

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
<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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P 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 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

N/A

Data analysis

We used R version 4.3.2 for all statistical analyses.

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](#)

All published Harvard Aging Brain Study (HABS) data have been deposited in the Synapse data sharing platform under accession code syn53910452 (www.synapse.org/habs). The HABS data, including all data used in this study, are individual-level human data available under restricted access. Access can be obtained by submitting a data request through the Synapse platform and signing a data use agreement.

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 consistently used the term sex in our study. We adjusted sex as a covariate in all multivariate analyses.

Reporting on race, ethnicity, or other socially relevant groupings

We used self-reported race in reporting the demographic characteristics of our participants (Table 1).

Population characteristics

See Table 1.

Recruitment

We recruited cognitively unimpaired volunteers between age 50-90 at their time of enrollment. While this is a convenience sample, our participant characteristics are representative of cognitively unimpaired older adults residing in the greater Boston area.

Ethics oversight

The protocols and procedures were approved by the Mass General Brigham Institutional Review Board (IRB), and all participants signed a written informed consent form before undergoing any study procedures.

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://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

HABS is a prospective cohort study.

Research sample

We recruited cognitively unimpaired volunteers between age 50-90 at their time of enrollment.

Sampling strategy

While HABS recruited its participants from a convenience sample (volunteers), our participant characteristics are representative of cognitively unimpaired older adults residing in the greater Boston area.

Data collection

We acquired clinical, cognitive, neuroimaging, and plasma biomarker data following standard procedures, as detailed in the manuscript.

Timing

HABS started its enrollment in 2010, and we used data collected and curated as of 8/29/2024.

Data exclusions

We excluded individuals with missing data from each analysis and indicated the number of participants included in each analysis.

Non-participation

We selected individuals with at least 2 timepoints of data; those without longitudinal participation data has been excluded.

Randomization

N/A

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	Involvement 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	Involvement in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Antibodies against pTau217 and npTau217 were used in the commercial assay from C2N, during the immunoprecipitation step.
Validation	These antibodies were validated at C2N, and is currently being used in the commercial products for research and clinical diagnosis.

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	Not applicable.
Study protocol	Full study description is available through the HABS page on the Synapse data sharing platform (www.synapse.org/habs).
Data collection	HABS started its enrollment in 2010, and we used data collected and curated as of 8/29/2024. HABS is a single-site prospective cohort study, managed by the team at Massachusetts General Hospital.
Outcomes	This longitudinal observational Study used established biomarkers (A-beta and tau PET) and cognitive composite (PACC5) as our the dependent variable.

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A