nature portfolio

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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	F-Search MPs software v3.7 is a commercial mass spectrometry software from Frontier Labs, Koriyama, Japan.
Data analysis	Statistical analyses were conducted with GraphPad Prism v10.4 (ANOVA, Shapiro-Wilks test, Mann Whitney). Regression analysis was conducted using R version 4.3.3. The MPVAT 2.0 macro was used in ImageJ for FTIR analysis

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

Data are posted in Dryad. https://doi.org/10.5061/dryad.b8gtht7p8

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Sex was reported for all decedent samples analyzed.
Population characteristics	Limited demographic data (age, sex, race/ethnicity, cause of death, date of death) were available due to the conditions of specimen approval; age of death, race/ethnicity, and sex are reported and considered in regression analyses. The cohort included randomly sampled subjects from the University of New Mexico Office of the Medical Investigator in Albuquerque, New Mexico, along with available samples from the east coast (NC, MD, MA).
Recruitment	Decedent samples were available from the Office of the Medical Investigator.
Ethics oversight	All studies were approved by the UNM Office of the Medical Investigator and UNM Human Research Protections Office, which specifically determined the decedent work to be "not human research".

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	No a priori samples size calculations were performed. Sample sizes were determined largely based on availability and feasibility. This began as an exploratory study with 2016 data and we built the subsequent comparator cohorts based on roughly equal samples sizes. Importantly, with the limited demographic data available, we were able to generate relatively balanced a comparable cohorts in terms of age, sex, and cause of death.
Data exclusions	No data were excluded.
Replication	Samples were prepared and analyzed in such a way that replication was not uniformly feasible due to the consumption of the biospecimens.
Randomization	Samples were procured at random, based on availability from the Office of the Medical Investigator and the collected east coast tissues available from our collaborator (Andrew West). There are no "experimental groups" but the comparisons across date of death trended significantly. We did aim to balance the study across a wide range of ages and causes of death, and collect relatively even male and female samples.
Blinding	Analytical chemistry was conducted without knowledge of decedent characteristics. We were not fully blinded in the sense that subsequent reviewer requests for dementia cases and earlier time frames (ie, "east coast samples") came in batches. Blinding did occur for other demographic data (sex, age, etc).

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

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging