

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                                                                                                                                                                                                                                                                                      |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The exact sample size ( <i>n</i> ) for each experimental group/condition, given as a discrete number and unit of measurement                                                                                                                               |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly                                                                                                                                    |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>                                                               |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of all covariates tested                                                                                                                                                                                                                     |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons                                                                                                                                        |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> 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) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted<br><i>Give P values as exact values whenever suitable.</i>                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings                                                                                                                                                                      |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes                                                                                                                                                |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i> ), 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   | MATLAB R2017b can be download at <a href="https://www.mathworks.com">https://www.mathworks.com</a> .<br>FSL (version 5.0.10) can be download at <a href="https://fsl.fmrib.ox.ac.uk/fsl/oldwiki/">https://fsl.fmrib.ox.ac.uk/fsl/oldwiki/</a> .<br>Freesurfer (version 7.1.1) can be download at <a href="https://surfer.nmr.mgh.harvard.edu/">https://surfer.nmr.mgh.harvard.edu/</a> .<br>Python 3.6 ( <a href="https://www.python.org/">https://www.python.org/</a> ) and R software (4.3.1; <a href="https://cran.r-project.org/">https://cran.r-project.org/</a> ) were used for statistical analysis (linear regression, Mann-Whitney U test and chi-squared test) and visualization.<br>The R package 'lavaan' (version 0.6-19; <a href="https://cran.r-project.org/web/packages/lavaan/index.html">https://cran.r-project.org/web/packages/lavaan/index.html</a> ) was used to perform the mediation analysis.<br>The study employed linear regression and mediation analysis implemented in R (version 4.3.1). The code for these two models is available ( <a href="https://github.com/fuyingji102/regional_adiposity">https://github.com/fuyingji102/regional_adiposity</a> ). |

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 UK Biobank data is a public health database. This work mainly includes demographic data, obesity measures derived from dual-energy X-ray absorptiometry (DXA), brain images, and cognitive tests. Researchers can apply for access to the data on the UK Biobank website (<https://www.ukbiobank.ac.uk>). Additional information regarding registration for data access is available at <http://www.ukbiobank.ac.uk/register-apply/>. The application number for this study is 57831.

## 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 This study use "sex" in the paper.

Reporting on race, ethnicity, or other socially relevant groupings This study categorized ethnicity as white and non-white.

Population characteristics This study leveraged publicly accessible demographic, phenotypic, image, and cognitive data from the UK Biobank, ensuring compliance with its ethical and data access guidelines. A detailed flowchart of participant selection is provided in Supplementary Fig. 1. During the first imaging visit, both DXA and brain MRI examinations were conducted. For this study, we identified 47,764 participants with available AFP, TFP, and LFP data and 40,072 participants with VAT measurements. We excluded participants who had major physical, neurological, or psychiatric disorders (Supplementary Methods), as well as those whose MRI scans did not meet quality standards. This resulted in analytic samples of 23,088 participants (mean age =  $62.5 \pm 7.40$  years, standard deviation; 45.2% male participants) and 18,886 participants (mean age =  $62.5 \pm 7.43$  years, standard deviation; 45.7% male participants) for fat percentage and VAT analyses, respectively. These analyses aimed to investigate the associations between regional adiposity measures and brain imaging metrics. Furthermore, participants who underwent cognitive function assessments at the assessment centers were selected to explore the relationships among regional adiposity, brain aging, and cognitive performance.

Recruitment This study utilized data from the UK Biobank recruitment, encompassing over 500,000 participants aged 40 years in the United Kingdom at baseline. For more detailed information, please refer to <http://www.ukbiobank.ac.uk>.

Ethics oversight We analysed data from the UK Biobank (application no. 57831), a nationwide population cohort that enrolled more than 500,000 adults at assessment centres across the United Kingdom between 2006 and 2010. The present analyses were conducted under the ethical approval granted to UK Biobank by the UK National Health Service National Research Ethics Service (reference 11/NW/0382). All participants provided written informed consent and could withdraw at any time without explanation. Study-related risk was considered minimal; however, UK Biobank maintains insurance arrangements that provide compensation for injuries arising from negligent conduct during participation.

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](https://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 formal sample size calculation was performed. All eligible participants were included from the publicly available UK Biobank dataset, comprising 23,088 participants with AFP, LFP, and TFP measurements and 18,886 participants with VAT measurements. The large sample size provides adequate statistical power, substantially exceeds that of similar studies, and ensures the robustness of the findings.

Data exclusions To examine the relationships between these adiposity measures and brain imaging metrics in a non-clinical adult sample, we further selected participants with multi-modal brain magnetic resonance imaging (MRI) data and excluded those with major physical, neurological, or psychiatric diseases (Supplementary Fig. 1).

Replication All available data were used to maximize statistical power of the analysis therefore we did not repeat the analysis.

## Randomization

In this study, covariates were selected based on their potential associations with obesity and brain characteristics, as reported in previous research. Age at the time of the imaging visit (the second follow-up wave) was included as a covariate. Additional baseline covariates encompassed demographics (sex, ethnicity, and handedness), socioeconomic status (years of education and employment status), lifestyle factors (physical activity, smoking frequency, and alcohol consumption frequency), and metabolic health, represented by the metabolic syndrome score. At the imaging visit, MRI scanning centers were considered to account for variability in imaging equipment, brain size was included to adjust for differences in brain morphology, and mean framewise displacement was included to control for head motion. Imaging sites (Cheadle, Reading, and Newcastle) were also included as a covariate to control potential differences due to scanner variability. More details can be found in the Supplementary Methods.

## Blinding

Blinding was not applicable to this study as this study is observational.

## 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                                  |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Antibodies                    |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Eukaryotic cell lines         |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Palaeontology and archaeology |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Animals and other organisms   |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Clinical data                 |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Dual use research of concern  |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Plants                        |

### Methods

- |                                     |                                                            |
|-------------------------------------|------------------------------------------------------------|
| n/a                                 | Involved in the study                                      |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> ChIP-seq                          |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Flow cytometry                    |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> MRI-based neuroimaging |

### Plants

Seed stocks

N/A

Novel plant genotypes

N/A

Authentication

N/A

## Magnetic resonance imaging

### Experimental design

Design type

Structural MRI, resting-state functional MRI, neurite orientation dispersion and density imaging (NODDI)

Design specifications

UK Biobank designed the imaging acquisition protocols including 6 modalities. This study primarily utilized T1-weighted structural images, resting-state functional MRI and diffusion-weighted imaging (DWI) images from these protocols.

Behavioral performance measures

N/A

## Acquisition

|                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Imaging type(s)               | Structural MRI, resting-state functional MRI, diffusion-weighted imaging (DWI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Field strength                | 3T                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Sequence & imaging parameters | The T1-weighted image was obtained using Magnetization Prepared Rapid Acquisition Gradient-Echo (MPRAGE) with 1×1×1 mm resolution, a field-of-view of 208×256×256 mm, TI/TR/TE of 880/2000/2.01 ms, and a flip angle of 8°. Resting-state fMRI (rs-fMRI) was acquired using gradient echo EPI (GE-EPI), interleaved multi-slice, gradient-echo, echo planar imaging (GE-EPI) sequence with 8 multislice acceleration; TR = 0.735 s, TE = 39 ms, flip angle = 52°, matrix = 88×88, resolution = 2.4 mm×2.4 mm; slice thickness = 2.4 mm; slice number = 64 slices; rs-fMRI acquisition time = 6 minutes. The standardized parameters can be referenced at <a href="https://biobank.ctsu.ox.ac.uk/crystal/crystal/docs/brain_mri.pdf">https://biobank.ctsu.ox.ac.uk/crystal/crystal/docs/brain_mri.pdf</a> . |
| Area of acquisition           | <i>State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Diffusion MRI                 | <input checked="" type="checkbox"/> Used <input type="checkbox"/> Not used                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

## Preprocessing

|                            |                                                                   |
|----------------------------|-------------------------------------------------------------------|
| Preprocessing software     | Freesurfer (version 7.1.1) and FSL (version 5.0.10)               |
| Normalization              | large deformation diffeomorphic metric mapping (LDDMM)            |
| Normalization template     | fsaverage and the JHU MNI atlas                                   |
| Noise and artifact removal | Before preprocessing, noisy images were removed from the study    |
| Volume censoring           | Before preprocessing, fMRI volumes with large motion were removed |

## Statistical modeling & inference

|                                           |                                                                                                                  |
|-------------------------------------------|------------------------------------------------------------------------------------------------------------------|
| Model type and settings                   | linear regression model                                                                                          |
| Effect(s) tested                          | The standardized beta coefficients were obtained for the linear regression models.                               |
| Specify type of analysis:                 | <input checked="" type="checkbox"/> Whole brain <input type="checkbox"/> ROI-based <input type="checkbox"/> Both |
| Statistic type for inference              | vertex-wise statistics, connectome statistics and volume-wise statistics                                         |
| (See <a href="#">Eklund et al. 2016</a> ) |                                                                                                                  |
| Correction                                | FDR, random field theory [RFT] correction                                                                        |

## Models & analysis

|                                          |                                                                              |
|------------------------------------------|------------------------------------------------------------------------------|
| n/a                                      | Involved in the study                                                        |
| <input type="checkbox"/>                 | <input checked="" type="checkbox"/> Functional and/or effective connectivity |
| <input checked="" type="checkbox"/>      | <input type="checkbox"/> Graph analysis                                      |
| <input checked="" type="checkbox"/>      | <input type="checkbox"/> Multivariate modeling or predictive analysis        |
| Functional and/or effective connectivity | Functional connectivity is measured using Pearson correlation                |