nature research

Corresponding author(s): Pengfei Liu, Yong Xu, Zheng Sun

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.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Ethovision XT(Noldus), Any-Maze Behavior Tracking Software (Stoelting), Digidata1440A (Axon Instruments), VersaMax (Autoscan Instruments), SAMtools V0.1.19 ,and BEDtools v2.17.0, SICER v1.1 , and Tophat v2.1.0
Data analysis	SPSS (V.21.0, IBM), GraphPad Prism 7 (Graphpad), packages “lme4” and “lmerTest” (statistical package R version 3.5.1.), Ethovision XT (Noldus), Any-Maze Behavior Tracking Software (Stoelting), ImageJ(NIH), Mini Analysis Program (Synaptosoft Inc.), pClamp 10.3 software (Axon Instruments), SICER v1.1, DESeq2 (version 1.8.2)

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 upon request. 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

RNA-seq and ChIP-seq data are available in GEO (GSE92452).

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	Sample size were based on literature and were not determined by statistical methods.
Data exclusions	Animals were excluded and euthanized before behavior tests if they showed distress, infection, bleeding, or anorexia due to surgery. Animals were excluded after behavior tests if they showed mis-injection at postmortem examination.
Replication	All the experiments were repeated at least once, except that the ChIP sequencing and RNA sequencing were only done once. All attempts at replication were successful.
Randomization	All animals were grouped according to their sex, age, genotype, w/wo surgery, and w/wo drug/virus.
Blinding	Data collection and analysis were not performed completely blind to the conditions of the experiments. Behavioral experiments were done by experimentalists who know the drug treatment information but do not know the genotype or surgery information. During the early stage of analysis such as counting the time duration from video clips, experimentalists were blind to both genotype and treatment information. The statistical analysis and data plotting was done by experimentalists who knew both genotype and treatment information.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Antibodies

Antibodies used

Anti-GABA-A Receptor alpha2 (Catlog #224104, Synaptic Systems), dilution 1:100
Anti-HDAC3 (AbCam, AB7030), IHC 1:100; WB 1:2000; IP 6µg per IP.
Anti-HDAC1 (AbCam, AB7028), IP 4µg per IP.
Anti-NCOR1 (Bethyl Laboratories, A301-146A), dilution 1:1000.
Anti-TBLR1 (IMGENEX, IMG591), dilution 1:1000.
Anti-GFP (D5.1) (Cell Signaling , 2956), IHC 1:100.
Anti Glutamate antibody, (Sigma, G6642), IHC 1:100.
Alexa Fluor 488 goat anti guinea pig IgG (H+L) (Life Tech, A11073), dilution 1:1000.
Alexa Fluor 488 goat anti rabbit IgG (H+L) (Life Tech, A11034), dilution 1:1000.

Alexa Fluor 546 goat anti rabbit IgG(H+L) (Life Tech, A11010), dilution 1:1000.
Alexa Fluor 647 goat ant rabbit IgG(H+L) (A32733, Life Tech), dilution 1:1000.

Validation

Anti-GABA-A Receptor alpha2 (Catlog #224104, Synaptic Systems). IHC on mouse; https://www.sysy.com/products/gaba-a/facts-224104.php; PMID: 24554721
Anti-HDAC3 (AbCam, AB7030). IHC, ChIP and WB on mouse; https://www.abcam.com/hdac3-antibody-chip-grade-ab7030-references.html#top-600; PMID: 24268577, & 22647876
Anti-HDAC1 (AbCam, AB7028). IP on mouse: https://www.abcam.com/hdac1-antibody-chip-grade-ab7028-references.html#top-310; PMID: 28115699
Anti-NCOR1 (Bethyl Laboratories, A301-146A). WB on mouse; PMID: 24268577
Anti-TBLR1 (IMGENEX, IMG591). WB on mouse; PMID: 24268577
Anti Glutamate antibody, (Sigma, G6642), IHC on mouse; https://www.sigmaaldrich.com/catalog/product/sigma/g6642?lang=en&region=US; PMID: 26098212
Anti-GFP (D5.1) (Cell Signaling , 2956). IHC on mouse; https://www.citeab.com/antibodies/124367-2956-gfp-d5-1-xp-rabbit-mab?utm_campaign=Widget+All+Citations&utm_medium=Widget&utm_source=Cell+Signaling+Technology; PMID: 29158396

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293T (ATCC)
Authentication	Morphology check by microscope and fluorescent Hoechst staining
Mycoplasma contamination	Negative for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	Not in ICLAC

Animals and other organisms

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

Laboratory animals	NS-DADm mice were generated from crossing N-DADm and S-DADm mice. Vgat-Cre mice and Rosa26-tdTomato mice were obtained from JAX. Hdac3loxP/loxP mice were published and can be obtained from JAX. The NCOR1/2loxP/loxP mice were provided by PHENOMIN, Institut Clinique de la Souris (ICS), CNRS, INSERM, University of Strasbourg, France (http://www.phenomin.fr/). NCOR1loxP/loxP/NCOR2loxP/loxP/Vgat-Cre (NS-V) mice were generated through crossbreeding. tdTomatoloxP/loxP/NCOR1loxP/loxP/NCOR2loxP/loxP/Vgat-Cre mice (tdTomato-labeled NS-V mice) were further generated for circuit mapping and electrophysiology studies. All mice were C57BL/6 genetic background. Male mice at the age of 2-6 months were used for all experiments except otherwise noted. Female mice (2-6 months old) were also used for some of the tests and no sexual dimorphism was observed for the phenotypes of NS-DADm mice or NS-V mice. For NS-DADm mice, wild-type littermates were used as control and referred to as WT. For the initial characterization of NS-V mice, NCOR1loxP/loxP/NCOR2loxP/loxP mice were used as control as referred to as WT. For electrophysiology studies, ribosomal profiling, circuit mapping, and chemogenetics experiments involving NS-V mice, Vgat-Cre mice or tdTomato/Vgat-Cre mice served as control and referred to as WT. All tests were repeated at least 2 times. 5 mice were housed in each cage in a 12-12 light-dark (7am - 7pm) facility with free access to water and food. After surgery, mice were housed singly in the same facility. All the animal care and use procedures followed the guidelines of the Institutional Animal Care and Use Committee in Baylor College of Medicine.
Wild animals	This study did not use wild animals.
Field-collected samples	This study did not use field-collected samples.

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=GSE92452 Token to access the data: clenkascfvmpdov
Files in database submission	Raw files: Run1_ZN5264_GCCAATGT_L001_R1_001.fastq.gz, Run2_ZN5264_GCCAATGT_L001_R1_001.fastq.gz, Run2_ZN5264_GCCAATGT_L002_R1_001.fastq.gz, Run1_ZN5624_CTTGTACT_L001_R1_001.fastq.gz, Run2_ZN5624_CTTGTACT_L001_R1_001.fastq.gz, Run2_ZN5624_CTTGTACT_L002_R1_001.fastq.gz Processed files : HDAC3.IP.bw, HDAC3.IN.bw
Genome browser session (e.g. UCSC)	https://genome.ucsc.edu/cgi-bin/hgTracks?db=mm10&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&nonVirtPosition=&position=chr2%3A112129023-112135205&hgsid=683266175_dnO3lAgpZ1spw8IDd6canmCY4GW7

Methodology

Replicates	One ChIP sample and one input sample were created and sequenced after pooling 4 independent ChIP
Sequencing depth	IP sample: Single end, 50bp, total reads: 234629536, uniquely aligned reads: 159488867 Input sample: Single end, 50bp, total reads:157256519, uniquely aligned reads: 97771305
Antibodies	Anti-HDAC3 (Abcam, ab7030)
Peak calling parameters	HDAC3 peaks were called using used SICER v1.1 by extending reads to 200bp in the 5′ to 3′ direction. A window size of 200nt, gap of 300nt and an FDR of 0.05 were set. HDAC3 ChIP samples were ratio normalized to their respective inputs and converted to bigwig format using the bamCompare (with --normalizeTo1x) module from deepTools.
Data quality	Read quality using fastqc: average phred score is greater than 34. ChIP-seq reads were aligned to the mus musculus genome (mm10) using Bowtie2 V2.1.0 with following parameters: -D 20 -R 3 -N 0 -L 20 -i S,1,0.50. The average mappability across all the samples was ~96%. HDAC3 ChIP samples were ratio normalized to their respective inputs and converted to bigwig format using the bamCompare (with --normalizeTo1x) module from deepTools.
Software	Bowtie2 V2.1.0, SAMtools V0.1.19, BEDtools v2.17.0, deepTools, SICER v1.1, Integrative Genome Browser (IGV) and ChIPseeker.