

Reporting Summary

Nature Research 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 Research policies, see [Authors & Referees](#) 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

We have included a code availability statement. Zeiss Axiozoom.V16 and Zen software V2 blue edition were used for collection of zebrafish seizure data.

Data analysis

GraphPad Prism (version 8.1.2), ImageJ 2.0, Marvin Sketch (19.25.0), ImageJ plugin Time Series Analyzer V3, SciPy package "find_peaks", ANYmaze software (version 6.2), TraceFinder 4.1, GraphPad Prism, RRID:SCR_002798; V8.0), EthoVision XT 14

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [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 list of figures that have associated raw data
- A description of any restrictions on data availability

Data are available at the following link <https://doi.org/10.6084/m9.figshare.11634795>.

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

Life sciences study design

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

Sample size	Appropriate sample sizes were predetermined based on reports in the literature, pilot experiments, or through power analysis.
Data exclusions	One animal was excluded from the alcohol consumption study as the bottle in its cage was leaking. Two rats (one male and one female) were excluded from the final heroin self-administration dataset due to defective catheters. Eight rats were excluded from the final sucrose self-administration dataset due to failure to acquire sucrose self-administration. These exclusions were indicated in the methods. No other data were excluded.
Replication	Details about replication of specific experiments are shown in Supplementary Table 1. All attempts at replication were successful.
Randomization	For cellular assays, treatment groups were always randomized across the plate and analyzed blinded. For animal studies, animal treatments were randomized.
Blinding	All cellular assays and animal work was analyzed by an experimenter blinded to the treatment condition.

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	☒	☐ MRI-based neuroimaging
☐	☒ Animals and other organisms		
☒	☐ Human research participants		
☒	☐ Clinical data		

Antibodies

Antibodies used	chicken anti-MAP2 antibody (1:10,000; EnCor, CPCA-MAP2)
Validation	This antibody was validated by the manufacturer by demonstrating selective labeling of neurons in neuron-glia co-cultures and by western blot. It has been utilized in the following papers, among many others: 1. Dehmelt, H and Halpain, S. The MAP2/Tau family of microtubule-associated proteins. Genome Biol. 6:204 (2005). 2. Nunez J. Immature and mature variants of MAP2 and tau proteins and neuronal plasticity. Trends Neurosci. 11:477-9 (1998).

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	HEK293 (gift from Craig January, University of Wisconsin, Madison); HEK Flp-In 293 T-Rex stable cell lines (Invitrogen)
Authentication	These cell lines were not authenticated
Mycoplasma contamination	These cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	N/A

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	The species, strain, sex, and age of animals are reported in the methods where appropriate and included 8 week old, male and female C57BL/6J mice; male and female, 7 dpf zebrafish; male and female, 6 dpf zebrafish; male and female, 6 hpf zebrafish;
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	male 9–10 week old C57BL/6J mice; male and female, 12 weeks old C57/BL6J mice; E18 rats (unknown sex); Male and female Thy1-GFP-M line mice (> 8 weeks old); male C57/BL6J mice (6-8 weeks old); male and female Wistar rats (>8 weeks old)
Wild animals	We did not use wild animals.
Field-collected samples	We did not use field-collected samples.
Ethics oversight	All experimental procedures involving animals were approved by either the UCD, UCSF, UCSC or CU Anschutz Institutional Animal Care and Use Committee (IACUC) and adhered to principles described in the National Institutes of Health Guide for the Care and Use of Laboratory Animals. The University of California, Davis (UCD), the University of California, San Francisco (UCSF), the University of California, Santa Cruz (UCSC), and the University of Colorado Denver, Anschutz Medical Campus (CU Anschutz) are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

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