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Supplementary Figures: 8

Supplementary Tables: 0

Supplementary Videos: 0

Reporting Checklist for Nature Neuroscience

This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. For more information, please read Reporting Life Sciences Research.

Please note that in the event of publication, it is mandatory that authors include all relevant methodological and statistical information in the manuscript.

Statistics reporting, by figure

- Please specify the following information for each panel reporting quantitative data, and where each item is reported (section, e.g. Results, & paragraph number).
- Each figure legend should ideally contain an exact sample size (n) for each experimental group/condition, where n is an exact number and not a range, a clear definition of how n is defined (for example x cells from x slices from x animals from x litters, collected over x days), a description of the statistical test used, the results of the tests, any descriptive statistics and clearly defined error bars if applicable.
- For any experiments using custom statistics, please indicate the test used and stats obtained for each experiment.
- Each figure legend should include a statement of how many times the experiment shown was replicated in the lab; the details of sample collection should be sufficiently clear so that the replicability of the experiment is obvious to the reader.
- For experiments reported in the text but not in the figures, please use the paragraph number instead of the figure number.

Note: Mean and standard deviation are not appropriate on small samples, and plotting independent data points is usually more informative. When technical replicates are reported, error and significance measures reflect the experimental variability and not the variability of the biological process; it is misleading not to state this clearly.

		TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
example	1a	one-way ANOVA	Fig. legend	9, 9, 10, 15	mice from at least 3 litters/group	Methods para 8	error bars are mean +/- SEM	Fig. legend	p = 0.044	Fig. legend	F(3, 36) = 2.97	Fig. legend
example	results, para 6	unpaired t-test	Results para 6	15	slices from 10 mice	Results para 6	error bars are mean +/- SEM	Results para 6	p = 0.0006	Results para 6	t(28) = 2.808	Results para 6
+ -												

		TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	FIGURE NUMBER	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
+ -	Fig. 1c	two-tailed t-test	Figure legend	n=5 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO FC p =.0018 HC p=.0037 STR p=0.0001 CBL p=0.5090	Figure legend	FC t(8) = 4.577 HC t(8) = 4.408 STR t(8) = 6.832 CBL t(8) = 0.6912	Figure legend
+ -	Fig. 1d	two-tailed t-test	Figure legend	n=5 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO FC p <0.0001 HC p=.0118 STR p=0.0059 CBL p=0.2536	Figure legend	FC t(8) = 23.06 HC t(8) = 3.247 STR t(8) = 3.715 CBL t(8) = 0.8062	Figure legend
+ -	Fig. 2a	two-tailed t-test	Figure legend	n=6 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO 3 weeks p=.9121 4 weeks p=.8579 5 weeks p=.8566 6 weeks p=.8901 7 weeks p=0.0460 8 weeks p=0.0008 9 weeks p<0.0001	Figure legend	3 weeks t(10) = 0.1132 4 weeks t(10) = 0.1838 5 weeks t(10) = 0.1854 6 weeks t(10) = 0.1417 7 weeks t(10) = 2.278 8 weeks t(10) = 4.72 9 weeks t(10) = 7.922	Figure legend
+ -	Fig. 3b	two-tailed t-test	Figure legend	CTL n=7 cDKO n=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO for all groups 0-10 min p=0.0267 0-20 min p=0.0003 0-30 min p=0.0001	Figure legend	0-10 min t(11) = 2.556 0-20 min t(11) = 5.129 0-30 min t(11) = 5.787	Figure legend
+ -	Fig. 3c	two-way Anova; Tukey post hoc analysis	Figure legend	CTL Saline n=5; CTL Flx n=6; cDKO Saline n=4; cDKO Flx n=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	p=0.0039 for interaction CTL Saline versus cDKO Saline p = 0.0024, cDKO Saline versus cDKO Flx p = 0.0119	Figure legend	F(1,17) = 11.1	Figure legend
+ -	Fig. 3d	two-tailed t-test	Figure legend	FC CTL n=7, cDKO n=6; STR CTL n=6, cDKO=7; HC CTL n=8, cDKO n=7; CBL CTL n=7, cDKO=4	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO for all groups FC p=0.0183 STR p=0.0437 HC p=.3640 CBL p=.2677	Figure legend	FC t(11) = 2.769 STR t(11) = 2.278 HC t(13) = 0.9407 CBL t(9)=1.181	Figure legend

+ -	Fig. 4c	two-tailed t-test	Figure legend	HDAC1 AAV-GFP n=7; AAV-GFP-Cre n=6; HDAC2 AAV-GFP n=7; AAV-GFP-Cre n=8	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	HDAC1 GFP vs Cre p=0.0491 HDAC2 GFP vs Cre p= 0.0013	Figure legend	HDAC1 GFP vs Cre t(11)=2.211 HDAC2 GFP vs Cre t(13)= 4.084	Figure legend
+ -	Fig. 4d	two-tailed t-test	Figure legend	AAV-GFP n=9; AAV-GFP-Cre n=8	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	GFP vs Cre for all groups 0-10 min p=0.0497 0-20 min p=0.0119 0-30 min p=0.0021	Figure legend	0-10 min t(15)=2.134 0-20 min t(15)=2.863 0-30 min t(15)=3.709	Figure legend
+ -	Fig. 4e	two-tailed t-test	Figure legend	AAV-GFP n=6; AAV-GFP-Cre n=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	GFP vs Cre p=0.0065	Figure legend	t(10)=3.425	Figure legend
+ -	Fig. 5b	two-tailed t-test	Figure legend	n=5 for all groups	replicates	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO p=.0429	Figure legend	t(8)=2.404	Figure legend
+ -	Fig. 5c	two-tailed t-test	Figure legend	CTL n=15; cKO n=12	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO for all groups 0-10 min p=0.0044 0-20 min p=0.0013 0-30 min p=0.0055	Figure legend	0-10 min t(25)=3.133 0-20 min t(25)=3.62 0-30 min t(25)=3.036	Figure legend
+ -	Fig. 5d	two-tailed t-test	Figure legend	n=4 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	p=0.0474	Figure legend	t(6)=2.487	Figure legend
+ -	Fig. 6c	two-way Anova; Holm-Sidak post hoc analysis	Figure legend	AAV-GFP CTL n=9; AAV-GFP MeCP2 cKO n=6; AAV-SAPAP3 CTL n=8; AAV-SAPAP3 MeCP2 cKO n=5	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	p=0.0103 for interaction CTL GFP vs cKO GFP p=0.0162; cKO GFP vs cKO SAPAP3 p=0.0027	Figure legend	F(1,24) = 7.752	Figure legend
+ -	Fig. 6d	two-way Anova; Tukey post hoc analysis	Figure legend	AAV-GFP CTL n=10; AAV-GFP Mecp2 cKO n=8; AAV-SAPAP3 CTL n=10; AAV-SAPAP3 Mecp2 cKO n=7	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	p=0.0190 for interaction CTL GFP vs cKO GFP p=0.0017; cKO GFP vs cKO SAPAP3 p=0.0158	Figure legend	F(1,31) = 6.13	Figure legend

+ -	Supp Fig. 1a	two-tailed t-test	Figure legend	CTL n=5; cKO n=7	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO 3 weeks p=.0642 4 weeks p=.9780 5 weeks p=.1483 6 weeks p=.4761 7 weeks p=0.3281 8 weeks p=0.3343 9 weeks p=.9017	Figure legend	3 weeks t(10) = 2.08 4 weeks t(10) = 0.0283 5 weeks t(10) = 1.566 6 weeks t(10) = 0.7404 7 weeks t(10) = 1.028 8 weeks t(10) = 1.015 9 weeks t(10) = 0.1267	Figure legend
+ -	Supp Fig. 1b	two-tailed t-test	Figure legend	CTL n=5; cKO n=7	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO 3 weeks p=.2707 4 weeks p=.2869 5 weeks p=.0720 6 weeks p=.6322 7 weeks p=0.1553 8 weeks p=0.1642 9 weeks p=.1222	Figure legend	3 weeks t(10) = 1.166 4 weeks t(10) = 1.125 5 weeks t(10) = 2.011 6 weeks t(10) = 0.4936 7 weeks t(10) = 1.537 8 weeks t(10) = 1.501 9 weeks t(10) = 1.680	Figure legend
+ -	Supp Fig. 1c	two-tailed t-test	Figure legend	CTL n=6; cKO n=5	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO p=.9301	Figure legend	t(9) = 0.0902	Figure legend
+ -	Supp Fig. 1d	two-tailed t-test	Figure legend	n=5 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO p=.1059	Figure legend	t(8) = 1.822	Figure legend
+ -	Supp Fig. 1e	two-tailed t-test	Figure legend	n=5 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO p<0.0001	Figure legend	t(8) = 13.04	Figure legend
+ -	Supp Fig. 3a	two-tailed t-test	Figure legend	n=5 for all groups	mice per group	Figure legend	mean value ± s.e.m (main); median, 25th and 75th percentile, and min and max value (inset)	Figure legend	CTL vs cDKO p=0.0187	Figure legend	t(8) = 2.939	Figure legend
+ -	Supp Fig. 3b	two-tailed t-test	Figure legend	CTL n=11; cDKO n=9	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO Complete center p=0.0002 Periphery p=0.0002	Figure legend	Complete center t(18) = 4.775 Periphery t(18) = 4.775	Figure legend
+ -	Supp Fig. 3c	two-tailed t-test	Figure legend	CTL n=7; cDKO n=5	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO for all groups 0-10 min p=0.0453 0-20 min p=0.0608 0-30 min p=0.0419	Figure legend	0-10 min t(10)=2.286 0-20 min t(10)=2.112 0-30 min t(10)=2.333	Figure legend
+ -	Supp Fig. 3d	two-tailed t-test	Figure legend	n=6 for all groups	mice per group	Figure legend	mean value ± s.e.m (main); median, 25th and 75th percentile, and min and max value (inset)	Figure legend	CTL vs cDKO p=0.0010	Figure legend	t(10)=4.571	Figure legend

+ -	Supp Fig. 3e	two-tailed t-test	Figure legend	CTL n=7; cDKO n=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO Complete center p=0.0258 Periphery p=0.0258	Figure legend	Complete center t(11) = 2.575 Periphery t(11) = 2.575	Figure legend
+ -	Supp Fig. 4a	two-tailed t-test	Figure legend	n=6 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO for all groups 0-10 min p=.3137 0-20 min p=.7916 0-30 min p=.6483	Figure legend	0-10 min t(10)=1.061 0-20 min t(10)=0.2714 0-30 min t(10)=0.4703	Figure legend
+ -	Supp Fig. 4b	two-tailed t-test	Figure legend	n=6 for all groups	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO for all groups 0-10 min p=.0675 0-20 min p=.5303 0-30 min p=.1773	Figure legend	0-10 min t(10)=2.05 0-20 min t(10)=0.6498 0-30 min t(10)=1.452	Figure legend
+ -	Supp Fig. 4c	two-way Anova; Tukey post hoc analysis	Figure legend	CTL Saline n=5; CTL Flx n=6; cDKO Saline n=4; cDKO Flx n=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	p=0.0004 for genotype CTL Saline vs cDKO Saline p = 0.0495 CTL Flx vs cDKO Flx p = 0.0119	Figure legend	F(1,17) = 18.97	Figure legend
+ -	Supp Fig. 4d	two-tailed t-test	Figure legend	FC CTL n=6, cKO n=6; HC CTL n=5, cKO n=6; STR CTL n=6, cKO=6; CBL CTL n=5, cKO=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO for all groups FC p=.6472 STR p=.6609 HC p=.3802 CBL p=.3064	Figure legend	FC t(10) = 0.4718 HC t(9) = 0.4535 STR t(10) = 0.918 CBL t(9) = 1.084	Figure legend
+ -	Supp Fig. 4d	two-tailed t-test	Figure legend	FC CTL n=6, cKO n=6; HC CTL n=5, cKO n=6; STR CTL n=5, cKO=6; CBL CTL n=6, cKO=6	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cKO for all groups FC p=.2123 STR p=.1887 HC p=.1892 CBL p=.9784	Figure legend	FC t(10) = 1.332 HC t(9) = 1.422 STR t(9) = 1.42 CBL t(10) = 0.0277	Figure legend
+ -	Supp Fig. 4f	two-tailed t-test	Figure legend	FC CTL n=8, cDKO n=7; STR CTL n=7, cDKO=7; HC CTL n=6, cDKO n=7; CBL CTL n=7, cDKO=4	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	CTL vs cDKO for all groups FC p=0.2344 STR p=0.0990 HC p=.3889 CBL p=.5793	Figure legend	FC t(13) = 1.247 STR t(12) = 1.788 HC t(11) =0 .897 CBL t(9)=0.5751	Figure legend

+ -	Supp Fig. 5a	two-tailed t-test	Figure legend	AAV-GFP n=9; AAV-GFP-Cre n=8	mice per group	Figure legend	mean value ± s.e.m (main); median, 25th and 75th percentile, and min and max value (inset)	Figure legend	GFP vs Cre p=0.7634	Figure legend	t(15)=0.3065	Figure legend
+ -	Supp Fig. 5b	two-way Anova; Bonferroni post hoc analysis	Figure legend	AAV-GFP n=9; AAV-GFP-Cre n=8	mice per group	Figure legend	mean value ± s.e.m	Figure legend	p=0.6524 for genotype	Figure legend	F(1,15) = 0.2112	Figure legend
+ -	Supp Fig. 5c	two-tailed t-test	Figure legend	AAV-GFP n=9; AAV-GFP-Cre n=8	mice per group	Figure legend	median, 25th and 75th percentile, and min and max value	Figure legend	GFP vs Cre complete center p=0.6125; periphery p=.6122	Figure legend	Complete center t(15) = 0.5173 Periphery t(15) = 0.5173	Figure legend
+ -	Supp Fig. 7a	one-way Anova; Tukey post hoc analysis		AAV-GFP CTL n=10; AAV-GFP Mecp2 cKO n=8; AAV-SAPAP3 CTL n=10; AAV-SAPAP3 Mecp2 cKO n=7	mice per group	Figure legend	mean value ± s.e.m (main); median, 25th and 75th percentile, and min and max value (inset)	Figure legend	p=.2036 for treatment	Figure legend	F(3,31) = 1.625	Figure legend
+ -	Supp Fig. 7b	two-way Anova; Tukey post hoc analysis		AAV-GFP CTL n=10; AAV-GFP Mecp2 cKO n=8; AAV-SAPAP3 CTL n=10; AAV-SAPAP3 Mecp2 cKO n=7	mice per group	Figure legend	mean value ± s.e.m	Figure legend	p<0.0001 for genotype CTL GFP vs cKO GFP p<0.0001; CTL GFP vs cKO SAPAP3 p=0.0023	Figure legend	F(3,248) = 16.74	Figure legend

Representative figures

1. Are any representative images shown (including Western blots and immunohistochemistry/staining) in the paper?

   If so, what figure(s)?

Immunostaining Fig. 1a, b, Fig. 6b,c
Western blot: Fig. 1c, d, Supp Fig. 6
Whole Brains: Fig. 2b, c
H&E staining: Fig. 2d-k
Mice: Fig. 3a
GFP signal: Fig. 4b
TUNEL staining: Supp Fig. 2, Supp Fig. 5d

2. For each representative image, is there a clear statement of how many times this experiment was successfully repeated and a discussion of any limitations in repeatability?

   If so, where is this reported (section, paragraph #)?

The number of replicates per experiment is indicated in the corresponding figure legend.

Statistics and general methods

1. Is there a justification of the sample size? If so, how was it justified? Where (section, paragraph #)? Even if no sample size calculation was performed, authors should report why the sample size is adequate to measure their effect size.	Sample size justification is listed in the Statistics section of the Methods. "No statistical methods were used to pre-determine sample sizes, however sample sizes were estimated based on similar experiments reported in previous publications from our lab."
2. Are statistical tests justified as appropriate for every figure? Where (section, paragraph #)?	Yes. Statistics section in the Methods
a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?	Yes. Statistical tests for each experiment is described in the corresponding figure legend, and a summary of the statistics used for the manuscript is described in the Statistics section of the Methods.
b. Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)? Where is this described (section, paragraph #)?	Yes. "Data distribution was assumed to be normal with similar variance between groups, however this was not formally tested" Statistics section in the Methods.
c. Is there any estimate of variance within each group of data? Is the variance similar between groups that are being statistically compared? Where is this described (section, paragraph #)?	"Data distribution was assumed to be normal with similar variance between groups, however this was not formally tested" Statistics section in the Methods
d. Are tests specified as one- or two-sided?	Yes, each corresponding figure legend states that tests are two-tailed.
e. Are there adjustments for multiple comparisons?	Yes, Tukey, Bonferonni, or Holm-Sidak post hoc analysis was used as appropriate.
3. To promote transparency, *Nature Neuroscience* has stopped allowing bar graphs to report statistics in the papers it publishes. If you have bar graphs in your paper, please make sure to switch them to dot-plots (with central and dispersion statistics displayed) or to box-and-whisker plots to show data distributions.	All graphs with multiple data points are represented as whisker-and-box plots or dot plots.
4. Are criteria for excluding data points reported? Was this criterion established prior to data collection? Where is this described (section, paragraph #)?	Yes. The Grubbs test was used when appropriate to identify and remove significant outliers. Statistics section in the methods.

5. Define the method of randomization used to assign subjects (or samples) to the experimental groups and to collect and process data. If no randomization was used, state so. Where does this appear (section, paragraph #)?	"Testing groups for behavioral cohorts were balanced by age and genotype, and randomization of experimental groups was not performed." Behavioral overview section in the Methods.
6. Is a statement of the extent to which investigator knew the group allocation during the experiment and in assessing outcome included? If no blinding was done, state so. Where (section, paragraph #)?	All behavioral experiments were performed and analyzed by an observer blind to genotypes and group assignments. Behavioral overview section in the Methods.
7. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included? Where (section, paragraph #)?	"All animal protocols were approved by the Institutional Animal Care and Use Committee at The University of Texas Southwestern Medical Center." Mice section in the Methods
8. Is the species of the animals used reported? Where (section, paragraph #)?	Mice. Behavioral overview section in the Methods.
9. Is the strain of the animals (including background strains of KO/ transgenic animals used) reported? Where (section, paragraph #)?	Yes, details of all mice used is reported. Mice section in the Methods.
10. Is the sex of the animals/subjects used reported? Where (section, paragraph #)?	Yes. "For all behavioral testing, experimental animals were male mice, and age matched littermates were used as CTLs." Behavioral overview section in the Methods.
11. Is the age of the animals/subjects reported? Where (section, paragraph #)?	The age of mice is reported in the corresponding figure legend, and/ or in the Methods. Figure legends and "Adeno-associated virus injection" section in the methods.
12. For animals housed in a vivarium, is the light/dark cycle reported? Where (section, paragraph #)?	"Mice were maintained on a 12 hour (hr) light/dark cycle with ad libitum access to food and water." Mice section in the Methods.
13. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported? Where (section, paragraph #)?	"Mice were housed 3-5 mice per cage, with the exception of when mice were singly housed for analyzing the lesion in cDKO mice." Mice section in the Methods.
14. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)? Where (section, paragraph #)?	"All experiments were conducted during the light cycle and scored by an observer blind to genotypes and group assignments." Behavioral overview section in the Methods.
15. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported? Where (section, paragraph #)?	"All injections were delivered intraperitoneally on naïve male mice." "Mice were naïve prior to the start of the initial behavioral test within each series of paradigms." Drug injections section in the Methods. Behavioral overview section in the Methods.

a. If multiple behavioral tests were conducted in the same group of animals, is this reported?

Where (section, paragraph #)?

"Mice were tested in cohorts for various behavioral tasks. Distinct cohorts of HDAC1 cKO, HDAC2 cKO, cDKO, and respective CTL mice were used to assess body weight and brain weight. Distinct cohorts of cDKO mice and CTLs were used to test locomotor activity and open field, and separate cohorts were used to test 6 week and 3 week old mice in each task. A distinct cohort of cDKO and CTL mice was used to score grooming behavior at 6 weeks old, and a separate cohort of cDKO and CTL mice was used to score grooming at 3 weeks old. Separate cohorts of HDAC1 cKO, HDAC2 cKO, and respective CTL mice were used to test grooming behavior. A distinct cohort of cDKOs and CTLs was used to test grooming behavior following one week of fluoxetine treatment, and the same cohort was scored for grooming behavior following 3 weeks of fluoxetine treatment. A distinct cohort of HDAC1loxP/loxP/HDAC2loxP/loxP mice was used for stereotaxic injections with AAV-GFP and AAV-GFP-Cre and after recovery this same cohort of mice was tested in multiple behavioral tasks in the following order; locomotor activity, open field, grooming, and rotarod. A distinct cohort of mice was used to assess grooming in MeCP2 cKO and CTL mice. For rescue experiments using AAV-GFP and AAV-SAPAP3, a distinct cohort of MeCP2 cKO and CTL mice was used for stereotaxic injections, and following recovery this same cohort of mice was tested in multiple behavioral tasks in the following order; locomotor activity, grooming, and rotarod."
Behavioral overview section in the Methods.

16. If any animals/subjects were excluded from analysis, is this reported?

Where (section, paragraph #)?

Yes.
Statistics section in the Methods. For surgeries this point is discussed in the Results section, page 8, paragraph 1.

a. How were the criteria for exclusion defined?

Where is this described (section, paragraph #)?

Following stereotaxic surgery, mice with off-target injected animals eliminated from further analysis.
Results section, page 8, paragraph 1.

b. Specify reasons for any discrepancy between the number of animals at the beginning and end of the study.

Where is this described (section, paragraph #)?

Following stereotaxic surgery, mice with off-target injected animals eliminated from further analysis.
Results section, page 8, paragraph 1.

Reagents

1. Have antibodies been validated for use in the system under study (assay and species)?

Yes.

a. Is antibody catalog number given?

Where does this appear (section, paragraph #)?

Yes.
Immunohistochemistry, Protein Quantification, and Chromatin Immunoprecipitation sections of the Methods.

b. Where were the validation data reported (citation, supplementary information, Antibodypedia)?

Where does this appear (section, paragraph #)?

Yes, citations.
Yes.
Immunohistochemistry, Protein Quantification, and Chromatin Immunoprecipitation sections of the Methods.

2. Cell line identity

a. Are any cell lines used in this paper listed in the database of commonly misidentified cell lines maintained by ICLAC and NCBI Biosample?

Where (section, paragraph #)?

N/A - no cell lines were used.

b. If yes, include in the Methods section a scientific justification of their use--indicate here in which section and paragraph the justification can be found.

N/A

c. For each cell line, include in the Methods section a statement that specifies:

- the source of the cell lines
- have the cell lines been authenticated? If so, by which method?
- have the cell lines been tested for mycoplasma contamination?

Where (section, paragraph #)?

N/A

Data availability

Provide a Data availability statement in the Methods section under "Data availability", which should include, where applicable:

- Accession codes for deposited data
- Other unique identifiers (such as DOIs and hyperlinks for any other datasets)
- At a minimum, a statement confirming that all relevant data are available from the authors
- Formal citations of datasets that are assigned DOIs
- A statement regarding data available in the manuscript as source data
- A statement regarding data available with restrictions

"The data that support the findings of this study are available from the corresponding author upon request."

Data availability section following the Methods section.

See our data availability and data citations policy page for more information.

Data deposition in a public repository is mandatory for:

a. Protein, DNA and RNA sequences
b. Macromolecular structures
c. Crystallographic data for small molecules
d. Microarray data

Deposition is strongly recommended for many other datasets for which structured public repositories exist; more details on our data policy are available here. We encourage the provision of other source data in supplementary information or in unstructured repositories such as Figshare and Dryad.

We encourage publication of Data Descriptors (see Scientific Data) to maximize data reuse.

Where is the Data Availability statement provided (section, paragraph #)?

Computer code/software

Any custom algorithm/software that is central to the methods must be supplied by the authors in a usable and readable form for readers at the time of publication. However, referees may ask for this information at any time during the review process.

1. Identify all custom software or scripts that were required to conduct the study and where in the procedures each was used.

N/A - No custom software was used.

2. If computer code was used to generate results that are central to the paper's conclusions, include a statement in the Methods section under "**Code availability**" to indicate whether and how the code can be accessed. Include version information as necessary and any restrictions on availability.

N/A

Human subjects

1. Which IRB approved the protocol?

   Where is this stated (section, paragraph #)?

N/A

2. Is demographic information on all subjects provided?

   Where (section, paragraph #)?

N/A

3. Is the number of human subjects, their age and sex clearly defined?

   Where (section, paragraph #)?

N/A

4. Are the inclusion and exclusion criteria (if any) clearly specified?

   Where (section, paragraph #)?

N/A

5. How well were the groups matched?

   Where is this information described (section, paragraph #)?

N/A

6. Is a statement included confirming that informed consent was obtained from all subjects?

   Where (section, paragraph #)?

N/A

7. For publication of patient photos, is a statement included confirming that consent to publish was obtained?

   Where (section, paragraph #)?

N/A

fMRI studies

For papers reporting functional imaging (fMRI) results please ensure that these minimal reporting guidelines are met and that all this information is clearly provided in the methods:

1. Were any subjects scanned but then rejected for the analysis after the data was collected?	No. N/A
a. If yes, is the number rejected and reasons for rejection described? Where (section, paragraph #)?	N/A
2. Is the number of blocks, trials or experimental units per session and/or subjects specified? Where (section, paragraph #)?	N/A
3. Is the length of each trial and interval between trials specified?	N/A
4. Is a blocked, event-related, or mixed design being used? If applicable, please specify the block length or how the event-related or mixed design was optimized.	N/A
5. Is the task design clearly described? Where (section, paragraph #)?	N/A
6. How was behavioral performance measured?	N/A
7. Is an ANOVA or factorial design being used?	N/A
8. For data acquisition, is a whole brain scan used? If not, state area of acquisition.	N/A
a. How was this region determined?	N/A
9. Is the field strength (in Tesla) of the MRI system stated?	N/A
a. Is the pulse sequence type (gradient/spin echo, EPI/spiral) stated?	N/A
b. Are the field-of-view, matrix size, slice thickness, and TE/TR/flip angle clearly stated?	N/A
10. Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and pre-processing clearly stated?	N/A

11. Is the coordinate space for the anatomical/functional imaging data clearly defined as subject/native space or standardized stereotaxic space, e.g., original Talairach, MNI305, ICBM152, etc? Where (section, paragraph #)?	N/A
12. If there was data normalization/standardization to a specific space template, are the type of transformation (linear vs. nonlinear) used and image types being transformed clearly described? Where (section, paragraph #)?	N/A
13. How were anatomical locations determined, e.g., via an automated labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?	N/A
14. Were any additional regressors (behavioral covariates, motion etc) used?	N/A
15. Is the contrast construction clearly defined?	N/A
16. Is a mixed/random effects or fixed inference used?	N/A
a. If fixed effects inference used, is this justified?	N/A
17. Were repeated measures used (multiple measurements per subject)?	N/A
a. If so, are the method to account for within subject correlation and the assumptions made about variance clearly stated?	N/A
18. If the threshold used for inference and visualization in figures varies, is this clearly stated?	N/A
19. Are statistical inferences corrected for multiple comparisons?	N/A
a. If not, is this labeled as uncorrected?	N/A
20. Are the results based on an ROI (region of interest) analysis?	N/A
a. If so, is the rationale clearly described?	N/A
b. How were the ROI's defined (functional vs anatomical localization)?	N/A
21. Is there correction for multiple comparisons within each voxel?	N/A
22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined?	N/A

Additional comments

Additional Comments