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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	Transmission electron microscope (Tecnai G2 F20; 200 kV; FEI), Leica STED confocal microscope, ZEISS Axio Imager M2 microscope, Olympus FV4000 laser scanning confocal microscope, PanoBrain slide scanner (Meca Scientific), ZEISS Axioskop2 plus Microscope (Carl Zeiss, Thornwood, NY), Thunder Imager (Leica DM6B), XF96 Analyzer (Seahorse Bioscience), Laser scanning confocal LSM980 two-photon imaging system, AvianQuick-Nano UPLC system (Thermo Fisher Scientific), Upright microscope (Olympus X51W), Patch-clamp amplifier (Axon Patch 700B), OmniPlex Neural Recording Data Acquisition System (Plexon), Fear conditioning apparatus (Labmaze Conditional Fear Video Analysis System, ZS-KJ), 9.4T uMR (United Imaging Life Science Instrument, Wuhan, China), Orbitrap Exploris 480 instrument with a nanoelectrospray ion source, Digidata 1500B (Molecular Devices, San Jose, CA), Axoclamp 700B,Tanon 5200 imaging system.
Data analysis	GraphPad Prism version 8.0, IMARIS 9.6.2, MatlabR2020b, ZEN, Python, Mini Analysis Program 6.0, CUDA Toolkit 10.2 software, ImageJ software, IMARIS 9.6.2 software (Bitplane), Panolyzer software, AxioVision Rel.4.7 software, EthoVision XT 14 software (Noldus, Wageningen, The Netherlands), Signal acquisition software (InperStudio), Analysis software (InperDataProcess).

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

scRNA sequencing data has been submitted and deposited in GEO database (GEO: GSE295882). The proteomics raw data are currently being uploaded to ProteomeXchange and make them public. Obtaining the accession ID or PRIDE Submission reference: https://www.ebi.ac.uk/pride/archive/projects/PXD064814 (glycogen binding proteomics raw data); https://www.ebi.ac.uk/pride/archive/projects/PXD064694 (ATAD3A binding proteomics raw data) .Microscopy data and any required information reported in this paper is available from the lead contact. And this study doesn't involve any original code.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Patients and samples were collected without regard to specific sex and gender. Supplementary Table 3 shows the details of the human brain tissue samples.
Reporting on race, ethnicity, or other socially relevant groupings	All sample sources comply with regulations and clinical ethics. The detailed information of those samples is summarized in Supplementary Table 3.
Population characteristics	Population characteristics is summarized in Supplementary Table 3 .
Recruitment	Our study does not involve patient recruitment.
Ethics oversight	The human brain tissue samples provided by the National Health and Disease Human Brain Tissue Resource Center (Ethical number: S2024052).All sample sources comply with regulations and clinical ethics. The detailed information of those samples was represented in Supplementary table3.

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	Sample size of each analysis and experiments is indicated in results description or figures and corresponding figure legends.
Data exclusions	No data exclusions were needed.
Replication	All experiments were repeated successfully, replicates are presented in bar plots.
Randomization	Mice were randomly picked and grouped for animal experiments.
Blinding	The investigators were blinded to group allocations during data collection and/or 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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[ ]	[x] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[x]	[ ] Flow cytometry
[ ]	[x] MRI-based neuroimaging

Antibodies

Antibodies used

Mouse monoclonal anti-Beta-Actin, Proteintech, Cat#66009-1-Ig , 1:10000
Rabbit polyclonal anti-GAPDH , Proteintech , Cat#10494-1-AP , 1:10000
Rabbit monoclonal, anti-Myc-Tag , ABclonal , Cat#AE070, 1:10000
Chicken polyclonal anti-GFAP , Abcam, Cat#ab4674, 1:500
Rat monoclonal anti-GFAP, Abcam, Cat#ab279291, 1:500
Goat Anti-Chicken IgY H&L (Alexa Fluor® 594), Abcam , Cat#ab150172, 1:200
Goat anti-Rat IgG (H+L) Cross-Adsorbed Secondary Antibody, Cyanine5 Thermo Fisher Scientific, Cat#A10525 , 1:200
Goat Anti-Rabbit IgG H&L (Alexa Fluor® 488), Abcam , Cat#ab150077, 1:200
Goat Anti-Rabbit IgG H&L (Alexa Fluor® 594), Abcam , Cat#ab150080 , 1:200
Goat Anti-Rabbit IgG H&L (Alexa Fluor® 647), Abcam , Cat#ab150079 , 1:200
Donkey Anti-Sheep IgG H+L(Alexa Fluor® 488) , jacksonimmuno, Cat#713-545-003 , 1:200
Goat anti-Chicken IgY (H+L) Secondary Antibody, Alexa Thermo Fisher Scientific, Cat#24134 , 1:200
Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 750 Thermo Fisher Scientific , Cat#A-21039, 1:200
Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 750 Thermo Fisher Scientific, Cat#A-2103 , 1:200
Goat Anti-Mouse IgG H&L (Alexa Fluor® 488), Abcam, Cat#ab150113 , 1:200
ATAD3A MaxPab rabbit polyclonal antibody (D01) , Abnova , Cat# H00055210-D01 , 1:4000
Rabbit polyclonal anti- MBP , Abcam, Cat# ab40390, 1:4000
Mouse monoclonal anti-SMI 32 , BioLegend, Cat# 801701, 1:4000
Mouse monoclonal anti-Drp1, Santa Cruz, Cat# sc-271583 , 1:2000
Mouse monoclonal anti-HDAC3, Proteintech, Cat# 67151-1-Ig , 1:4000
Rabbit polyclonal anti-HDAC3 , Proteintech, Cat#10255-1-AP , 1:4000
Mouse monoclonal anti-EPM2AIP1, Abnova, Cat#10R-6910, 1:4000
Mouse monoclonal anti-STBD1, Proteintech , Cat# 67018-1-Ig, 1:4000
Rabbit polyclonal anti-IgG Proteintech, Cat#30000-0-AP , 1:10000
Mouse polyclonal anti-IgG Proteintech, Cat#B900620 , 1:10000
Rabbit monoclonal anti- Acetylated-Lysine , Sigma-Aldrich, Cat# SAB5600275 , 1:4000
Mouse monoclonal anti-Pan Acetylation , Proteintech, Cat# 66289-1-Ig , 1:4000
Rabbit polyclonal anti-Acetylated-Lysine, Cell signaling Technology, Cat#9441S , 1:4000
Mouse monoclonal anti-GFP-Tag , ABclonal , Cat#AE012 , 1:10000
Rabbit monoclonal anti-HA-Tag, Cell signaling Technology , Cat#AE012, 1:10000
Rabbit polyclonal anti-His-Tag, Cell signaling Technology, Cat#2365T , 1:10000
HRP-conjugated Streptavidin , Proteintech , Cat#SA00001-0 , 1:4000
Mouse monoclonal anti-Flag, Sigma-Aldrich , Cat#F3615 , 1:10000
Rabbitpolyclonalanti-phospho-Drp1(humanSer616/mouseSer579) , CellSignaling Technology, Cat#3455, 1:4000
Rabbit polyclonal anti-Phospho-DRP1 (Ser637) (humanSer637/mouseSer600) , Affbiotech, Cat#DF2980 , 1:4000
Rabbit polyclonal anti-GYS1, Solarbio , Cat#K003385P , 1:4000
Mouse monoclonal anti-GYS1, Santa Cruz , Cat#sc-81173 , 1:4000
Mouse monoclonal anti-beta III Tubulin, servicebio , Cat#GB15139-100 , 1:4000
Sheep polyclonal anti- GFAP , Abcam, Cat#ab90601 , 1:500
Mouse monoclonal anti-HDAC6 , Proteintech, Cat#67250-1-Ig, 1:4000
Goat Anti-Mouse IgG, Peroxidase - Conjugated, H+L Biosharp, Cat, # BL001A, 1:20000
Goat Anti-Rabbit IgG, Peroxidase Conjugated, H+L Biosharp, Cat# BL003A, 1:20000
Mouse monoclonal anti-ATAD3, A Santa Cruz, Cat#sc-376185 , 1:4000
Rabbit polyclonal anti-STBD1, Affinity , Cat#DF12326, 1:200
Rabbit polyclonal anti-GBE1, Proteintech, Cat#20313-1-AP, 1:200
Anti-Iba1 antibody, Abcam, Cat#ab5076, 1:200

Validation

The manufacturers validated the commercially available antibodies,which were then utilized in accordance with those manufacturers instructions.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HEK293T(Procell, CL-0005), Hela (ATCC, CRM-CCL-2) and SVG p12(ATCC, CRL-8621).
Authentication	The STR was used for authentication.
Mycoplasma contamination	All cell lines were used after confirming that they were Mycoplasma negative after testing with the detection kit.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines in the ICLAC database were used.

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	ATAD3A fl/fl (stock no: NM-CKO-2102515) and G6PT-/- mice were obtained from Shanghai Model Organisms Center, Inc. Aldh1l1-CreERT (stock no: C001288) mice were purchased from Cyagen Biosciences, Inc. Aldh1l1-CreERT mice were crossed with ATAD3A fl/fl mice to generate Aldh1l1-CreERT mice. To obtain astrocytic ATAD3A heterozygous knockout mice (ATAD3A Ast Het), male Aldh1l1-CreERT; ATAD3A fl/Δmice aged six weeks were subjected to five daily intraperitoneal injections of 20 mg/kg tamoxifen (TAM, dissolved in corn oil) to generate ATAD3A Ast KO and control male littermates under corn oil treatment (ATAD3A Ast WT). Astrocyte-specific secretion protein mice (Aldh1l1-CreERT; ER-BioID HA) were generated by crossing Aldh1l1-CreERT mice with C57BL/6-Tg (CAG-EGFP, -birA*)1Fink/J mice (Jackson Laboratory, Stock No: 036203). Aldh1l1-CreERT; ER-BioID HA mice aged six weeks were subjected to five daily intraperitoneal injections of 20 mg/kg tamoxifen (TAM, dissolved in corn oil) to generate Ast ER-BioID HA mice. Astrocyte specific diphtheria toxin A (DTA) expression-based mouse strain was established by Aldh1l1-CreERT mice crossed with ROSA26iDTR (Jackson laboratory, Stock No: 007900). ROSA26iDTR; Aldh1l1-CreERT mice aged at six weeks were pretreated with administrated with 20 mg/kg tamoxifen for 5 consecutive days to induce Cre-inducible expression of DTR. 100 ng diphtheria toxin (DT, Aladdin, Cat# D684675-1mg) in 1 × PBS was injected intraperitoneally 3x daily for 10 d to obtain astrocyte specific ablation mouse.
Wild animals	No wild animals were used in the study.
Reporting on sex	Female mice were used in the study.
Field-collected samples	No field-collected samples were used in the study.
Ethics oversight	All the animal experiments were approved by the Institutional Animal Care and Use Committee at the University of Science and Technology of China (Ethical number: No. 2022-N(A)-175).

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	This study is an observational study, not a clinical trial.
Study protocol	No study protocol.
Data collection	Clinical data were collected from medical records.
Outcomes	NA.

Plants

Seed stocks	NA.
Novel plant genotypes	NA.
Authentication	NA.

Magnetic resonance imaging

Experimental design

Design type	Resting state
Design specifications	Each subject underwent one session of DTI acquisition. Total acquisition time: 20 minutes per subject.
Behavioral performance measures	NA.

Acquisition

Imaging type(s)	Diffusion.
Field strength	9.4 Tesla.
Sequence & imaging parameters	DTI and T2-weighted images were obtained via the following parameters: (1) DTI: TR/TE = 5728/28 ms; acquisition matrix = 148×192; field of view (FOV) = 15×19 mm; slices = 30; slice thickness = 0.5 mm; number of excitations (NEX) = 4; b-values = 0, 1000, 2000 s/mm² (for the x, y, and z directions); and 5 averages. (2) T2W-MRI: TR/TE = 3000/49 ms; acquisition matrix = 331×368; FOV = 18×20 mm; slices = 20; slice thickness = 0.5 mm; rare factor = 13.
Area of acquisition	Whole brain.

Diffusion MRI ☒ Used ☐ Not used

Parameters: Diffusion scheme: multi-shell; Number of diffusion directions: 32 per shell; b-values: 0, 1000, 2000 s/mm².

Preprocessing

Preprocessing software	Data were preprocessed using the manufacturer's built-in workstation.
Normalization	Data were non-linearly normalized to standard space. FA images were used for transformation.
Normalization template	MNI152 standard space.
Noise and artifact removal	Motion correction was applied using eddy_current correction in FSL. Physiological noise was modeled but not regressed.
Volume censoring	Volumes with excessive motion (FD > 0.5 mm) were censored using FSL's motion outliers tool. Less than 10% of volumes were censored per subject.

Statistical modeling & inference

Model type and settings	Mass univariate analysis. First-level fixed-effects modeling was followed by a second-level one-sample t-test (random effects).
Effect(s) tested	The primary effect tested was the inter-group difference in fractional anisotropy (FA) values at each voxel of the mean white matter skeleton.

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

Statistic type for inference (See Eklund et al. 2016)	Voxel-wise, using Threshold-Free Cluster Enhancement (TFCE) with 5000 permutations.
Correction	Preprocessing included rigid-body realignment for motion correction.

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	NA.
Graph analysis	NA.