

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 (<i>n</i>) 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> 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 <i>d</i> , Pearson's <i>r</i>), 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	EthoVision XT 15 (Noldus), Leica SP8, Clampex (Molecular Devices V11)
Data analysis	Prism v10 (GraphPad), EthoVision XT 15 (Noldus), Fiji (ImageJ), Clampfit (Molecular Devices V11), EasyElectrophysiology (V2.8.0), Python (3.12.11)

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 data, code and materials used in this study are available in some form to any researcher for purposes of reproducing or extending the analysis. RNA-seq data is accessible through GEO: GSE283741. Map sequencing reads to transcriptome in the mouse mm9 (GRCm37) reference genome. The custom Python scripts used for

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

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	Sample size was determined by prior experience, existing literature, or power analyses as appropriate.
Data exclusions	To identify and exclude any potential outliers, Grubbs' or ROUT tests were used to identify outliers with α or $Q = 0.05$ (for Figure 4k).
Replication	We adhered to accepted standards for rigorous study design and reporting to maximize the reproducibility and translational potential of our findings as described by Landis, S.C et al., 2012 and in Arrive Guidelines by Kilkenny, C., et al., 2010. Representative images and traces were selected from experiments that were independently replicated with similar results across analyzed mice and cells.
Randomization	Age-matched mice were used for this study and cagemates were randomly assigned to groups during virus injection
Blinding	All experimenters were blind to treatment conditions throughout data collection, scoring, and analyses

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

Antibodies

Antibodies used	PV (rabbit, Swant PV25, 1/5000, RRID:AB_10000344; goat, Swant PVG213, RRID:AB_2721207, 1/1000); RGS14 (mouse, NeuroMab 75-170, RRID:AB_2179931, 1/500; rabbit, Proteintech 16258-1-AP, RRID:AB_2179918, 1/500); Synaptotagmin 2 (mouse, Abcam AB154035-1001, RRID:AB_2916272, 1/250); RFP (rabbit, Rockland 600-401-370, RRID:AB_2209751, 1/1000; goat, Sicgen AB1140-100, RRID:AB_2877097, 1/500); cFOS (guinea pig, Synaptic Systems 226-004, RRID:AB_2619946, 1/3000); GFP (chicken,
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Invitrogen A10262, RRID:AB_2534023, 1/500); Gephyrin (rabbit, Synaptic Systems 147-008, RRID:AB_2619834, 1/500); MEIS2 (rabbit, Protein Tech 11550-1-AP, RRID:AB_2143028, 1/400); BCL11a (mouse, Abcam ab19487, RRID:AB_444947, 1/500); TBR1 (rabbit, Abcam ab31940, RRID:AB_2200219, 1/200); GFAP (Chicken, Millipore AB5541, RRID:AB_177521, 1/2000); IBA1 (rabbit, FujiFilm 019-19741, RRID:AB_839504, 1/500); SST (mouse, Santa Cruz G-10, RRID:AB_831726, 1/500). Fluorescent-label-coupled secondary antibodies (Alexa-Fluor-488-conjugated donkey anti-rabbit IgG, 711-545-152, 1:500; Cy3-conjugated donkey anti-rabbit-IgG, 711-165-152, 1:500; Alexa-Fluor-488-conjugated donkey anti-mouse-IgG, 715-545-151, 1:500; Cy3-conjugated donkey anti-mouse-IgG, 715-165-151, 1:500; Alexa-Fluor-488-conjugated donkey anti-chicken-IgG, 703-545-155, 1:500; Cy3-conjugated donkey anti-goat-IgG, 705-165-147, 1:500; 647-conjugated donkey anti-guinea pig-IgG, 706-605-1481; Cy3-conjugated donkey anti-guinea-pig-IgG, 706-165-148, Jackson ImmunoResearch, in 1/500 dilution.

Validation

All antibodies used are commercially available and were selected because they were previously validated for mouse reactivity and for immunohistochemistry use. These antibodies have been widely used in peer reviewed publications. RRID of antibodies are provided in the Method section.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s) 293FT Cell Line from ThermoFisher Scientific (catalog number R70007) was used for lentiviruses production.

Authentication Successful lentiviral packaging reaction was assessed using Lenti-X GoStick titer test (Takara 631281). Lentiviruses were injected in mice and expression of the reporter was assessed by IHC.

Mycoplasma contamination cell lines are routinely tested for mycoplasma and deemed free of contamination prior to study

Commonly misidentified lines (See [ICLAC](#) register) None were included in this study

Animals and other research organisms

Policy information about [studies involving animals; ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals C57Bl/6J, adult mice (2 months) and Cntnap2^{-/-} mice, Pvalb-cre mice, Amigo2-Cre, and Rpl22HA mice were obtained from the Jackson Laboratories.

Wild animals This study did not involve wild animals

Reporting on sex This study include both male and female mice

Field-collected samples This study did not involve field-collected samples.

Ethics oversight All mice were group housed and experiments were conducted in accordance with procedures approved by the Institutional Animal Care and Use Committees at the Massachusetts General Hospital and NIH guidelines (IACUC 2011N000084) and Tufts University Medical School.

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