

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	The reads obtained from RNA-seq experiments were uniquely mapped to the mouse (mm10) genome with the use of HISAT2 (version 2.1.0), and counted with featureCounts (version 2.0.0). The reads obtained from ChIP-seq and ATAC-seq experiments in this study were uniquely mapped to the mouse (mm10) genome with the use of Bowtie software (version 2.2.3), and duplicated reads were removed with samtools (version 1.9).
Data analysis	RNA-seq data were analyzed by using DESeq2 (version 1.26.0), DAVID, and GSEA software (version 4.3.2). ATAC-seq and ChIP-seq data were analyzed by using MACS peak caller (version 3.0.0), deepTools (version 3.5.4), TOBIAS, and GREAT (version 4.0.4).

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](#)

RNA-seq, ChIP-seq and ATAC-seq data have been deposited in GEO under the accession numbers GSE263334 and GSE288732.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

NA

Reporting on race, ethnicity, or other socially relevant groupings

NA

Population characteristics

NA

Recruitment

NA

Ethics oversight

NA

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](https://www.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

No statistical methods were used to predetermine sample sizes, but sample size was similar to those generally employed in the field.

Data exclusions

No data were excluded from the analyses.

Replication

The experimental findings were reliably reproduced through repeated experiments.

Randomization

All individual mice or samples were randomly allocated to the experimental groups.

Blinding

The experimenters were blinded to mouse genotype during data collection.

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
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	Rabbit polyclonal antibodies to CHD8 were generated in-house and used for immunoblot analysis, and a rat monoclonal antibody to CHD8 was used for ChIP. Other antibodies included those to CUX1 (11733-1-AP, Proteintech, 1:100), to CTIP2 (ab18465, abcam, 1:500), to TBR1 (ab31940, abcam, 1:500), to SOX2 (ab97959, abcam, 1:500), to SATB2 (ab51502, abcam, 1:25), to BrdU (B35128, Thermo Fisher Scientific, 1:10), to Ki67 (550609, BD Biosciences, 1:500), and to cleaved caspase-3 (9661, Cell Signaling Technology, 1:500) for immunofluorescence staining, and those to FLAG (F1804, Sigma-Aldrich, 1:2000) and to HSP90 (610419, BD Biosciences, 1:2000) for immunoblot analysis.
Validation	Antibody validation was reported from the companies that provide the antibodies or from cited literatures.

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	Rosa26+/LSL-Chd8 mice were generated in this study. A pair of loxP sites flanking stop cassette of Rosa26+/LSL-Chd8 mice was deleted by crossing with Zp3-Cre mice to yield Rosa26+/Chd8 mice (Chd8 KI mice). Chd8+/- mice were crossed with Chd8 KI mice to produce Chd8+/-/Chd8 KI mice. All mice in this study were backcrossed to the C57BL/6 background for more than six generations.
Wild animals	NA
Reporting on sex	Both sexes were used for body and brain weight measurements, MRI analysis as well as behavioral analysis for genetic and pharmacological rescue experiments. The experiments for immunoblot, RT and real-time PCR analysis, immunofluorescence staining did not distinguish based on the sex of the mice. For RNA-seq, ChIP-seq, and ATAC-seq analyses, we used samples from male mice, as previous studies primarily employed male mice, and we aimed to compare our results with those studies. Behavioral battery tests were also conducted exclusively on male mice. For some of those behavioral tests where significant differences were observed, we performed same tests on female mice and found similar behavioral abnormalities.
Field-collected samples	NA
Ethics oversight	Periments were performed under the approval of the Animal Care Committee of Kanazawa University (Permission No. AP-224334). Guidelines for the Care and Use of Laboratory Animals at the University of Toyama and approved by the Ethics Committee for Animal Experiments at the University of Toyama (Permission No. A2022OPR-2 and A2019OPR-2).

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

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA

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.

GSE263334

Files in database submission

ChIP-seq input E14 forebrain CHD8 WT rep1
ChIP-seq input E14 forebrain CHD8 WT rep2
ChIP-seq input E14 forebrain CHD8 WT rep3
ChIP-seq CHD8 E14 forebrain CHD8 WT rep1
ChIP-seq CHD8 E14 forebrain CHD8 WT rep2
ChIP-seq CHD8 E14 forebrain CHD8 WT rep3
ChIP-seq input E14 forebrain CHD8 KI rep1
ChIP-seq input E14 forebrain CHD8 KI rep2
ChIP-seq input E14 forebrain CHD8 KI rep3
ChIP-seq CHD8 E14 forebrain CHD8 KI rep1
ChIP-seq CHD8 E14 forebrain CHD8 KI rep2
ChIP-seq CHD8 E14 forebrain CHD8 KI rep3

Genome browser session

(e.g. [UCSC](#))

IGV

Methodology

Replicates

Biological replicates, n = 3

Sequencing depth

ChIP-seq input E14 forebrain CHD8 WT rep1, 18939251 (paired-end)
ChIP-seq input E14 forebrain CHD8 WT rep2, 20415912 (paired-end)
ChIP-seq input E14 forebrain CHD8 WT rep3, 19215040 (paired-end)
ChIP-seq CHD8 E14 forebrain CHD8 WT rep1, 21346779 (paired-end)
ChIP-seq CHD8 E14 forebrain CHD8 WT rep2, 22196401 (paired-end)
ChIP-seq CHD8 E14 forebrain CHD8 WT rep3, 20124727 (paired-end)
ChIP-seq input E14 forebrain CHD8 KI rep1, 19447385 (paired-end)
ChIP-seq input E14 forebrain CHD8 KI rep2, 21072615 (paired-end)
ChIP-seq input E14 forebrain CHD8 KI rep3, 20850390 (paired-end)
ChIP-seq CHD8 E14 forebrain CHD8 KI rep1, 19394782 (paired-end)
ChIP-seq CHD8 E14 forebrain CHD8 KI rep2, 21037888 (paired-end)
ChIP-seq CHD8 E14 forebrain CHD8 KI rep3, 20752045 (paired-end)

Antibodies

A rat monoclonal antibody to CHD8 was used for ChIP.

Peak calling parameters

Markedly enriched regions of the genome were identified with the use of the MACS peak caller ($P < 1 \times 10^{-12}$ or $P < 1 \times 10^{-18}$)

Data quality

CHD8_WT_rep1.narrowPeak, 5989 peaks
CHD8_WT_rep2.narrowPeak, 6003 peaks
CHD8_WT_rep3.narrowPeak, 6168 peaks
CHD8_TG_rep1.narrowPeak, 8309 peaks
CHD8_TG_rep2.narrowPeak, 7692 peaks
CHD8_TG_rep3.narrowPeak, 2482 peaks
(cut off, $P < 1 \times 10^{-12}$)

Software

ChIP-seq data were analyzed by using MACS peak caller (version 3.0.0), deepTools (version 3.5.4), TOBIAS, and GREAT (version 4.0.4).

Magnetic resonance imaging

Experimental design

Design type

Structure MRI for ex vivo samples

Design specifications

Image acquisition is performed once per sample.

Behavioral performance measures

NA

Acquisition

Imaging type(s)	Structural
Field strength	11.7 T
Sequence & imaging parameters	The structural images were acquired using 3D T2-weighted multi-slice rapid acquisition with relaxation enhancement (RARE) with the following parameters: repetition time = 2000 ms, echo time = 75 ms, spatial resolution = 100 × 100 × 100 μm, RARE factor = 32, and averages = 4.
Area of acquisition	A whole brain scan
Diffusion MRI	☐ Used ☒ Not used

Preprocessing

Preprocessing software	SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK), and in-house software written in MATLAB (MathWorks, Natick, MA, USA)
Normalization	The segmented images were spatially normalized into a study-specific template that was created with all data using a Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) algorithm.
Normalization template	A study-specific template was created with all data using a DARTEL.
Noise and artifact removal	Before preprocessing, the images were applied by the trapezoid filter to remove the gibbs artifact and denoising process to remove the background noise using ParaVision 360 (version 3.6, Bruker Biospin GmbH)
Volume censoring	NA

Statistical modeling & inference

Model type and settings	2nd level two-sample t-test for whole-brain comparisons of gray matter volume
Effect(s) tested	NA
Specify type of analysis:	☒ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	voxel-wise
(See Eklund et al. 2016)	
Correction	a cluster-level family-wise error (FWE) corrected p-value < 0.05, with an individual voxel threshold of an uncorrected p-value = 0.001

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis