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\# Main Figures: 7

\# Supplementary Figures: 9

\# Supplementary Tables: 1

\# 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

FIGURE NUMBER	TEST USED		n			DESCRIPTIVE STATS (AVERAGE, VARIANCE)		P VALUE		DEGREES OF FREEDOM & F/t/z/R/ETC VALUE	
	WHICH TEST?	SECTION & PARAGRAPH #	EXACT VALUE	DEFINED?	SECTION & PARAGRAPH #	REPORTED?	SECTION & PARAGRAPH #	EXACT VALUE	SECTION & PARAGRAPH #	VALUE	SECTION & PARAGRAPH #
+/-	ALL STATISTICAL INFO IS PROVIDED IN SUPP. TABLE 1										

▶ Representative figures

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

   If so, what figure(s)?

   > Yes, representative sections exposed to I-125 MPPI of dentate gyrus and raphe nucleus or CA1 are shown in Figures 1b, 2b, and 4b. In addition representative in situs are shown in Supplementary Figure 3 and representative sections of YPet immunostaining are shown in Supplementary Figure 5.

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 #)?

   > Yes, this info is provided in Supplementary Table 1 or the Figure Legends. The I-125 MPPI experiments are quantified for figures 1b and 2b.

▶ 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.

   > It is generally accepted in the field that behavioral groups require 15-25 per group to assess anxiety and depression-related tasks. Various published papers using these group sizes are referenced throughout the text and online methods sections. Our group sizes are mentioned throughout the figure legends and in detail in Supplementary Table 1.

2. Are statistical tests justified as appropriate for every figure?

   Where (section, paragraph #)?

   > Yes. ANOVA (with Tukey's posthoc tests where appropriate) was used throughout the manuscript except for assessment of Novelty Suppressed Feeding. NSF requires non-parametric stats as described in the online methods (Statistics).

   a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?

   > Yes, the Statistics section in the online methods describes the statistical test for each experiment.

   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 #)?

   > All data meet the assumption except for NSF (described in Statistics section of online 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 #)?

> Yes, the variance was similar between the groups.

d. Are tests specified as one- or two-sided?

> Yes

e. Are there adjustments for multiple comparisons?

> Yes, for one-way ANOVA posthoc tests were only performed if the ANOVA was significant. For two-way ANOVA, posthoc tests were only performed if there was a significant interaction. For Kaplan-Meier Survival Analysis, a Bonferroni correction was performed for multiple comparisons. This is all discussed in the online methods (Statistics).

3. Are criteria for excluding data points reported?

Was this criterion established prior to data collection?

Where is this described (section, paragraph #)?

> No data points were excluded.

4. 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 #)?

> Treatment and pre-treatment groups were randomly assigned within larger groups determined by genotype. The groups were assigned so that every homecage contained animals from multiple pretreatment and treatment groups (mentioned in Experimental Mice section in online methods).

5. 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 #)?

> For some tests (Elevated Plus Maze, Forced Swim Test, corticosterone measurements), the data was counted and analyzed with computer programs (described in online methods section for each test). For NSF, neurogenesis counting, and I-125 MPPI the experimenter performing the counting was blinded to the treatment and genotype of the mice.

6. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included?

Where (section, paragraph #)?

> Yes, this statement is included in the Husbandry section of the online methods.

7. Is the species of the animals used reported?

Where (section, paragraph #)?

> Yes, mice were used. This is mentioned throughout the results, figure legends, and online methods.

8. Is the strain of the animals (including background strains of KO/transgenic animals used) reported?

Where (section, paragraph #)?

> Mixed background strains (C57/129) were used for all experiments.

9. Is the sex of the animals/subjects used reported?

Where (section, paragraph #)?

> Yes, only male mice were used (experimental mice section in online methods).

10. Is the age of the animals/subjects reported?

Where (section, paragraph #)?

> Yes, timelines for the experiments (including age of mice) are presented in each figure and are described in the figure legends.

11. For animals housed in a vivarium, is the light/dark cycle reported?

Where (section, paragraph #)?

Yes, the mice were maintained on a 12:12 light/dark schedule (husbandry section of online methods).

12. 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 per cage (husbandry section of online methods).

13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)?

Where (section, paragraph #)?

Yes, all behavioral experiments were performed between 10am and 3pm (behavioral testing section of online methods).

14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported?

Where (section, paragraph #)?

Yes, timelines for the experiments (including history of exposure to behavioral tests and treatments) are presented in each figure and are described in the figure legends.

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

    Where (section, paragraph #)?

Yes, timelines for the experiments (including history of exposure to behavioral tests and treatments) are presented in each figure and are described in the figure legends. This is also mentioned throughout the results section.

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

Where (section, paragraph #)?

No animals were excluded

    a. How were the criteria for exclusion defined?

    Where is this described (section, paragraph #)?

N/A

    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 #)?

N/A

▶ Reagents

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

Yes, the antibodies used to assess neurogenesis are described in the relevant sections of the online methods

    a. Is antibody catalog number given?

    Where does this appear (section, paragraph #)?

Supplier, species, and dilutions are reported in the online methods

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

    Where does this appear (section, paragraph #)?

A citation is provided in the online methods.

2. If cell lines were used to reflect the properties of a particular tissue or disease state, is their source identified?

   Where (section, paragraph #)?

   N/A

   a. Were they recently authenticated?

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

      N/A

▶ Data deposition

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.

1. Are accession codes for deposit dates provided?

   Where (section, paragraph #)?

   N/A

▶ 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

2. Is computer source code/software provided with the paper or deposited in a public repository? Indicate in what form this is provided or how it can be obtained.

   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?

   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

All statistical information, including tests used, cohort sizes, full ANOVA tables and posthoc test results are provided in Supplementary Table 1.