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.

<table>
<thead>
<tr>
<th>TEST USED</th>
<th>n</th>
<th>DESCRIPTIVE STATS (AVERAGE, VARIANCE)</th>
<th>P VALUE</th>
<th>DEGREES OF FREEDOM &amp; F/T/Z/R/ETC VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHICH TEST?</td>
<td>SECTION &amp; PARAGRAPH #</td>
<td>EXACT VALUE</td>
<td>DEFINED?</td>
<td>REPORTED?</td>
</tr>
<tr>
<td>one-way ANOVA</td>
<td>Methods para 8</td>
<td>error bars are mean +/- SEM</td>
<td>Fig. legend</td>
<td>p = 0.044</td>
</tr>
<tr>
<td>unpaired t-test</td>
<td>Results para 6</td>
<td>error bars are mean +/- SEM</td>
<td>Results para 6</td>
<td>p = 0.0006</td>
</tr>
<tr>
<td>FIGURE</td>
<td>TEST USED</td>
<td>n</td>
<td>DESCRIPTIVE STATS (AVERAGE, VARIANCE)</td>
<td>P VALUE</td>
</tr>
<tr>
<td>--------</td>
<td>-----------</td>
<td>---</td>
<td>--------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>1d</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations</td>
<td>average + SD</td>
</tr>
<tr>
<td>1c</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations</td>
<td>fig. legend</td>
</tr>
<tr>
<td>2b</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations; 10 neurons/preparation analyzed</td>
<td>methods (image analysis)</td>
</tr>
<tr>
<td>2d</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations; 12 neurons/preparation analyzed</td>
<td>methods (image analysis)</td>
</tr>
<tr>
<td>2e</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations; 12 neurons/preparation analyzed</td>
<td>methods (image analysis)</td>
</tr>
<tr>
<td>2g</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations : control shRNA: n=15; Ube3a1 shRNA: n=12</td>
<td>fig. legend</td>
</tr>
<tr>
<td>2h</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 cells from 3 different preparations : control shRNA: n=15; Ube3a1 shRNA: n=12</td>
<td>fig. legend</td>
</tr>
<tr>
<td>3c</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations; 10 neurons/preparation analyzed</td>
<td>methods (image analysis)</td>
</tr>
<tr>
<td>3d</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
<td>3 neurons from 3 independent preparations; 10 neurons/preparation analyzed</td>
<td>methods (image analysis)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>3f</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>4c</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>4e</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>4f</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>5b</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>5c</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>5d</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>5e</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>5g</td>
<td>One sample Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>6a</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>6b</td>
<td>Student’s T-test (two-tailed, type 2)</td>
<td>methods (last paragraph)</td>
</tr>
</tbody>
</table>
### Representative figures

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

   If so, what figure(s)?

   - Fig. 1B, 1E, 2A, 2C, 2F, 3B, 3E, 4A, 4B, 5F, 6C

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 #)?

   - Fig. 1B: repeated three times (figure legend)
   - Fig. 1E: repeated three times (figure legend)
   - Fig. 2A: refers to quantifications in Fig. 2B
   - Fig. 2C: refers to quantifications in Fig. 2D, E
   - Fig. 2F: refers to quantifications in Fig. 2G, H
   - Fig. 3B: not explicitly stated, but repeated three times (once in HEK293 cells, twice in neurons)
   - Fig. 3E: refers to quantifications in Fig. 3F
   - Fig. 4A: not explicitly stated, but repeated three times
   - Fig. 4B: refers to quantifications in Fig. 4C
   - Fig. 5F: refers to quantifications in Fig. 5G
   - Fig. 6C: refers to quantifications in Fig. 6D

### 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.

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

   Where (section, paragraph #)?

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

   power analysis (G-power) was performed to calculate required sample size. For most experiments, effect size is sufficiently high to use n=3. Otherwise (Fig. 2G,H; 5G; 6A,B,D,F,G), larger sample sizes were used. Result of power analysis is reported for Fig. 6D, G (cf. figure legend).

   As outlined in the methods section, paragraph "Statistics", One-way ANOVA followed by post-hoc T-test was used for multiway comparisons, two-sided Student’s T-Test for single comparisons.

   yes (online methods, “Statistics”)

Nature Neuroscience: doi:10.1038/nn.3996
b. Do the data meet the assumptions of the specific statistical test you chose (e.g. normality for a parametric test)?
   Data distribution was assumed to be normal, but this was not formally tested unless otherwise stated (Online methods, "Statistics").

   Where is this described (section, paragraph #)?

   c. Is there any estimate of variance within each group of data?

   Is the variance similar between groups that are being statistically compared?

   For most statistical analyses, ANOVA was used (described in figure legends). Otherwise, as illustrated by the error bars, variance was comparable between groups (not described).

   Where is this described (section, paragraph #)?

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

   two-sided (Online methods, "Statistics")

   e. Are there adjustments for multiple comparisons?

   no, but no more than 3 comparisons were performed in each data set

3. Are criteria for excluding data points reported?
   Was this criterion established prior to data collection?
   not applicable

   Where is this described (section, paragraph #)?

4. Define the method of randomization used to assign subjects (or samples) to the experimental groups and to collect and process data.

   In the animal studies, the animals were assigned to the various groups randomly. In imaging studies, cell selection was performed randomly, excluding unhealthy cells and cells not easily identified as pyramidal neurons. Data was collected and processed randomly. (online methods, "Statistics")

   If no randomization was used, state so.

   Where does this appear (section, paragraph #)?

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.

   for all microscopy and patch-clamp analysis, investigator was blinded to the experimental conditions (stated in online methods, "Statistics")

   Where (section, paragraph #)?

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

   statement of compliance is provided in the online methods ("Animal experiments")

   Where (section, paragraph #)?

7. Is the species of the animals used reported?

   species of animals (rats, mice) used reported in online methods section ("Animal experiments") and respective figure legends.

   Where (section, paragraph #)?

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

   rat (Wistar, Sprague Dawley, purchased from Harlan and Charles River, respectively) and mouse strains (C57BL/6, purchased from Charles River or Taconic Artemis) reported in the online methods section ("Animal experiments").

   Where (section, paragraph #)?

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

   for rat behaviour experiments, only male rats were used ("Animal experiments"). Otherwise, sex-matched groups of mice were compared.

   Where (section, paragraph #)?

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

    age of animals reported in online methods section ("animal experiments") and in respective figure legends.

    Where (section, paragraph #)?
11. For animals housed in a vivarium, is the light/dark cycle reported?
   Where (section, paragraph #)?
   yes (Online methods, "Animal experiments")

12. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported?
   Where (section, paragraph #)?
   for rats: 3-5 per cage (unless isolated) for mice: 4-6 per cage (Online methods, "Animal experiments")

13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)?
   Where (section, paragraph #)?
   rat behavioural testing was performed during the light cycle (Online methods, "Animal experiments")

14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported?
   Where (section, paragraph #)?
   not applicable

   a. If multiple behavioral tests were conducted in the same group of animals, is this reported?
      Where (section, paragraph #)?
      not applicable

15. If any animals/subjects were excluded from analysis, is this reported?
    Where (section, paragraph #)?
    In Fig. 6B, a random subset of animals analyzed for Fig. 6A was used (figure legends 6A and 6B)

    a. How were the criteria for exclusion defined?
       Where is this described (section, paragraph #)?
       not applicable

    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 #)?
       not applicable

### Reagents

1. Have antibodies been validated for use in the system under study (assay and species)?
   yes, only validated antibodies from commercial sources were used in this study.

   a. Is antibody catalog number given?
      Where does this appear (section, paragraph #)?
      yes (Online methods, "Antibodies")

   b. Where were the validation data reported (citation, supplementary information, Antibodypedia)?
      validation of antibodies is provided on the respective suppliers’ webpages (not reported in the manuscript)
2. If cell lines were used to reflect the properties of a particular tissue or disease state, is their source identified?

Where (section, paragraph #)?

   a. Were they recently authenticated?

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

   not applicable

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.

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

1. Are accession codes for deposit dates provided?

   Where (section, paragraph #)?

   Provisional Genbank accession number for the rat Ube3a1 3’UTR (KP742805) provided in the main text, results, section 5.

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.

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.

Human subjects

1. Which IRB approved the protocol?

   Where is this stated (section, paragraph #)?

2. Is demographic information on all subjects provided?

   Where (section, paragraph #)?
3. Is the number of human subjects, their age and sex clearly defined?  
   Where (section, paragraph #)?

4. Are the inclusion and exclusion criteria (if any) clearly specified?  
   Where (section, paragraph #)?

5. How well were the groups matched?  
   Where is this information described (section, paragraph #)?

6. Is a statement included confirming that informed consent was obtained from all subjects?  
   Where (section, paragraph #)?

7. For publication of patient photos, is a statement included confirming that consent to publish was obtained?  
   Where (section, paragraph #)?

**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?  
   a. If yes, is the number rejected and reasons for rejection described?  
      Where (section, paragraph #)?

2. Is the number of blocks, trials or experimental units per session and/or subjects specified?  
   Where (section, paragraph #)?

3. Is the length of each trial and interval between trials specified?  

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.

5. Is the task design clearly described?  
   Where (section, paragraph #)?

6. How was behavioral performance measured?  

7. Is an ANOVA or factorial design being used?
8. For data acquisition, is a whole brain scan used? If not, state area of acquisition.

   a. How was this region determined?

9. Is the field strength (in Tesla) of the MRI system stated?

   a. Is the pulse sequence type (gradient/spin echo, EPI/spiral) stated?

   b. Are the field-of-view, matrix size, slice thickness, and TE/TR/flip angle clearly stated?

10. Are the software and specific parameters (model/functions, smoothing kernel size if applicable, etc.) used for data processing and pre-processing clearly stated?

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 #)?

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 #)?

13. How were anatomical locations determined, e.g., via an automated labeling algorithm (AAL), standardized coordinate database (Talairach daemon), probabilistic atlases, etc.?

14. Were any additional regressors (behavioral covariates, motion etc) used?

15. Is the contrast construction clearly defined?

16. Is a mixed/random effects or fixed inference used?

   a. If fixed effects inference used, is this justified?

17. Were repeated measures used (multiple measurements per subject)?

   a. If so, are the method to account for within subject correlation and the assumptions made about variance clearly stated?

18. If the threshold used for inference and visualization in figures varies, is this clearly stated?

19. Are statistical inferences corrected for multiple comparisons?
a. If not, is this labeled as uncorrected?

20. Are the results based on an ROI (region of interest) analysis?
   a. If so, is the rationale clearly described?
   b. How were the ROI’s defined (functional vs anatomical localization)?

21. Is there correction for multiple comparisons within each voxel?

22. For cluster-wise significance, is the cluster-defining threshold and the corrected significance level defined?

› Additional comments

Additional Comments