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 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	No software was used.
Data analysis	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

All data supporting the findings are included within this manuscript and its Supplementary information. Source data are provided with this paper.

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 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	N numbers range from n=3 to n=8, with n=biological replicates (in vitro experiments) and n=individual animal (in vivo experiments).
Data exclusions	No data were excluded from the analyses.
Replication	All attempts at replication were successful.
Randomization	All cells and animals were randomly divided into groups before underwent specific treatment or spinal cord injury followed by administration.
Blinding	The investigators were blinded to the group allocation during data collection and 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

Methods

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

Antibodies

Antibodies used

Mouse monoclonal anti-Nestin (Rat-401) Cell Signaling Technology Cat# 4760, RRID: AB_2235913
Rabbit monoclonal anti-β3-Tubulin (D71G9) Cell Signaling Technology Cat# 5568, RRID: AB_10694505
Rabbit monoclonal anti-GFAP (E4L7M) Cell Signaling Technology Cat# 80788, RRID: AB_2799963
Mouse monoclonal anti-GFAP (GA5) Cell Signaling Technology Cat# 3670, RRID: AB_561049
Rabbit monoclonal anti-UCHL1 (D3T2E) Cell Signaling Technology Cat# 13179, RRID: AB_2798141
Rabbit monoclonal anti-MBP (D8X4Q) Cell Signaling Technology Cat# 78896, RRID: AB_2799920
Rabbit monoclonal anti-CNPase (D83E10) Cell Signaling Technology Cat# 5664, RRID: AB_10705455
Mouse monoclonal anti-Neurofilament-L (DA2) Cell Signaling Technology Cat# 2835, RRID: AB_490808
Rabbit polyclonal anti-Doublecortin Cell Signaling Technology Cat# 4604, RRID: AB_561007
Rabbit polyclonal anti-5-HT(Serotonin) Immunostar Cat# 20080, RRID: AB_572263
Chicken polyclonal anti-MAP2 abcam Cat# ab5392, RRID: AB_2138153
Rabbit polyclonal anti-SOX2 abcam Cat# ab97959, RRID: AB_2341193
Rat monoclonal anti-Nestin (7A3) abcam Cat# ab81462, RRID: AB_1640724
Rabbit monoclonal anti-NeuN (EPR12763) abcam Cat# ab177487, RRID: AB_2532109
Rabbit polyclonal anti-C3 abcam Cat# ab11887, RRID: AB_298669
Mouse monoclonal anti-C3aR Santa Cruz Cat# sc-133172, RRID: AB_2066736
Mouse monoclonal anti-NG2 Santa Cruz Cat# sc-53389, RRID: AB_784821
Mouse monoclonal anti-Nrf2 abcam Cat# ab89443, RRID: AB_2041334
Rabbit monoclonal anti-Synaptophysin (YE269) abcam Cat# ab32127, RRID: AB_2286949
Rabbit polyclonal anti-Ki67 abcam Cat# ab15580, RRID: AB_443209
Rabbit polyclonal anti-Caspase 3 Affinity Biosciences Cat# AF6311, RRID: AB_2835170
Rabbit polyclonal anti-Cleaved-Caspase 3 Affinity Biosciences Cat# AF7022, RRID: AB_2835326
continued
Rabbit polyclonal anti-Proteasome 20S LMP2 Affinity Biosciences Cat# DF6606, RRID: AB_2838568
Rabbit monoclonal anti-GAPDH Cell Signaling Technology Cat# 5174, RRID: AB_10622025
Mouse monoclonal anti-β-Actin Cell Signaling Technology Cat# 58169, RRID: AB_2750839
Human TNFα neutralizing antibody (D1B4) Cell Signaling Technology Cat# 7321, RRID: AB_10925386
Mouse IL-1α/ IL-1F1 antibody R&D Systems Cat# AF-400-NA,
Goat anti-Human C1q Quidel Cat# A301, RRID: AB_452502
Normal Goat IgG control R&D Systems Cat# AB-108-C
Goat anti-chicken IgG (H&L) Secondary Antibody, Alexa Flour 647 conjugate abcam Cat# ab150171
Goat anti-rabbit IgG (H&L) Secondary Antibody, Alexa Flour 488 conjugate abcam Cat# ab150077, RRID: AB_2630356
Goat anti-rat IgG (H&L) Secondary Antibody, Alexa Flour 488 conjugate abcam Cat# ab150157, RRID: AB_2722511
Goat anti-mouse IgG (H+L) Cross-Adsorbed Secondary Antibody-Alexa Flour 488 conjugate Thermo Fisher Scientific Cat# A-11001, RRID: AB_2534069
Goat anti-rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Flour 594 conjugate Thermo Fisher Scientific Cat# A-11012, RRID: AB_2534079
Goat anti-rabbit horseradish peroxidase (HRP)-conjugated IgG Secondary Antibodies Beyotime Biotechnology Cat# A0208
Goat anti-mouse horseradish peroxidase (HRP)-conjugated IgG Secondary Antibodies Beyotime Biotechnology Cat# A0216
Mouse monoclonal anti-Nestin (Rat-401) Cell Signaling Technology Cat# 4760, RRID: AB_2235913
Rabbit monoclonal anti-β3-Tubulin (D71G9) Cell Signaling Technology Cat# 5568, RRID: AB_10694505
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Rabbit polyclonal anti-Cleaved-Caspase 3 Affinity Biosciences Cat# AF7022, RRID: AB_2835326
continued
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Rabbit monoclonal anti-GAPDH Cell Signaling Technology Cat# 5174, RRID: AB_10622025
Mouse monoclonal anti-β-Actin Cell Signaling Technology Cat# 58169, RRID: AB_2750839

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Mouse IL-1α/ IL-1F1 antibody R&D Systems Cat# AF-400-NA,
Goat anti-Human C1q Quidel Cat# A301, RRID: AB_452502
Normal Goat IgG control R&D Systems Cat# AB-108-C
Goat anti-chicken IgG (H&L) Secondary Antibody, Alexa Flour 647 conjugate abcam Cat# ab150171
Goat anti-rabbit IgG (H&L) Secondary Antibody, Alexa Flour 488 conjugate abcam Cat# ab150077, RRID: AB_2630356
Goat anti-rat IgG (H&L) Secondary Antibody, Alexa Flour 488 conjugate abcam Cat# ab150157, RRID: AB_2722511
Goat anti-mouse IgG (H+L) Cross-Adsorbed Secondary Antibody-Alexa Flour 488 conjugate Thermo Fisher Scientific Cat# A-11001, RRID: AB_2534069
Goat anti-rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Flour 594 conjugate Thermo Fisher Scientific Cat# A-11012, RRID: AB_2534079
Goat anti-rabbit horseradish peroxidase (HRP)-conjugated IgG Secondary Antibodies Beyotime Biotechnology Cat# A0208
Goat anti-mouse horseradish peroxidase (HRP)-conjugated IgG Secondary Antibodies Beyotime Biotechnology Cat# A0216

Validation

All antibodies have been validated in the official website and Resource Identification Portal RRID database (https://scicrunch.org/resources). please reference to the Supplementary Materials for more details about antibodies used in the manuscript.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Neural stem cells were obtained from the fetal brain of embryonic 14-day SD rats, and neural stem cells in passage 3-4 were used in the study. Astrocytes were isolated from the brains of the postnatal 2-day SD rats.
Authentication	Neural stem cells were authenticated with the specific markers Nestin and SOX2 by immunofluorescence staining. Astrocytes were identified by the typical marker GFAP using the immunofluorescence staining and flow cytometry.
Mycoplasma contamination	All cell lines were negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	not used

Palaeontology and Archaeology

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). Permits should encompass collection and, where applicable, export.*
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.*

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

Ethics oversight: *Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

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

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	Female Sprague Dawley (SD) rats (age, 8~10 weeks; weight, 180~200 g) and C57BL/6 mice (half male and female; age, 8~10 weeks; weight, 15~20 g) were purchased from the Guangdong Medical Laboratory Animal Center and housed under standard specific pathogen free (SPF) condition. All animals were housed in standard cages under a regulated environment (12-h light/dark cycle) with free access to food and water about one week before surgery.
Wild animals	not used
Reporting on sex	Sex was not considered in the study design.
Field-collected samples	not used
Ethics oversight	All animal experimental procedures using laboratory animals were conducted in accordance with the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996) and approved by the Animal Care and Use Committee of Sun Yat-sen University

(SYSU-IACUC-2021-000438).

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 *May remain private before publication.*	*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 (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	Cells were fixed as mentioned above, then permeabilized with 0.5% Triton X-100/PBS on ice and gently shake for 30 min. After washed twice with PBS 500 µl of freshly diluted 1:10000 PROTEOSTAT Aggresome Detection Reagent was applied to incubate cells for 30 min under protection from light. Proteasome activity assays were performed by a proteasome activity probe according to the instructions. The treated cells were incubated with the 5 µM proteasome activity probe Me4BodipyFl-Ahx3Leu3VS (Boston Biochem) for 2 h at 37°C, then

	washed and analyzed via flow cytometry. Cell proliferation in vitro was examined by EdU incorporation. NSCs were incubated with a culture medium supplemented with 10 μM EdU overnight before harvesting. Cells were fixed with 4% paraformaldehyde (PFA) followed by permeabilization, then washed twice with 3% bovine serum albumin (BSA) and stained using Click-iT EdU assay kit (US Everbright INC.) in accordance to the manufacturer's instructions. After washed once, the cells were resuspended with Hoechst solution (2 ug/ml; US EVERBRIGHT INC.) for DNA counterstaining prior to analysis on Cytoflex LX or laser scanning confocal microscope (LSCM).
Instrument	Cytoflex LX
Software	Cytoflex LX; Flow JO 10.0
Cell population abundance	30000-100000 cells were collected per group.
Gating strategy	initial SSC/FSC was gated generously, followed by FSC-W/FSC-A to exclude doublets. Then using the blank group or mono-color group as controls, the positive cells were gated out in different treatments.

☒ 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.*

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.*