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	Single-cell RNA-sequencing data acquisition: Illumina Novaseq 6000 and 10x Genomics with Chromium Controller Readiness Test; electrophysiological recordings: HEKA Patch master (v2.65), MultiClamp 700B Microelectrode Amplifiers and pClamp software (v11.2).
Data analysis	Single-cell RNA-sequencing data analysis using Cell Ranger (10x Genomics, v3.0.2). Scrublet (v0.2.1), Scanpy (v1.9.1), Harmony (v0.1.0), python (v3.10.4), R (v4.1.3), Seurat (v4.1.0), dplyr (v1.0.9), ggplot2 (v3.3.5), Matrix (v1.4-1), seaborn (v0.11.2), matplotlib (v3.5.3), pandas (v1.4.4), numpy (v1.20.3) for primary analysis of single-cell RNA-sequencing data. Images were processed and analyzed using Zeiss ZEN software suites (v23). Analysis of electrophysiology data was performed using MATLAB (v9.7). Computer code to process the scRNA-seq data is available as jupyter notebooks at GitHub (https://github.com/leitang607/macaque_Neural_cell).

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

The data supporting the findings of this study are available within the article, the primary supporting research paper of macaque hippocampus. The scRNA-seq datasets shown in Figs. 4-6 are publicly available at ArrayExpress under the accession codes E-MTAB-12399.

Human research participants

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

Reporting on sex and gender	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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	No statistical method was used to predetermine sample sizes. For single-cell RNA-sequencing (10x Genomics), whole cells were isolated from six macaques.
Data exclusions	During transcriptomic data analysis, some cells within each sample were excluded for the following reasons: 1) high mitogene percentage (>30%), and 2) low UMI count (< 200), and 3) clusters were identified as doublets and excluded if they had elevated doublet score and the combined marker gene expression profiles of more than one cell type. The criteria was determined based on the distribution of the datasets and applied equally to all samples.
Replication	Single-cell RNA-sequencing (10x Genomics) data were acquired from the six macaques used in the study. For single-cell RNA sequencing, all attempts at replication were successful. The observations were validated by previous work or other methodology including immunofluoscent staining.The experiments were performed based on the availability of the animals without a set frequency.
Randomization	Randomization was not applicable for this study. There is no treatment or intervention to the samples. Therefore there is no need for randomization.
Blinding	Blinding was not applicable for this study. To avoid bias, all samples were treated equally with the same rigorous criteria.

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-HMGB2, clone 3E5, Sigma, Cat# WH0003148M5, 1: 2000 dilution
Mouse monoclonal anti-Nestin, clone rat-401, Millipore, Cat# MAB353, 1:2000 dilution
Rabbit monoclonal anti-Ki-67, Invitrogen, clone SP6, Cat# MA5-14520, 1: 200 dilution
Rabbit polyclonal anti-beta III Tubulin, Abcam Cat# ab18207, 1: 2000 dilution
Mouse monoclonal anti-MAP2, clone AP-20, Sigma, Cat# M1406, 1:2000 dilution
Rabbit polyclonal anti-PAX6, Millipore, Cat# AB2237, 1:3000 dilution
Rabbit monoclonal anti-Vimentin, clone EPR3776, Abcam, Cat# ab92547, 1: 1000 dilution
Mouse monoclonal anti-sox4, clone CL5634, Abcam, Cat# ab243041, 1: 1000 dilution
Chicken anti-Glial Fibrillary Acidic Protein, Millipore, Cat# AB5541, 1:2000 dilution
Rabbit Sox2 (D6D9) Rabbit mAb, clone D6D9, Cell Signaling Technology, Cat# 9092, 1: 200 dilution
Mouse monoclonal anti-CNPase, clone 11-5B, Sigma, Cat# C5922, 1: 500 dilution
Rabbit polyclonal anti-NeuN, Millipore, clone NA.41, Cat# ABN78, 1: 500 dilution
Mouse monoclonal anti- Synapsin I, clone 46.1, Cat# 106011, 1:2000 dilution

Validation

HMGB2, Sigma: Validated by the vendor with IHC staining, western blotting, and ELISA.
https://www.sigmaaldrich.com/HK/zh/product/sigma/wh0003148m5

Nestin, Millipore: Validated in the references provided by the vendor.
DOI: 10.3389/fnmol.2013.00023. DOI: 10.1371/journal.pone.0051294
https://www.sigmaaldrich.cn/CN/zh/product/mm/mab353

SOX2, Cell Signaling Technology: Validated by the vendor. ICC: Mouse embryonic stem cells.IHC-P: Human Spermatogonia.
https://www.cellsignal.cn/products/primary-antibodies/ips-cell-reprogramming-antibody-kit/9092?site-search type=Products&N=4294956287&Ntt=9092&fromPage=plp&_requestid=9610859

MKI67, Invitrogen: Validated by the vendor. ICC: Hela cells, IHC-P: Human breast tissue. IHC: Human tonsil. FC:Hela cells.
https://www.thermofisher.cn/cn/zh/antibody/product/Ki-67-Antibody-clone-SP6-Recombinant-Monoclonal/MA5-14520

Tuj1, Abcam: This Anti- beta III Tubulin Protein Antibody is validated by the vendor for use in ICC with PC12 cells, IF with E18 rat hippocampal brain, IH(P) with rat cerebellum formalin, WB with HAP1 cells for the detection of Tuj1.
https://www.abcam.com/beta-iii-tubulin-antibody-neuronal-marker-ab18207.html

Map2, Sigma: Validated by the vendor with ICC in cortical cell and IHC staining in rat brain, western blotting in rat brain.
https://www.sigmaaldrich.cn/CN/zh/product/sigma/m1406

Pax6, Millipore: This Anti- PAX6 Protein Antibody is validated by the vendor for use in WB with rat and mouse brain.
https://www.sigmaaldrich.cn/CN/zh/product/mm/ab2237

Vimentin, Abcam: Validated by the vendor. WB: HeLa, HEK293, Jurkat, A549, NIH3T3, PC12, HUVEC, Daudi, Caco-2 and COS-1 cell lysates; mouse and rat brain tissue lysates. IHC-P: Human kidney, colon, breast adenocarcinoma, cervical carcinoma and ovarian cancer tissues, mouse brain and kidney, E17 rat cheek and rat skin tissue sections; Rhesus monkey retina tissue. IHC-Fr: Mouse testis tissue. ICC/IF: HeLa, human adenocarcinoma, human schlemms canal endothelium and wild-type HAP1 cells. Flow Cyt (intra): HeLa cells.
https://www.abcam.com/vimentin-antibody-epr3776-cytoskeleton-marker-ab92547.html

Sox4, Abcam: Validated by the vendor.IHC: human glioma brain tumour tissue, mouse brain. tumour,ICC: human neuroblastoma cell.
https://www.abcam.cn/sox4-antibody-cl5634-ab243041.html

GFAP, Glial Fibrillary Acidic Protein, Millipore: This Anti-Glial Fibrillary Acidic Protein Antibody is validated by the vendor for use in IC, IH,IH(P), WB for the detection of GFAP.
https://www.merckmillipore.com/HK/en/product/Anti-Glial-Fibrillary-Acidic-Protein

CNPase, Sigma: Validated in the references provided by the vendor for use in ICC staining, IHC staining, western blotting.
DOI: 10.1186/1477-5956-11-18
https://www.sigmaaldrich.cn/CN/zh/product/sigma/c5922

NeuN, Millipore: Validated by the vendor using immunofluorescent staining in human and mouse brain.
https://www.sigmaaldrich.cn/CN/zh/product/mm/abn78

Synapsin I, Synaptic Systems: Validated by the vendor. WB: rat cerebellum homogenate,
ICC: mouse hippocampus neuron, rat hippocampus neurons. IHC: mouse hippocampus. IHC-P: mouse hippocampus.
https://www.sysy.com/product/106011

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	We used adult macaque monkeys (Macaca fascicularis) at the age of 4-15 YO.
Wild animals	The study did not involve wild animals.
Reporting on sex	There are one female and five male macaques in 10x Genomics dataset. It is therefore challenging to explore genes with sex-related differences in our analysis.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All experiments involving animals should be performed in accordance with the relevant guidelines for animal care and use, and should be approved by the appropriate institutional regulatory board. All animal procedures in this protocol were conducted under protocols approved by the Animal Care and Use Committee of Zhongshan Ophthalmic Center, Sun Yat-sen University. The work was performed in accordance with the Principles for the Ethical Treatment of Non-Human Primates.

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