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- Accession codes, unique identifiers, or web links for publicly available datasets

All data supporting the findings of this study are available within the paper.

- For clinical datasets or third party data, please ensure that the statement adheres to our policy

- A description of any restrictions on data availability

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Last updated by author(s):	May 21, 2023

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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

Statistics				
For all statistical an	alyses, 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 stateme	ent 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 descript	ion of all covariates tested			
A descript	ion 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 Give <i>P</i> values as exact values whenever suitable.				
For Bayes	ian analysis, information on the choice of priors and Markov chain Monte Carlo settings			
For hierar	chical 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 <u>statistics for biologists</u> contains articles on many of the points above.			
Software an	d code			
Policy information	about <u>availability of computer code</u>			
Data collection	pCLAMP 10 and 11 software was used to			
Data analysis	Statistical analyses were computed using GraphPad Prism version 9 and StatView.			
	s 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 encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.			
Data				
'	about <u>availability of data</u> ust include a <u>data availability statement</u> . This statement should provide the following information, where applicable:			

Research involving human participants, their data, or biological material

Policy information about studies with <u>human participants or human data</u>. See also policy information about <u>sex, gender (identity/presentation)</u>, <u>and sexual orientation</u> and <u>race, ethnicity and racism</u>.

Reporting on sex and gender

Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected.

Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Reporting on race, ethnicity, or other socially relevant groupings

Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status).

Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.)

Please provide details about how you controlled for confounding variables in your analyses.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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			

Data exclusions Data were excluded when input-output curves indicated that the slice was not viable, by significant Grubbs outlier tests, or when an animal was found to have a brain tumor that could have impacted synaptic plasticity (some tumors are common in aged rodents).

Replication

Sample size

Because of limited equipment availability, and the nature of LTP experimentation, data from only 1 animal per day could be collected, by a single experimenter throughout the entire study. This allowed multiple replications across months of study. Care was taken to repeat each collection exactly the same way each day.

Randomization

Animals were randomly assigned to conditions.

Blinding

Experimenters were blinded to group allocation during data collection.

Sample sizes were determined based on previous similar studies.

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	Methods
n/a Involved in the study	n/a Involved in the study
Antibodies	ChIP-seq
Eukaryotic cell lines	Flow cytometry
Palaeontology and archaeology	MRI-based neuroimaging
Animals and other organisms	·
Clinical data	
Dual use research of concern	
Plants	
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Animals and other research organisms

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research, and <u>Sex and Gender in Research</u>

Laboratory animals	Young adult (3 months old) and aged (24 months old) F344xBN F1 rats were used.
Wild animals	The study did not involve wild animals.
Reporting on sex	Only male rats were used in this study. Unfortunately, female rats of this strain and ages, exclusively available through the NIA rodent colony, were not available at the time these studies were conducted.
Field-collected samples	The study did not involve samples that were collected in the field.
Ethics oversight	All experiments were conducted in accordance with protocols approved by the Ohio State University Institutional Animal Care and Use Committee.

Note that full information on the approval of the study protocol must also be provided in the manuscript.