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.

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
- 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
- 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

Data and images were collected using mFLPI2Meas (v2.0, Moor Instruments), OmniPlex (v1.13.0, Plexon), Smart (V3.0, Harvard Apparatus), pClamp (V9, Molecular Devices), FV30-SW (Olympus), SciScan (v1.4, Scientifica), ZEN (V2.6, Carl Zeiss AG), Tanon (6100C, Tanon), Xcalibur (v4.3, Thermo Fisher Scientific), and the following software: moorFLPIReview (V50, Moor Instruments); NeuroExplorer (V5, Nex Technologies); Smart (V3.0, Harvard Apparatus); pClamp (V9, Molecular Devices); ImageJ (v1.52k, NIH); Imaris (V9.2, Oxford Instruments); ZEN (V2.6, Carl Zeiss AG); MaxQuant (v.1.5.2.8, Max Planck Institute of Biochemistry); MeV (v4.9); InterProScan (v.5.15-3.0, EMBL-EBI).

Before statistical comparison, data and image analyses were collected using corresponding software (listed below). When only two groups were generated, a two-tailed unpaired t-test was used for normally distributed data. For multiple groups, a one-way ANOVA was used with appropriate post hoc tests for comparison between groups. Appropriate sample sizes were based on best practices in the literature as well as on ethical standards to minimize numbers of animals for experiments and were dictated by the magnitude of experiment-to-experiment variation. 1ANOVA was followed by a post hoc Fisher’s LSD, Tukey’s Sidak’s or Dunnett’s test to identify significant groups as indicated in the figure legends. 2ANOVA with repeated measures over time was applied to the analysis of LFPs, LTP recordings, distance traveled to the platform, and escape latency in the spatial acquisition test of MWM to detect significant differences between groups on different days or treatments. The statistical analysis was performed in Graphpad Prism (v7.0, GraphPad Software) and SPSS (v22.0, IBM).

Software: moorFLPIReview (V50, Moor Instruments); NeuroExplorer (V5, Nex Technologies); Smart (V3.0, Harvard Apparatus); pClamp (V9, Molecular Devices); ImageJ (v1.52k, NIH); Imaris (V9.2, Oxford Instruments); ZEN (V2.6, Carl Zeiss AG); MaxQuant (v.1.5.2.8, Max Planck Institute of Biochemistry); MeV (v4.9); InterProScan (v.5.15-3.0, EMBL-EBI).
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 data supporting the findings of this study is available with the article and its Supplementary Information file, or is available from the corresponding author upon request. The source data underlying Fig.1b-g, j-m, o-r; Fig. 2c-e; Fig. 3b-h; Fig. 4a-b, d-g; Fig 5a, b, d-e; Fig. 6e-l; Fig. 7b-d; Fig. 8; Supplementary Figs. 1b, c, f, g, i-n; Supplementary Fig. 2b, c, e-h; Supplementary Fig. 4; Supplementary Fig. 5; Supplementary Fig. 6, and Supplementary Fig. 8d-h are provided as a Source Data file. The mouse brain atlas images on the left of Supplementary Fig. 2a was derived from Allen Mouse Brain atlas (http://atlas.brain-map.org/atlases/1plate=100960240). Supplementary Fig. 8a protein sequence alignment was performed using CLUSTALW multiple sequence alignment at https://www.genome.jp/tools-bin/clustalw.

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.

- [X] 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**
Sample sizes were selected based on the previous examples of similar work in the literature. Adult male C57Bl/6 mice (3 months old) and adult male Thy1-YFP-H mice (3 months old) mice were used in this study. A total of 112 mice with the same age (3-month-old) and sex (male) were first randomly assigned to two groups (56 each) to receive Sham or 2VO surgery, respectively. For stroke behavioral analyses, each group had at least 7 mice to allow for statistic analyses. For electrophysiological recordings, at least 3 mice with more than 10 brain slices were used. These sample size allowed for acceptable statistical analyses to be performed while minimize numbers of animals for experiments dictated by the magnitude of experiment-to-experiment variation.

**Data exclusions**
Efforts were made to minimize the number of mice used. The inclusion criterion was based on the identical age and sex of the mice. The exclusion criterion was when the mouse failed to survive 2VO surgery at the end of the 14 d periods of the experimentation. Data derived from all qualified animals were included in the analyses and presentation of the results.

**Replication**
To achieve meaningful statistical differences, minimal of 5 mice per group were used in the LFP in vivo recordings, behavioral studies, RGS12 gene expression modifications experiments as indicated in the figure legends. For tissue section staining and Western blotting experimentation, at least 3 mice per group were used except 2 mice in western blotting of 3day. Where representative images are shown, at least three repeats have been performed with similar results.

**Randomization**
Mice used in the current study were randomly assigned into each group to maintain a total randomization. After the surgery, mice in each group were randomly assigned to receive LED light or occluded LED treatment.

**Blinding**
Investigators were blinded to groups allocation during data collection and data analysis as stated in the method section.

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**

- [X] Antibodies
- [X] Eukaryotic cell lines
- [X] Palaeontology
- [X] Animals and other organisms
- [X] Human research participants
- [X] Clinical data

**Methods**

- [X] ChIP-seq
- [X] Flow cytometry
- [X] MRI-based neuroimaging
Antibodies

| Antibodies used | Validation |
|-----------------|------------|
| Anti-Iba1 antibody [EPR16589](Abcam, ab178847); Anti-GFAP antibody(Abcam, ab7260); Anti-RGS 12 antibody (A-2)(Santa Cruz Biotechnology, sc-514173);Anti-Parvalbumin antibody(Abcam, ab11427); Anit-beta Actin(Abcam, ab6276). The dilutions of these anyibodies used have been described in the Source data file under Key reagents and in the Methods section. | All antibodies are commercially available and have been extensively validated by the manufacturer and in the literature. |

Eukaryotic cell lines

| Policy information about | cell lines |
|-------------------------|------------|
| Cell line source(s)     | State the source of each cell line used. |
| Authentication          | Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated. |
| Mycoplasma contamination | Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination. |
| Commonly misidentified lines | Name any commonly misidentified cell lines used in the study and provide a rationale for their use. |

Palaeontology

| Specimen provenance | Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). |
|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Specimen deposition | Indicate where the specimens have been deposited to permit free access by other researchers. |
| Dating methods      | If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided. |

Animals and other organisms

| Policy information about | studies involving animals. ARRIVE guidelines recommended for reporting animal research |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Laboratory animals      | Adult male C57Bl/6 mice (3 months old) and adult male Thy1-YFP-H mice (3 months old) mice were used in this study. |
| Wild animals            | No wild animals were used in the study. |
| Field-collected samples | No field collected samples were used in the study. |
| Ethics oversight        | All animal experiments were conducted according to protocols approved by the Animal Care Committee of the Southern University of Science and Technology (Shenzhen, China). Efforts were made to minimize the number of animals used. ARRIVE guidelines were followed. |

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

Human research participants

| Policy information about | studies involving human research participants |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Population characteristics | Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, 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.
Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration
Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.

Study protocol
Note where the full trial protocol can be accessed or if not available, explain why.

Data collection
Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.

Outcomes
Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.

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
For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.

Files in database submission
Provide a list of all files available in the database submission.

Genome browser session
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
Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.

Instrument
Identify the instrument used for data collection, specifying make and model number.

Software
Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.
### 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

Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.

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 | Indicate task or resting state; event-related or block design. |
|-------------|-------------------------------------------------------------|
| 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. |

#### 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: | \[\text{Whole brain} \quad \text{ROI-based} \quad \text{Both}\] |
| 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.*