nature portfolio

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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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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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.
X	A description of all covariates tested
\boxtimes	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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\times	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
X	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
X	Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection

Tucker-Davis Technologies Synapse (Version 90-39473P), MicroManager (Version 1.4), Olympus Fluoview (FV10), Arduino IDE (Version 1.8.15), MathWorks Matlab (R2019a, R2019b)

Data analysis

MathWorks Matlab (R2019a, R2019b), FIJI (Version 1.53c), GraphPad Prism 8.4.3, R, Python

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 <u>guidelines for submitting code & software</u> 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

All data supporting the findings of this study are available upon request.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

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 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.

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 <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size Sample size was determined based on similar studies in the literature and our experience. No statistical method was used to determine the sample size prior to the study.

Data exclusions

Animals in which post-hoc histological examination showed that viral targeting or the position of implanted fiber were in the incorrect location were excluded from analysis. This exclusion criteria was predetermined.

Replication

We performed multiple independent experiments as noted in the figure legends. Results were reproducible.

Randomization

Stimuli order was random, otherwise in situations as described in the manuscript where no randomization was used, the stimuli were interspersed and repeated among trials.

Blinding

Investigators were not blinded to group allocation, as data analysis was performed automatically with the same scripts executed for each experimental group.

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 & experime	ntal systems	Methods
n/a Involved in the study		n/a Involved in the study
Antibodies		ChIP-seq
Eukaryotic cell lines		Flow cytometry
Palaeontology and a	archaeology	MRI-based neuroimaging
Animals and other o	organisms	
Clinical data		
Dual use research o	f concern	
Z		
A collection		
Antibodies		
beta (R&D Systems, D' TNF-alpha (R&D Syste		, 226004, Guinea Pig, 1:5000), anti IL-6 (R&D Systems, DY406, Capture, 1:120, Detection, 1:60), anti IL-1 Capture, 1:120, Detection, 1:60), anti IL-10 (R&D Systems, DY417, Capture, 1:120, Detection, 1:60), anti /410, Capture, 1:125, Detection, 1:60), anti-CXCL-1(R&D Systems, DY45305, Capture, 1:120, Detection, nvitrogen, EIACORT, 1:7) and anti-DBH SAP (Advanced Targeting Systems, IT-03, 40 ng)
Validation	3210, (2019); Li, et al. Natur levels in mouse blood sampl Reports, 38(10): 110462, (20 eabf0466, (2021); CXCL-1: G	dated extensively by immuno-staining on mouse brain sections (Song, et al. Science advances, 5(2): eaat e, 60: 722, (2022)). Cytokine antibodies have been validated in ELISA experiments measuring cytokine es (IL-6: Peruzzo, et al. Nature Communications, 12(1):2103, (2021); IL-1 beta: Sugisawa, et al. Cell 202); IL-10: Csoka, et al. Diabetes, 63(3): 850, (2014); TNF-alpha: Virga, et al. Science Advances, 7(19): awish, et al. Elife, 11(0): e78291, (2022); Corticosterone: You et al. Nature Communications, 14: 6875, I antibody (anti-DBH SAP) has been validated to be highly effective in selectively killing DBH-neurons in, 145(1):154-167)
Animals and othe	r research organ	isms
Policy information about <u>st</u> <u>Research</u>	udies involving animals; Al	RRIVE guidelines recommended for reporting animal research, and Sex and Gender in
Laboratory animals	Mice both male and female	and at least 7 weeks of age were used in the study. C56BL/6J (JAX 000664); Myd88-/- (JAX 009088);

Wild animals No wild animals were used.

Reporting on sex

Animals of both sexes were used in the immune-challenging and imaging studies, without bias.

Field-collected samples No field-collected samples were used.

Ethics oversight

All procedures were carried out in accordance with the US National Institutes of Health (NIH) guidelines for the care and use of laboratory animals, and were approved by the Institutional Animal Care and Use Committee at Columbia University.

TRAP2 (JAX 030323); Dbh-cre (JAX 033951); Vip-IRES-cre (JAX 010908); Gpr65-IRES-cre (JAX 029282); Piezo2-cre (JAX 027719); Oxtr-IRES-cre (JAX 030543); Vglut2-IRES-cre (JAX 028863); Vgat-IRES-cre (JAX 016962); Ai939 (JAX 007909); Ai96 (JAX 028866); Ai162 (JAX 031562); Rosa-iDTR (JAX, 007900) were obtained from the Jackson Laboratory. Trpa1-IRES-cre6 was generated in the Zuker lab.

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

Calca-cre mice were a generous gift of Richard Palmiter.