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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	Supplementary Files 2&3 contain Igor Pro routines used for brain partitioning, sample randomization and de-randomization
Data analysis	Supplementary File 1 contains the markdown of the RNAseq analysis, which was done in Python. Supplementary File 4 contains the Python code used for the conversion of the image of the brain slab to Neuroimaging Informatics Technology Initiative (NIfTI) format. Data was analyzed and graphed using Igor Pro (Wavemetrics, Lake Oswego, OR; RRID:SCR_000325), Python Programming Language (RRID: SCR_008394) and Prism 8.0 software (GraphPad Software Inc, San Diego, CA; RRID:SCR_002798).

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

Provide your data availability statement here.

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	Brain donor sex (male) was self-reported. Sex/gender were not considered in the study design. A single brain for the study was chosen based on it's toxicological and neurological records, short postmortem interval and age of the donor at the time of death.
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	New York State Psychiatric Institute, New York, NY, USA

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	This proof-of-principle study was performed on a frozen coronal hemisphere from a single donor brain. Number of voxels/samples was based on the physical size of the brain slab, which was partitioned at 3x3x3mm resolution, similar to MRI resolution. This yielded 703 samples and required >20,000 independent assays to measure mitochondria abundance and OxPhos enzyme activities.
Data exclusions	Some voxels/samples were excluded from the analysis due to 1) missing readouts from some of the assays, due to technical or sensitivity issues, or 2) imperfect transformation of the physical voxels into the MNI space, which resulted in some of them having less than 70% of gray +white matter.
Replication	Assays for mitochondria abundance and OxPhos enzyme activities were performed in duplicates or triplicates.
Randomization	All samples/voxels were randomly assigned to 96-well assay plates by a locally written Igor Pro routine available in Supplementary Data2&3.
Blinding	To minimize potential batch effects and to blind the experimenter to the origin of the voxel, samples were scrambled using an Igor Pro routine: unique coordinates of each sample on the brain map were substituted with new, randomly generated coordinates on 96-well assay plates.

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
☒	☐ Plants

Methods

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

Plants

Seed stocks — *Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*

Novel plant genotypes — *Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*

Authentication — *Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

Magnetic resonance imaging

Experimental design

Design type: Template based multimodal imaging

Design specifications: We used neuroimaging templates derived from 2 databases (Human Connectome Project and Ishare) to produce a predictive model of the mitochondrial brain features

Behavioral performance measures: N/A

Acquisition

Imaging type(s): Structural, Diffusion and task (free movie watching) and resting state fMRI

Field strength: 3T & 7T

Sequence & imaging parameters: Parameters for the free movie watching task fMRI are reported in https://www.humanconnectome.org/hcp-protocols-ya-7t-imaging, T1w and T2w imaging at https://www.humanconnectome.org/hcp-protocols-ya-3t-imaging, DIffusion and resting state fMRI parameters in Tsuchida, A. et al. The MRi-Share database: brain imaging in a cross-sectional cohort of 1870 university students. Brain Struct. Funct. 226, 2057–2085 (2021).

Area of acquisition: Whole brain

Diffusion MRI ☒ Used ☐ Not used

Parameters: Parameters of acquisitions are reported in Tsuchida, A. et al. The MRi-Share database: brain imaging in a cross-sectional cohort of 1870 university students. Brain Struct. Funct. 226, 2057–2085 (2021).

Preprocessing

Preprocessing software: FSL, MRtrix, ANTs

Normalization: Diffeomorphic

Normalization template: MNI152

Noise and artifact removal: N/A

Volume censoring: N/A

Statistical modeling & inference

Model type and settings	N/A
Effect(s) tested	N/A

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

Statistic type for inference (See Eklund et al. 2016)	N/A
Correction	N.A

Models & analysis

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

Multivariate modeling and predictive analysis	Independent variables are values for axial diffusivity, fractional anisotropy , radial diffusivity, streamlines density, intracellular volume fraction, extracellular volume fraction, mean diffusion, orientation dispersion index, T1w, T2w, T1w/T2w, FLAIR, cortical thickness, inner cortical surface area, outer cortical surface area, probability of grey and white matter, fMRI maximum activity during free movie watching , shannon entropy during free movie watching, regional homogeneity at rest, amplitude of low-frequency fluctuation, ratio between low and and high frequency fluctuations. Dependant variables were CI, CII, CIV, MitoD, TRC and MRC.