***eLife’s* transparent reporting form**

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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

There was no sample-size estimation, as we used all relevant data currently available from UK Biobank (nearly 20,000 subjects), and, for the analyses in question, there is no existing suitable data that could feed into a meaningful prospective power calculation. Section 4.8 (Methods) describes final genetic sample sizes.

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
* If you encountered any outliers, you should describe how these were handled
* Criteria for exclusion/inclusion of data should be clearly stated
* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

The core replication was of the GWAS analyses, which used a different set of subjects (samples) for the replication. This is described in Sections 2.3 (Results) and 4.8 (Methods).

The estimation of the brain-aging modes was validated via repeated randomized split-half testing across subjects. There was also validation of data-driven modes’ age correlations. This is all described in Section 4.2 (Methods).

All source data is available from UK Biobank, as described in Section 5. That section also describes the full availability of all of our code used for this work, and additional supplementary materials.

Description of how outliers were handled (extreme outlier removal and quantile normalization), inclusion criteria, and results regarding patterns of missing data, are given in Sections 4.1 and 4.7 (Methods).

**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

Statistical methods are described throughout the Methods section, and recapitulated where necessary in Results. This includes corrections for multiple comparisons, which in general are (where appropriate) Bonferroni, and for single-phenotype GWAS, the standard threshold of -Log10P=7.5 (followed by replication testing).

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

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N/A.

**Additional data files (“source data”)**

* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
* Include code used for data analysis (e.g., R, MatLab)
* Avoid stating that data files are “available upon request”

Please indicate the figures or tables for which source data files have been provided:

All source data is available from UK Biobank, as described in Section 5. That section also describes the full availability of all of our code used for this work, and additional supplementary materials.