

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <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	Data are provided as freely available resource available to all scientists. No software was used for data collection.
Data analysis	The processing scripts and custom analysis software used in this work are available in a publicly accessible GitHub repository with instructions on how to set up a similar computation environment and with examples of key visualizations in the paper: https://github.com/ksaltoun/asymptath_age_progression It is also available at the following Zenodo: Software used for data analysis: FMRIB UKBioBank Normalisation, Parsing And Cleaning Kit (FUNPACK; version 2.5.0) PHEnome Scan ANalysis Tool (PHESANT; https://github.com/MRCIEU/PHESANT) sklearn (version: 1.0.2) nilearn (version 0.9.2) nibabel (version 4.0.2) numpy (version: 1.22.1) pandas (version 1.4.3) python (version 3.10.0)

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](#)

Individual-level data are under controlled access to protect the sensitive information of the study participants, and may be requested by application to the UKBB (<https://www.ukbiobank.ac.uk/enable-your-research/register>). Source data are provided with this paper.

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

We identified the full set of ~1,400 UK Biobank participants with two sets of structural MRI images without exclusions. Among these participants, 49% were men and 51% were women. Sex was self-reported. Sex was not considered when constructing asymmetry patterns (deconfounding and z-scoring were done in a sex-independent manner; see previous paper by Saltoun and colleagues 2023 <https://doi.org/10.1038/s41562-022-01461-0>) or asymmetry pattern changes. Sex effects were assessed after asymmetry changes were calculated to elucidate how structural hemispheric asymmetry changes differs between sexes (Figure 2B; Supplementary Figure 1D)

Reporting on race, ethnicity, or other socially relevant groupings

Ethnicity, race and socioeconomic status were not considered when evaluating asymmetry pattern change. Self-reported socioeconomic indicators obtained during UK Biobank questionnaire were used to how structural hemispheric asymmetry changes relate to broad population-level characteristics (socioeconomic status, mental health, cognitive function) as assessed during UK Biobank visits. A full accounting of UK Biobank recruitment and population characteristics is available in work by Sudlow and colleagues 2015 (<https://doi.org/10.1371/journal.pmed.1001779>)

Population characteristics

Of the ~40,000 UK Biobank imaging participants, a subset of 1,425 (49% male) participants were scanned on two occasions that were 2-3 years apart (27.4 ± 1.4 months between visits). These participants were aged 62.5 ± 7.2 years old at first imaging visit). Error bounds are standard deviation.

Recruitment

Recruitment was done as part of the UK biobank initiative by flyers and other means common in epidemiological research. For details on representativeness see Frey et al., 2017.

Ethics oversight

UK Biobank participants gave written, informed consent for the study, which was approved by the Research Ethics Committee under application 11/NW/0382.

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

We used all subject data with multiple MRI imaging visits from the 40,000 imaging UK Biobank release (February 2020) for a total of 1,425 subjects (2 MRI images per subject), no exclusions. No power calculation was needed in advance and we used all samples available (see below).

Data exclusions

We first identified the full set of ~1,400 participants who had also been imaged twice by UK Biobank, without exclusions. We used all subjects who had both structural and diffusion-weighted MRI data.

Replication

All bootstrap replications were successful. As such, we have performed rigorous bootstrap resampling schemes: All linear regressions were repeated based on bootstrap-resampled subset of participants and assessed against results derived from the full UKBB cohort

Randomization

UK Biobank is an observational prospective epidemiological study, and the analyses in our study use all available subjects that fulfill the criteria described above. Hence there is no equivalent process of randomization that comes into this analysis (this is not a controlled randomised study).

Blinding

For exactly the same reasons (this is not a controlled randomised study), there is no step equivalent to blinding involved.

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	N/A
Novel plant genotypes	N/A
Authentication	N/A

Magnetic resonance imaging

Experimental design

Design type	Please see "Methods" for full details. Our analyses include data from Structural MRI (T1), and diffusion MRI.
Design specifications	MRI data processing (to generate imaging-derived phenotypes) was done previously and is full described in references (Miller et al. 2016 and Alfaro-Almagro et al. 2018.).
Behavioral performance measures	Behavioral performance in the MRI scanner was not used in this study.

Acquisition

Imaging type(s)	Please see "Methods" for full details. Our analyses include data from Structural MRI (T1), and diffusion MRI.
Field strength	3T
Sequence & imaging parameters	MRI data acquisition for the structural and functional modalities covers several pages of full detail, which is fully provided previously in references (Miller et al. 2016 and Alfaro-Almagro et al. 2018.).
Area of acquisition	Siemens' auto-align was used to include the full brain in the imaged field-of-view; this was checked (and corrected if necessary) by the radiographer.
Diffusion MRI	☒ Used ☐ Not used
Parameters	See above (covered previously in full detail in Miller et al. 2016 and Alfaro-Almagro et al. 2018.).

Preprocessing

Preprocessing software	See above (covered previously in full detail in Miller et al. 2016 and Alfaro-Almagro et al. 2018.).
Normalization	See above (covered previously in full detail in Miller et al. 2016 and Alfaro-Almagro et al. 2018.).

Normalization template	MNI 152
Noise and artifact removal	See above (covered previously in full detail in Miller et al. 2016 and Alfaro-Almagro et al. 2018).
Volume censoring	See above (covered previously in full detail in Miller et al. 2016 and Alfaro-Almagro et al. 2018).

Statistical modeling & inference

Model type and settings	n/a
Effect(s) tested	n/a
Specify type of analysis:	☐ Whole brain ☒ ROI-based ☐ Both
Anatomical location(s)	ROIs were generated based on Harvard-Oxford atlas (111 regions from T1-weighted structural MRI); Diedrichsen cerebellar atlas (25 ROIs based on T1-weighted MRI) and Johns Hopkins University Atlas (48 ROIs derived from diffusion-weighted MRI)
Statistic type for inference (See Eklund et al. 2016)	Our analysis was conducted using singular vector decomposition on measures of hemispheric asymmetry between homologous brain pairs
Correction	Adjusted R2 score were used for testing linear regression. FDR and Bonferroni corrections were used for testing linear association strength.

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	We used singular value decomposition (SVD) for diffusion-weighted and structural MRI data. We used L2-penalized linear regression for extracted latent dimensions (asymmetry patterns)