pronounced differences between two test groups require a smaller number of animals to detect the effect and vice versa. Incorporation of appropriate controls, for instance, brains from postnatal wild-type littermates, is essential for analyses of angiogenesis and vascular network architecture in genetically modified mice during postnatal CNS development as well as in adulthood. For all quantitative analysis in the different brain regions (Figures 5-10, Extended Data Figures 5-8, and Supplementary Figures 2-9), we used 4-6 postnatal (P10), and 8-12 adult (P60) animals, respectively.
Data exclusions	We have sorted all samples by VVF and manually excluded nearly empty and/or degenerate datasets. Manual selection was required as VVF alone is not sufficient to discover nearly empty and/or degenerate datasets. It does not cover corner-cases like samples at region borders that show a clear cut in the data but also contain a very dense vessel network (high vvf, still degenerate and not usable for all volume related stats).
Replication	All steps in this protocol can be replicated with the listed materials and reagents, and by following the described imaging and analysis steps.
Randomization	Four study groups were used: P10 wildtype mice, P10 Nogo-A-/- mice, P60 wildtype mice, and P60 Nogo-A-/- mice. Randomization for these mice was not necessary. Brains from adult mice for immunofluorescence staining, were selected randomly.
Blinding	Blinding was not possible as stains and image analysis were performed by the same researchers.

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	DAPI (4',6-Diamidino-2-Phenylindole, Dihydrochloride) Nucleic Acid Stain (Invitrogen™) (excitation/emission maxima: 358/461 nm) FluoroMyelin™ Red Fluorescent Myelin Stain (Invitrogen™) (excitation/emission maxima: 558/654 nm)
Validation	All antibodies used for this protocol were comercially available and validated by the manufacturer.

Validation	- DAPI, information regarding validation of this antibody can be found at https://www.thermofisher.com/order/catalog/product/D1306#/D1306 - FluoroMyelin Red, information regarding validation of this antibody can be found at https://www.thermofisher.com/order/catalog/product/F34652#/F34652

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	10-d-old and 2-month-old mice (wild type and Nogo-A-/- C57BL/6, male or female) (Charles River Laboratories)
Wild animals	The study did not involve wild animals
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All the animal experiments herein were performed in accordance with governmental, institutional (University of Zurich), and ARRIVE guidelines, and had been approved by the Veterinary Office of the Canton of Zurich (license number 173/2010).

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