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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

Statistical parameters

When statistical analyses are reported	, confirm that the following items are	e present in the relevant	location (e.g. figu	re legend, table	legend, mair
text, or Methods section).					

n/a	onfirmed	
	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.	
\boxtimes	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 <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (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>	
\boxtimes	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings	
\boxtimes	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes	
\boxtimes	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 <u>statistics for biologists</u> may be useful.

Software and code

Policy information about availability of computer code

Data collection Graph-Pad Software Inc, Version 5.01 was used for all data display.

Data analysis Graph-Pad Software Inc, Version 5.01 was used for statistical analysis.

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 <u>data availability statement</u>. 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

All data generated or analyzed during this study are included in this published article and its supplementary information files. The source data underlying Figs 1-10 and Supplementary Figs 1-15 are provided as two Source Data files.

Field spe	ecific reporting				
<u>.</u>	ecific reporting				
	est 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				
Tor a reference copy or	the decument with an account, see <u>natural or policies reporting annually nation</u>				
Life scier	nces study design				
All studies must dis	close on these points even when the disclosure is negative.				
Sample size	No sample-size calculations was performed. Sample sizes are considered to be sufficient based on solid statistical results between groups.				
Data exclusions	No data were excluded from the analyses.				
Replication	Replicate experiments were successful.				
Randomization	All mice sacrificed for experiment were not random. Mice analyzed were litter mates and sex-matched whenever possible.				
Blinding	Investigators were not blinded to mouse genotypes and drug application during experiments. All image analyses, behavioral experiments, and other experiments were done blind to the experimental condition whenever possible. Data from no blinded experiments were not subjective but based on objectively acquired by related experimental software.				
Materials & expension of the materials and the materials are separated in the material of the materials and the materials are separated in the material are separated in the materials are separated in the material are separa	logical materials ChIP-seq Flow cytometry Cell lines MRI-based neuroimaging				
Antibodies used	The antibodies used for the experiments were provided in Antibodies and drugs section in Supplementary methods/pages 29-30 in Supplementary information .				
Validation	Description of all antibodies used in this study can be found in Antibodies and drugs section in Supplementary methods/pages 29-30 in Supplementary information.				
Animals and	other organisms				
Policy information	about <u>studies involving animals</u> ; <u>ARRIVE guidelines</u> recommended for reporting animal research				
Laboratory anima	Description of research mice used for experiments can be found in the relevant figure legends. Animal section in Methods/page				

Laboratory animals

Description of research mice used for experiments can be found in the relevant figure legends, Animal section in Methods/page 24 in the main text, and Animal section in Supplementary Methods/pages 28-29 in Supplementary information.

Wild animals

No wild animal was used .

No field-collected samples

No field-collected sample was used.