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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 Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	For Sholl analyses images were analyzed using the ImageJ(v1.51a-1.51h) Plugin Sholl Analysis v3.6.4; tracing individual neuronal processes was performed using ImageJ software.
Data analysis	Details about data analysis and visualization are provided in the Online Methods section of the paper. The following versions were used: Bioconductor package TopGO v2.3.1 employing the default algorithm weight01, GraphPad Prism v6.01, Igor Pro6 6.0.3.0; Custom R packages were used:TopHat v2.0.8, SAMTOOLS v.0.1.19, HTSeq v0.5.4p1. DESeq2 v1.3.0, FactoMineR v1.34, Seurat v1.4, Monocle2 v2.6.4, igraph v1.2.1, Seurat v2.1-2.2

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/reviewers upon request. 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 scRNA-seq data used in this study have been in the Gene Expression Omnibus (GEO) under accession number GSE113036. The data that support the findings of this study are available from the corresponding author upon reasonable request. Correspondence and requests for materials and data should be addressed to M.K. (marisa.karow@med.uni-muenchen.de), and B.T. (barbara_treutlein@eva.mpg.de), and B.B. (berningb@uni-mainz.de).

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-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 (Karow et al., Cell Stem Cell 2012; Treutlein et al., Nature 2016)
Data exclusions	No data points were excluded for the analysis, except for cells in the scRNA-seq analyses not fulfilling the required criteria. For the fluidigm C1 scRNA-seq data: We excluded cells that had less than 100,000 reads, did not express > 1000 genes, or did not express either of two housekeeping genes ACTB and GAPDH. For the 10x Genomics scRNA-seq data: only single cells with 1,000-7,000 genes were included; cells with lower or higher number of detected genes were excluded.
Replication	For all experiments all replicates are indicated in the figure legends or the methods sections. We have provided all informations to reproduce the experiments. All replications were successful.
Randomization	Samples (pericyte donors, coverslips in 24-well plates, T25 or T75 cell culture flasks) were randomly assigned for transduction with different viruses.
Blinding	scRNA-sequencing analyses were performed unbiasedly and therefore blinding is not applicable. Regarding all other data, if not indicated otherwise (e.g. Sholl analysis), data collection and analysis were not performed blind to the conditions of the experiments. These experiments were performed by a single experimentator (MK)

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☐ Eukaryotic cell lines
☐	☐ Palaeontology
☐	☐ Animals and other organisms
☐	☒ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All unique material (Ascl1/Sox2 encoding viruses) are available from the authors upon

Obtaining unique materials	reasonable request. Any other material is published elsewhere or commercially available.

Antibodies

Antibodies used	Mouse (IgG2b) anti-TUBB3 (Sigma; cat.no. T8660; 1:300), rat IgG2a anti-CD49f-PE (Miltenyi Biotec; cat.no. 130-100-096; 1:11), recombinant human anti-CD4 (Miltenyi; cat.no. 130-109-537; 1:11), rabbit anti-GABA (Abcam; cat.no. ab17413; 1:1000), chick anti-GFP (Aves; cat.no. GFP-1020; 1:500), mouse (IgG1) anti-Pvalb (Swant; cat.no. PV-235; 1:1000), rabbit anti-Pdgfrb (Cell Signaling; cat.no. 3169S; 1:300), rat anti-RFP (Chromotek; cat.no. 5F8; 1:500), mouse (IgG2b) anti-SMA (Sigma; cat.no. A5228; 1:500), rabbit anti-VGLUT1 (Synaptic Systems, cat.no. 135302; 1:500). For FACS: mouse (IgG2b) anti-LEPR Al647 (BD Pharmingen; cat.no. 564376; 1:20), corresponding isotype control (BD Pharmingen; cat.no. 557903; 1:20).
Validation	Antibodies were selected according to the antibody validation reported by the distributing companies.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	no eukaryotic cell lines used
Authentication	no eukaryotic cell lines used
Mycoplasma contamination	no eukaryotic cell lines used
Commonly misidentified lines (See ICLAC register)	no eukaryotic cell lines used

Palaeontology

Specimen provenance	no specimen used
Specimen deposition	no specimen used
Dating methods	no specimen used

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Animals and other organisms

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

Laboratory animals	no animals or other organisms used
Wild animals	no animals or other organisms used
Field-collected samples	no animals or other organisms used

Human research participants

Policy information about studies involving human research participants

Population characteristics	no human research participants
Recruitment	no human research participants

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	no ChIP-seq data included in this study
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	*Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.*
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	*Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.*

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 sorting of transduced cells for further i) culturing, ii) bulk RNA-sequencing, iii) scRNA-sequencing, primary pericytes were detached from the culture dish using TrypLE for 4-6 minutes and subsequently resuspended in 500-1000 µl pericyte growth medium. For the separation of LEPR-positive and -negative pericyte populations, pericyte cultures were detached from the culture dish using TrypLE for 4-6 minutes and subsequently 1-5 x 105 cells were resuspended in 100 µl staining solution (PBS plus 0.5% BSA).
Instrument	FACS Aria (BD)
Software	FACS Diva Software
Cell population abundance	The purity of the fluorescent reporter-positive populations that were used for (bulk- and) scRNA-sequencing was confirmed via quantification of the reporter gene expression and resulted in a purity of more than 92%. Due to limitations of using the directly PE conjugated anti-LepR antibody, the purity of the post-sort fraction of the LepR-positive cell population could not be confirmed by additional post-FACS immunohistochemistry.
Gating strategy	For sort of transduced cells: Gating was achieved via subtracting the autofluorescence of non transduced cells and control (DsRed or GFP only) transduced cells were used as respective controls. For the LEPR-based sort: An Alexa647-conjugated isotype control antibody (1:100, BD Pharmingen) was used to gate the proper populations.

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

Magnetic resonance imaging

Experimental design

Design type	no MRI imaging used in this study
Design specifications	*Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.*
Behavioral performance measures	*State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).*

Acquisition

Imaging type(s) — *Specify: functional, structural, diffusion, perfusion.*

Field strength — *Specify in Tesla*

Sequence & imaging parameters — *Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.*

Area of acquisition — *State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.*

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software — *Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).*

Normalization — *If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.*

Normalization template — *Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.*

Noise and artifact removal — *Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).*

Volume censoring — *Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.*

Statistical modeling & inference

Model type and settings — *Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).*

Effect(s) tested — *Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.*

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016) — *Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.*

Correction — *Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).*

Models & analysis

n/a	Involved in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity — *Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).*

Graph analysis — *Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).*

Multivariate modeling and predictive analysis — *Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.*