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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	Participants. Superagers and typical older adults. These groups were selected from the Vallecas Project cohort, a single-center longitudinal study of 1213 elderly adults. Participants were between 69 and 86 years old at baseline and were independent, community-dwelling individuals with no neurological or psychiatric disorders. Detailed information regarding this cohort's inclusion and exclusion criteria have been described previously (https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2015.00181/full.). From this cohort, a sample of 64 superagers and 55 typical older adults was selected. Participants. Young adults. rs-fMRI data from healthy young adults was obtained from the Cambridge Buckner dataset (released by Randy L. Buckner as principal investigator at Cambridge, MA, USA). A sample of 147 subjects aged between 20 and 30 years was selected. The data were accessed through the 1000 Functional Connectomes Project (http://fcon_1000.projects.nitrc.org/index.html), an open-access dataset repository.
Data analysis	CONN (functional connectivity toolbox) v.19; the Statistical Parametric Mapping (SPM) software v. SPM12.; R v.4.0.2

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

Anonymized data can be accessed upon request at direccioncientifica@fundacioncien.es.

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	Sex was determined based on self-reporting. We have not performed any sex- and gender-based analyses. All participant provided written informed consent.
Reporting on race, ethnicity, or other socially relevant groupings	In our research, we did not apply any categorization, classification, or grouping based on ethnicity or race.
Population characteristics	Superagers and typical older adults. These groups were selected based on their age (at or above 79.5 years old) and their cogntive performance from the Vallecas Project cohort, a single-center longitudinal study of 1213 elderly adults. All participants were independent, community-dwelling individuals with no neurological or psychiatric disorders. Detailed information regarding this cohort's inclusion and exclusion criteria have been described previously in https://www.frontiersin.org/journals/aging-neuroscience/articles/10.3389/fnagi.2015.00181/full. Young adults. A sample of 147 subjects aged between 20 and 30 years was selected from the Cambridge Buckner dataset.
Recruitment	Volunteers in the Vallecas project cohort were enlisted through radio and television campaigns, leaflet distribution, and visits by the research team to community centers for the elderly.
Ethics oversight	The Ethics Committee of the Instituto de Salud Carlos III.

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	A sample of 64 superagers and 55 typical older adults was selected from the Vallecas Project cohort and 147 young adults from the Cambridge Buckner dataset
Data exclusions	No data were excluded from our analyses.
Replication	Established pipelines and statistical packages have been used in our analyses.
Randomization	Two experimental groups including superagers and typical older adults were selected from the Vallecas Project cohort, a single-center longitudinal study of 1213 elderly adults. From this cohort, a sample of 64 superagers and 55 typical older adults was selected based on 1) age 2) episodic memory 3) non-memory cognitive performance. Additionally, a group of young healthy adults was obtained from the Cambridge Buckner dataset (released by Randy L. Buckner as principal investigator at Cambridge, MA, USA80). A sample of 147 subjects aged between 20 and 30 years was selected. The data were accessed through the 1000 Functional Connectomes Project (http://fcon_1000.projects.nitrc.org/index.html), an open-access dataset repository.
Blinding	Blinding was not necessary in our study, as we were not evaluating a treatment intervention. Instead, our focus was on observational data collection and 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
☒	☐ 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

Resting state

Design specifications

Resting state scanning lasted 5 minutes and 10 seconds

Behavioral performance measures

No behavioural performance. During resting state scanning participants were instructed to stay awake with their eyes open.

Acquisition

Imaging type(s)

Functional and structural MRI

Field strength

MRI images of the Vallecas Project were acquired using a 3-Tesla MRI (Sigma HDxt GEHC, Waukesha, USA) with a phased array 8-channel head coil.
MRI images of the Cambridge_Buckner dataset were acquired using a 3-Tesla MRI (Siemens Trim Trio).

Sequence & imaging parameters

MRI images of the Vallecas Project: T1-weighted images (3D fast spoiled gradient echo with inversion recovery preparation) were collected using a repetition time (TR) of 10 ms, echo time (TE) of 4.5 ms, a field of view (FOV) of 240 mm, and a matrix size of 288 x 288 with a slice thickness of 1 mm, yielding a voxel size of 0.5 x 0.5 x 1 mm. The rs-fMRI gradient echo echoplanar image (EPI) acquisition had the following parameters: TR 2500 ms; TE 27 ms; flip angle 81°; FOV 240 mm; matrix size 96 x 96; slice thickness of 2.6 mm and slice spacing 0.5 mm; yielding voxel size of 2.5 x 2.5 x 2.6 mm; slice order interleaved.

MRI images of the Cambridge_Buckner dataset: T1-weighted images were collected with MPRAGE with the following parameters: slices = 192, matrix size = 144 x 192, and voxel resolution = 1.20 x 1.00 x 1.33 mm. The open-eye rs-fMRI acquisition was performed using EPI, which lasted ~6 minutes with the following parameters: TR = 3000 ms; TE = 30 ms; flip angle 85°; FOV 216 mm; voxel size = 3.0 x 3.0 x 3.0 mm; 47 interleaved axial slices in 119 timepoints.

Area of acquisition

The rs-fMRI scans from the Vallecas Project did not yield whole-brain coverage in the z-axis in all subjects, such that uppermost portions of brain were not acquired in some subjects which is evident in Figure 2 in our manuscript. The rest of the acquisitions have whole-brain coverage.

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	The default preprocessing pipeline of the CONN toolbox v.19, which is an extension to the Statistical Parametric Mapping (SPM) software (www.fil.ion.ucl.ac.uk/spm/), was employed to preprocess the rs-fMRI data. These images were first realigned using SPM12's realign & unwarp procedure, where each participant's EPI time series was co-registered and resampled to each subject's own T1 structural image. In the unwarp step, distortion correction was also performed to correct the absolute deformation state of the reference image. Temporal misalignment between different slices of the rs-fMRI images was corrected using SPM12's slice-timing correction procedure, where the rs-fMRI images were time-shifted and resampled by sinc-interpolation to fit the time in the middle of each acquisition time. Potential outlier scans were identified from the global BOLD signal and the rate of subject-motion in the scanner, where acquisitions with framewise displacement above 0.9 mm or global BOLD signal changes above 5 standard deviations were excluded from further analyses as potential outliers. rs-fMRI and structural T1 images were then normalized into standard Montreal Neurological Institute (MNI) space, resampled at 2 x 2 x 2 mm3 voxel size and segmented into grey matter, white matter, and cerebrospinal fluid tissue classes using SPM12 unified normalization and segmentation procedure. Lastly, functional data were spatially smoothed with an 8-mm full-width at half maximum (FWHM) isotropic Gaussian kernel. Head motion parameters were individually controlled for all participants and excluded at a +/- 3 mm displacement criterion. The computed mean head motion in CONN was used as a covariate of no interest in our models to consider head motion artefacts.
Normalization	The "default preprocessing pipeline" in CONN was used for normalization, during which functional (and anatomical) images were non-linearly warped into standard space.
Normalization template	Montreal Neurological Institute (MNI) space
Noise and artifact removal	Head motion parameters were individually controlled for all participants and excluded at a +/- 3 mm displacement criterion. The computed mean head motion in CONN was used as a covariate of no interest in our models to consider head motion artefacts.
Volume censoring	No censoring was applied in our analyses.

Statistical modeling & inference

Model type and settings	First level analysis: a mass-univariate general linear model was used to compute the Pearson correlation between BOLD time series (then Fisher z-transformed). Second-level analysis: Mass univariate general linear model across subjects
Effect(s) tested	First-level analysis: Fixed-effect model (within-subject), restimates a single correlation value per ROI pair or voxel per subject. Second-level analysis: Random-effects model, treating each subject's functional connectivity as an independent observation.

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

Anatomical location(s): Brainnetome Atlas

Statistic type for inference (See Eklund et al. 2016)	A mass-univariate general linear model, at a voxel-wise threshold of $p < 0.005$ and a cluster-level threshold of p-FWE< 0.001 (two-tailed).
Correction	FWE, FDR

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	Pearson correlation with Fisher z-transformation; First-level model: mass-univariate general linear model, fixed-effect (prior to modeling, confounds including head motion and grey matter volume were regressed out, and data is band-pass filtered (e.g., 0.008–0.09 Hz); Second-level model: mass-univariate general linear model, random effects (second level functional connectivity values are independent and normally distributed).
Graph analysis	Pearson correlation with Fisher z-transformation; Graphs were constructed on thresholded ROI-to-ROI functional connectivity matrices, First-level: descriptive graph metrics such as degree centrality were generated; Second-level: mass-univariate general linear models (random-effects) were used to compare graph metrics across groups; Inference: general linear model contrast, multiple comparison correction (FDR).
Multivariate modeling and predictive analysis	Group differences in the demographic and neuropsychological variables were tested with Chi-squared tests for categorical data, and two-sample t-tests (two-tailed) and Mann-Whitney U test if numerical, with the significance level set at 0.05. Machine learning-based classification: The feature selection method of choice was statistical hypothesis testing, which is a wrapper that holds a set of features with the highest ranks according to a criterion. We

used a p-value of 0.05 from completed hypothesis testing as the ranking criterion. Then, we applied the sequential forward selector (SFS) algorithm in MATLAB R2020b.The classification method of choice was support vector machine (SVM) in MATLAB R2020b. Soft margin parameters C and γ (Gaussian kernel width) were optimized using a grid search and 5-fold stratified cross-validation (CV) on the training dataset to achieve an optimal hyperparameter for kernel-based SVM. The classification performance was assessed using an ROC-AUC (receiver operating characteristic-area under the curve) analysis.

Longitudinal Analysis. ROI-wise graph theory analysis testing longitudinal group differences was carried out in several steps. The anteroposterior gradient for degree centrality was computed by relating the degree centrality of 246 ROIs (excluding cerebellar regions) with the MNI y-coordinate at the center of each ROI. We tested for group differences in degree centrality along the anteroposterior axis with a linear mixed-effects model, fitting degree centrality as a function of the y-coordinate, adding the interaction with group (superagers, typical older adults, and young adults). The model also included a random slope of the anteroposterior coordinate and a random intercept per participant to capture interindividual variability in the anteroposterior gradient. The degree centrality data was further divided into tertiles of equal topological distance (-99.43 ≤ Y ≤ -46.79 mm for the posterior tertile, -43.89 ≤ Y ≤ 7.96 mm for the middle tertile, and 8.6 ≤ Y ≤ 61.35 mm for the anterior tertile). A one-way ANOVA was conducted to assess group differences within each tertile, followed by post-hoc pairwise comparisons using Tukey's Honest Significant Difference test. Between-group longitudinal differences in the anteroposterior degree centrality gradient and the mean degree centrality were analyzed using a linear mixed-effects model implemented in R's lme4 package, which accounts for missing data due to participant attrition. The model included group, scaled age, and their interaction as fixed effects, while participant intercept and scaled age slope were specified as random effects. All statistical analyses of anteroposterior gradients and tertiles were conducted in R 4.0.2 (www.r-project.org/).