Corresponding author(s): Dahua Chen
Zhao-Qian Teng
Peng Jin

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	Z-stack images (at 0.3-µm intervals) were obtained on a ZEISS 710 confocal laser-scanning microscope with an X63 oil-immersion lens at an electronic zoom factor of 1 or 2. Image analyses and quantification were performed using ImageJ software. Behavioral assays: Data were collected blindly using the software Smart V3.0.03 (Panlab, Barcelona, Spain). Electrophysiology: The fEPSP signals were digitized using the Digidata 1440A interface board. Traces were obtained by pClamp 10.6 and analyzed using the Clampfit 10.6 (Axon Instruments, Foster City, CA).
Data analysis	Image analyses and quantification were performed using ImageJ software (1.49v). For RNAseq data, short read alignment, transcript expression estimation, and differential analysis were carried out using the Tophat2 (v2.1.1) and Cufflinks (v2.2.1) pipelines. The short reads were aligned against a reference gene database (Ensembl: Mus musculus, NCBIM37.62) without attempting to assemble novel transcripts. Proteomics data analysis was performed by our JUMP software (version 1.0.55) with improved sensitivity and specificity. Gene ontology (GO) analysis was performed by Database for Annotation, Visualization and Integrated Discovery (DAVID v6.8). The WEB-based GEne SeT AnaLysis Toolkit (WebGestalt) was used for additional GO analysis. GeneMANIA and Pathway Commons were used to predict the function and interaction of the differentially expressed genes. Predicted ASD-associated gene interaction networks were performed by genome-wide predictions of autism-associated genes (http://asd.princeton.edu/). Sylamer software (https://www.ebi.ac.uk/research/enright/software/sylamer) was used to assess 3'UTR miRNA seed match enrichment p-values across the ranked protein list. A FASTA file containing 3'UTRs of protein-encoding genes was obtained and exported from Sylarray software (available at https://www.ebi.ac.uk/research/enright/software). All statistical analyses were performed using Prism 7.0 (GraphPad Software). Pearson's Chi-squared tests with Yates' continuity correction were performed in R software (http://www.rproject.org/). Conserved miR-137 predicted targets were obtained from TargetScanMouse Release 7.1 (http://www.targetscan.org/mmu_71/). Schizophrenia-

associated genes were obtained from Schizophrenia Gene Resource (http://bioinfo.mc.vanderbilt.edu/SZGR/) and Gene List Automatically Derived For You (GLAD4U). ASD-associated genes were obtained from SFARI (https://gene.sfari.org/autdb/HG_Home.do). ID-associated genes were obtained from the Intellectual Disability Project (http://gfuncpathdb.ucdenver.edu/iddrc/home.php). A detailed gene list can be found in Supplementary Table 4. Galaxy online tools were used to overlap different gene lists.

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

Genome-wide datasets are deposited at GEO under accession number GSE79661 (RNA-seq) and at the ProteomeXchange database under accession number PXD003874 (proteomics).

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	No statistical methods were used to predetermine sample sizes; however, sample sizes were similar to those reported in previous publications (e.g., Ref. 45).
Data exclusions	No animals were excluded from the study: all analysis includes data from all animals. However, for whole cell recordings, series resistance was monitored by a –3 mV step throughout the entire experiment of whole cell access and if it fluctuated more than 20%, the data were excluded from the analysis.
Replication	All experiments were replicated through multiple cohort/mice analysis. All replication attempts were successful and have similar results.
Randomization	Samples were allocated to groups by genotypes (wildtype/heterozygous/homozygotous miR-137 knockout mice).
Blinding	Littermates were housed in the same cage. For behavioral assays and electrophysiological experiments, each cage contains mixed genotypes, and the people who in charge of data collection do not know the mice information during the experiments.

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All unique materials used are readily available from the authors.

Antibodies

Antibodies used	Immunostaining: mouse microtubule-associated protein 2 (MAP2, 1:400; MAB3418; Millipore), mouse postsynaptic density protein 95 (PSD-95; 1:500; ab2723; Abcam); mouse synaptophysin (1:300; ab8049; Abcam); goat anti–mouse Alexa Fluor 568 (1:500; A11031;Invitrogen); goat anti–mouse Alexa Fluor 488 (1:500; A11001; Invitrogen); fluorescent nuclear dye DAPI (D9542; Sigma-Aldrich). Western blot: Anti-PDE10A (SAB2700582; Sigma-Aldrich), anti-SATB2 (ab34735; Abcam), anti-PTPN2 (MABS1753; Millipore), anti-DNMT3A (3598S; CST), anti-PKA C-α (4782S; CST), anti-Phospho-PKA C (Thr197) (5661S; Cell Signaling Technology) and anti-PSD-95 (MAB1598; Millipore) were used as primary antibodies at a 1:1,000 dilution. HRP-labeled secondary antibodies were obtained from Cell Signaling Technology (7074S & 7076S) and were used at a dilution of 1:5,000. The antibodies against GAPDH (AM4300; Thermo Fisher) or Actin (A5060; Sigma-Aldrich) were used for loading controls.
Validation	All antibodies used in our study are either validated by the antibody companies. Immunostaining: MAP2: http://www.emdmillipore.com/US/en/product/Anti-MAP2-Antibody-clone-AP20,MM_NF-MAB3418?bd=1 PSD-95: https://www.abcam.com/psd95-antibody-6g6-1c9-ab2723.html Synaptophysin: https://www.abcam.com/synaptophysin-antibody-sy38-ab8049.html Goat anti–mouse Alexa Fluor 568: https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11031 Goat anti–mouse Alexa Fluor 488: https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11001 DAPI: https://www.sigmaaldrich.com/catalog/product/sigma/d9542?lang=en&region=US Western blot: PDE10A: https://www.sigmaaldrich.com/catalog/product/sigma/sab2700582?lang=en&region=US SATB2: https://www.abcam.com/satb2-antibody-ab34735.html PTPN2: http://www.emdmillipore.com/US/en/product/Anti-TC-PTPase-PTPN2-Antibody-clone-9E9.1,MM_NF-MABS1753 DNMT3A: https://www.cellsignal.com/products/primary-antibodies/dnmt3a-d23g1-rabbit-mab/3598 PKA C-α: https://www.cellsignal.com/products/primary-antibodies/pka-c-a-antibody/4782 Phospho-PKA C (Thr197): https://www.cellsignal.com/products/primary-antibodies/phospho-pka-c-thr197-d45d3-rabbit-mab/5661 PSD-95: http://www.emdmillipore.com/US/en/product/Anti-Post-Synaptic-Density-Protein-95-Antibody-clone-7E3-1B8,MM_NF-MAB1598 Anti-rabbit IgG, HRP-linked Antibody: https://www.cellsignal.com/products/secondary-antibodies/anti-rabbit-igg-hrp-linked-antibody/7074 Anti-mouse IgG, HRP-linked Antibody: https://www.cellsignal.com/products/secondary-antibodies/anti-mouse-igg-hrp-linked-antibody/7076 GAPDH: https://www.thermofisher.com/antibody/product/GAPDH-Antibody-clone-6C5-Monoclonal/AM4300 Actin: https://www.sigmaaldrich.com/catalog/search?term=A5060

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	We used 293 FT and Neuron-2A cell lines.
Authentication	These commonly used commercial cell lines were not further authenticated.
Mycoplasma contamination	All cell lines were tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other organisms

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

Laboratory animals	All mice used were on the 129S6/SvEvTac genetic background. We designed a targeting vector to disrupt the Mir-137 gene via homologous recombination in mouse ES cells, where two loxP sites were inserted upstream (~2 kb) and downstream (~0.6 kb) of the Mir137 gene. By crossing with either Zp3-Cre or Nestin-Cre line, we were able to specifically delete Mir137 in germline or central and peripheral nervous system, and to generate the heterozygous global knockout (gKO) and conditional knockout (cKO) mice. For morphological analysis and H&E staining, mouse from embryonic day 15.5 (E15.5) to postnatal day 14 were used,

	including both male and female. For Immunohistochemistry, P18 and 8-week-old mice were used, including both male and female. For behavioral assays, only 2- to 3-month-old male mice obtained from at least two independent cohorts were used for behavioral testing. For electrophysiological measures, 4-week-old mice were used, including both male and female. For RNA-seq and proteomics analyses, P12 mice were used, including both male and female.
Wild animals	This study did not involve wild animals.
Field-collected samples	This study did not involve samples collected from the field.