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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	Behavior, electrophysiology, or calcium imaging data was acquired using Clampex (10.7, Molecular Devices), High-speed Data Acquisition (DI-2108, Dataq Instruments), or Prairie View Imaging software (Bruker).
Data analysis	Behavior, electrophysiology, or calcium imaging data data was analyzed using Matlab (R2015a, MathWorks). RNA-Seq, ChIP-Seq, DHS, HiC, and PLAC-Seq data was analyzed using HISAT2/Bowtie2 on the public server at usegalaxy.org or bwa mem for genome alignment, EdgeR on the public server at bioinf-galaxian.erasmusmc.nl/galaxy for differential gene expression and ChIP-Seq signals, WGCNA using the R package, DAVID Bioinformatics Resources for gene ontology, MACS2 for peak calling, Homer for transcription factor motif analyses, UCSC genome browser for visualizing ChIP-Seq and RNA-Seq datasets, MAPS for PLAC-Seq analyses, Juicebox for visualizing HiC and PLAC-Seq datasets, and Juicer (HiCCUPS or Eigenvector) or FIRE for HiC 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/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

ChIP-Seq, RNA-seq, DHS, HiC, and PLAC-Seq data are available in the Gene Expression Omnibus (GEO) database under the reference number GSE127995.

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 sizes were determined by the standards of the field. All statistical tests were made between groups with similar sample sizes. For animal experiments, 3 to 20 mice per group were used. For ChIP-Seq, RNA-Seq, DHS, HiC, and PLAC-Seq experiments, 2-4 biological replicates per group were used.
Data exclusions	In calcium imaging experiments testing how neural coding transforms following successful learning, two mice that failed to acquire conditioned responses after 8 days of delay tactile startle conditioning were excluded. In HiC analyses, promoter-enhancer interactions greater than 5kb were considered due to the resolution limits of chromatin conformation approaches. In MAPS analyses of PLAC-Seq data, intra-chromosomal bins between 20Kb and 1Mb were used to identify long-range chromatin interactions, since the majority of raw count frequency beyond 1Mb was extremely sparse. No other data was excluded.
Replication	Biological replicates were performed for all experiments and only reproducible results are reported.
Randomization	All mice were allocated into sex-matched, littermate-matched experimental groups.
Blinding	Investigators were not blinded to allocation during experiments and outcome assessment. Animal behavior experiments were automated and did not require blinding.

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
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used	histone H3K4me3 (Abcam ab8580), histone H3K27ac (Abcam ab4729), histone H2A.z (Abcam ab4174), histone H3K27me3 (Abcam ab6002), CTCF (Millipore 07-729), Rad21 (Abcam ab992), Calbindin (Millipore AB1778), GFP (Abcam ab13970), and DsRed (Clontech 632496)
Validation	All antibodies are commercially available and have been tested in mice.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	6-12 weeks old mice (mus musculus) of both sexes on a mixed background were used.
Wild animals	not applicable
Field-collected samples	not applicable
Ethics oversight	All animal experiments were done according to protocols approved by the Animal Studies Committee of Washington University

Ethics oversight: School of Medicine in accordance with the National Institutes of Health guidelines.

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

ChIP-seq

Data deposition

☒ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☒ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.

https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE127995

Files in database submission

P56 H3K4me3 home1, P56 H3K4me3 home2, P56 H3K4me3 opto1, P56 H3K4me3 opto2, P56 H3K27ac home1, P56 H3K27ac home2, P56 H3K27ac opto1, P56 H3K27ac opto2, P56 H3K27me3 home1, P56 H3K27me3 home2, P56 H3K27me3 home3, P56 H3K27me3 opto1, P56 H3K27me3 opto2, P56 H3K27me3 opto3, P56 H2A.z home1, P56 H2A.z home2, P56 H2A.z home3, P56 H2A.z opto1, P56 H2A.z opto2, P56 H2A.z opto3, P56 CTCF home1, P56 CTCF home2, P56 CTCF home3, P56 CTCF home4, P56 CTCF opto1, P56 CTCF opto2, P56 CTCF opto3, P56 CTCF opto4, P56 Rad21 home1, P56 Rad21 opto1

Genome browser session
(e.g. UCSC)

N/A

Methodology

Replicates

2-4 biological replicates were performed for all ChIP-Seq experiments. All replication attempts were successful

Sequencing depth

36bp paired-end reads were generated for all ChIP-Seq experiments.

Stats: Condition; total # of paired-end fragments; uniquely mapped paired-end fragments
P56 H3K4me3 home1 26609170 22276973
P56 H3K4me3 home2 29270907 23363574
P56 H3K4me3 opto1 27595064 22663638
P56 H3K4me3 opto2 28612043 21707440
P56 H3K27ac home1 27285187 23967809
P56 H3K27ac home2 24853568 21679983
P56 H3K27ac opto1 28243874 25004217
P56 H3K27ac opto2 25362900 21603725
P56 H3K27me3 home1 22578964 17303533
P56 H3K27me3 home2 26523437 21035529
P56 H3K27me3 home3 24609405 19019379
P56 H3K27me3 opto1 25587942 20063674
P56 H3K27me3 opto2 30983079 24349185
P56 H3K27me3 opto3 25021827 18799939
P56 H2A.z home1 29914410 24115624
P56 H2A.z home2 35044605 28767504
P56 H2A.z home3 29257380 24434771
P56 H2A.z opto1 31751564 26264444
P56 H2A.z opto2 29964135 25088776
P56 H2A.z opto3 31705781 26188674
P56 CTCF home1 26656517 21563083
P56 CTCF home2 26854777 21394138
P56 CTCF home3 26545783 19548334
P56 CTCF home4 24151141 18092971
P56 CTCF opto1 30161606 23876679
P56 CTCF opto2 23803862 18551819
P56 CTCF opto3 23415452 17347855
P56 CTCF opto4 23357342 16615928
P56 Rad21 home1 35840764 25724992
P56 Rad21 opto1 38547840 26600264
P56 input home 20382945 17265984
P56 input opto 15681266 13265137

Antibodies

histone H3K4me3 (Abcam ab8580), histone H3K27ac (Abcam ab4729), histone H2A.z (Abcam ab4174), histone H3K27me3 (Abcam ab6002), CTCF (Millipore 07-729), Rad21 (Abcam ab992)

Peak calling parameters

Reads were aligned to the mm10 reference genome using Bowtie2 and peaks were called using MACS2 on the public server at usegalaxy.org using default parameters.

Data quality

Using a FDR<0.05, score>=100: 39,624 peaks for H3K27ac; 23,459 peaks for CTCF; 58,043 peaks for H2A.z, and 21,689 peaks for H3K4me3 were identified

Software

Reads were aligned to the mm10 reference genome using Bowtie2 and peaks were called using MACS2 on the public server

Software

at usegalaxy.org. Differential binding with optogenetic stimulation was analyzed using EdgeR on the public server at bioinf-galaxian.erasmusmc.nl/galaxy