

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 |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> 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> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of all covariates tested |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> 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) |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> 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> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> 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 | ANY-maze 6.18 |
| Data analysis | For analyses the following software was used: ANY-maze 6.18, ImageJ 1.54, GraphPad Prism 9, IMARIS, R (version 4.2.1), SPM12, NeuroLucida, Hisat2 (version 2.0.5), FeatureCounts (version 1.5.0-p3), QuantStudio |

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](#)

RNAseq data have been deposited in Gene Expression Omnibus under accession number GSE256468. All other data are included in the manuscript and/or SI Appendix.

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

n.a.

Reporting on race, ethnicity, or other socially relevant groupings

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](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

Given the exploratory nature of the analyses, no sample size was calculated a priori.

Data exclusions

Outliers were identified as values greater than 2 times the standard deviation (SD) from the mean (M) and excluded from analyses.

Replication

Independent replication datasets were not included.

Randomization

Mice were randomly assigned to experimental groups.

Blinding

During data collection and analysis, the investigators were blinded to group allocation.

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 |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Antibodies |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Eukaryotic cell lines |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Palaeontology and archaeology |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> Animals and other organisms |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Clinical data |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Dual use research of concern |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Plants |

Methods

- | | |
|-------------------------------------|--|
| n/a | Involved in the study |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> ChIP-seq |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Flow cytometry |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> MRI-based neuroimaging |

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 | FKBP51-Nex or NEX-Cre mice at 5-8 months of age on a C57Bl/6n background. All animals were bred at the in-house breeding facility of the Max Plank Institute of Psychiatry in Martinsried, Munich, DE. |
| Wild animals | n.a. |
| Reporting on sex | Data were obtained in both male and female mice and reported accordingly. |
| Field-collected samples | n.a. |
| Ethics oversight | All experiments were in accordance with the European Communities Council Directive 2010/63/EU and were approved by the committee for the Care and Use of Laboratory animals of the Government of Upper Bavaria. |

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

Plants

| | |
|-----------------------|------|
| Seed stocks | n.a. |
| Novel plant genotypes | n.a. |
| Authentication | n.a. |

Magnetic resonance imaging

Experimental design

| | |
|---------------------------------|-------------------------------------|
| Design type | deformation based morphometry (DBM) |
| Design specifications | n.a. |
| Behavioral performance measures | n.a. |

Acquisition

| | |
|-------------------------------|---|
| Imaging type(s) | structural |
| Field strength | 9.4 |
| Sequence & imaging parameters | 3D gradient echo, cartesian k-space sampling, field of view 19.8 x 12.8 x 15.8 mm ³ , matrix size 256 x 166 x 205, coronal read orientation, TE/TR/flip angle 6.253ms/34.1ms/10 degree |
| Area of acquisition | whole brain scan |
| Diffusion MRI | <input type="checkbox"/> Used <input checked="" type="checkbox"/> Not used |

Preprocessing

| | |
|----------------------------|---|
| Preprocessing software | SPM12 on Matlab R2022b, brain extraction based on tissue probability maps, SPM12 "old segment" function, isotropic smoothing kernel size = 5.7 x voxel size |
| Normalization | non-linear registration (DARTEL), flow fields transformed to jacobian deformation fields |
| Normalization template | study specific template, aligned with the Hikishima C57Bl6 mouse MRI template (Hikishima et al., Sci Rep 7, 85 (2017)) |
| Noise and artifact removal | spatial adaptive non-local means denoising filter (CAT12) |

Volume censoring

n.a.

Statistical modeling & inference

Model type and settings

deformation based morphometry

Effect(s) tested

two-way ANOVA (early life stress x genotype and interaction if statistically significant), corrected for total brain volume

Specify type of analysis: ☒ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference

cluster

(See [Eklund et al. 2016](#))

Correction

FWE correction at the cluster level ($p_{FWE,cluster} < 0.05$), with a cluster collection threshold of $p < 0.005$ uncorrected

Models & analysis

n/a

Involved in the study

☐ Functional and/or effective connectivity☐ Graph analysis☐ Multivariate modeling or predictive analysis