nature neuroscience

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Main Figures: 4

Supplementary Figures: 10

Supplementary Tables: 7

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
+ -	1	permutation	Methods - sec 4	36	human brains	methods - sec 1	coverage	methods - sec 4	FWER < 1e-4	supp table 2	empirical	methods - sec 4

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		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 #
+ -	2	PCA	results -sec 3	487	human brains	results - sec 3	Principal components (PCs)	fig leg.	n/a	n/a	n/a	n/a
+ -	3	spearman correlation	results - sec 4	7	mouse brains	results - sec 4	mean fold change	fig leg.	p < 1e-100	results - sec 4	0.805, 0.342, 0.460	fig legend
+ -	4	PCA	results - sec 5	121	tissues and cell lines	results - sec 5	PCs	fig leg.	n/a	n/a	n/a	n/a
+ -	Res sec 1	F-test	Res para 1	36	independent replication cohort	methods - sec 4	F-test	methods - sec 4	p < 0.05	Res para 1	F(6,29)	methods - sec 4
+ -	Res sec 1	hypergeometric test	Table S3 leg	Varies, between 9-13k	Gene Ontology gene sets	Res sec 1 para 1	Proportion	Res sec 1 para 1,2	Given in text	Table S3	1	Table S3
+ -	Res sec 2	Proportion test	Res sec 2, para 2	16615	Number of intronic DERs, overlap of lncRNAs	Figure S4	Odds	Res sec 2, para 2	p = 1.58e-3, p= 8.61e-5, p < 1e-100	Res sec 2, para 2	1	Res sec 2, para 2
+ -	Res sec 2	Spearman correlation	Res sec 2, para 3	6	cytosolic fractions of 6 brains	Res sec 2, para 3	mean fold change	Figure S4	p < 1e-100	Figure S4	ρ=0.914, 0.927, 0.664, 0.820	Figure S4
+ -	Res sec 3	Spearman correlation	Res sec 3	487	human brains	Res sec 3	Fold changes	table 1 leg	All are listed in Table 1	Table 1	see Table 1	Table 1
+ -	Res sec 5	Spearman correlation	Res sec 5, para 3	121	tissues and cell lines	results - sec 5	mean fold change	results sec 5	Figures S8, S9	Figures S8, S9	Figures S8, S9	Figures S8, S9
+ -	Res sec 7	Linear regression	Res sec 7, para 1	36	human brains	Res sec 7, para 1	p-values for regression slope	Res sec 7, para 1	p=9.59e-8, p=2.40e-11, p=4.41e-23; p < 9.89e-7	Res sec 7, para 1	t(34)	Res sec 7, para 1

Representative figures

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

   If so, what figure(s)?

   no

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 #)?

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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.	The sample size was selected based on available tissue that would allow strong effect sizes given our experiences with microarray data on the majority of these subjects.
2. Are statistical tests justified as appropriate for every figure? Where (section, paragraph #)?	Yes, in the main text of each section and figure legends
a. If there is a section summarizing the statistical methods in the methods, is the statistical test for each experiment clearly defined?	Yes, several subsections in the Methods section describe the statistical tests
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 #)?	We mostly used statistics that were more robust to assumptions (e.g. spearman correlation, empirical p-values). These are described in the Methods section
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 - we show the variability within and between groups in Figure 1 and Figure 4
d. Are tests specified as one- or two-sided?	Two-sided
e. Are there adjustments for multiple comparisons?	Yes, we used genome-wide permutations
3. Are criteria for excluding data points reported? Was this criterion established prior to data collection? Where is this described (section, paragraph #)?	We did not remove data points.
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 #)?	Details of tissue acquisition, handling, processing, dissection, clinical characterization, diagnoses, neuropathological examinations, RNA extraction and quality control measures were performed uniformly, as described in the Methods Section #1
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 #)?	We allocated samples to flow cells, but the generation of the RNAseq data is unbiased.

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6. For experiments in live vertebrates, is a statement of compliance with ethical guidelines/regulations included? Where (section, paragraph #)?	N/A
7. Is the species of the animals used reported? Where (section, paragraph #)?	N/A
8. Is the strain of the animals (including background strains of KO/ transgenic animals used) reported? Where (section, paragraph #)?	N/A
9. Is the sex of the animals/subjects used reported? Where (section, paragraph #)?	N/A
10. Is the age of the animals/subjects reported? Where (section, paragraph #)?	N/A
11. For animals housed in a vivarium, is the light/dark cycle reported? Where (section, paragraph #)?	N/A
12. For animals housed in a vivarium, is the housing group (i.e. number of animals per cage) reported? Where (section, paragraph #)?	N/A
13. For behavioral experiments, is the time of day reported (e.g. light or dark cycle)? Where (section, paragraph #)?	N/A
14. Is the previous history of the animals/subjects (e.g. prior drug administration, surgery, behavioral testing) reported? Where (section, paragraph #)?	N/A
a. If multiple behavioral tests were conducted in the same group of animals, is this reported? Where (section, paragraph #)?	N/A
15. If any animals/subjects were excluded from analysis, is this reported? Where (section, paragraph #)?	N/A
a. How were the criteria for exclusion defined? Where is this described (section, paragraph #)?	N/A

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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)?

N/A

a. Is antibody catalog number given?

Where does this appear (section, paragraph #)?

N/A

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

Where does this appear (section, paragraph #)?

N/A

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

Where (section, paragraph #)?

Only publicly available data generated from cell lines, which we cite in the Methods section 9

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 #)?

We have set up a BioProject (PRJNA245228) and are depositing the alignment data in the next two weeks. We have created summary-level data available as a UCSC Track Hub in Results Section 6

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.

A collection of R code was provided with the submission

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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.	Yes, on GitHub: https://github.com/lcolladotor/derfinder

Human subjects

1. Which IRB approved the protocol? Where is this stated (section, paragraph #)?	The Institutional Review Board of the University of Maryland at Baltimore and the State of Maryland approved the protocol, and the tissue was donated to the Lieber Institute for Brain Development under the terms of a Material Transfer Agreement - Methods section 1
2. Is demographic information on all subjects provided? Where (section, paragraph #)?	Yes, Supp Table 1
3. Is the number of human subjects, their age and sex clearly defined? Where (section, paragraph #)?	Yes, Supp Table 1
4. Are the inclusion and exclusion criteria (if any) clearly specified? Where (section, paragraph #)?	Yes, Methods Section 1
5. How well were the groups matched? Where is this information described (section, paragraph #)?	Loosely matched on sex, Supp Table 1
6. Is a statement included confirming that informed consent was obtained from all subjects? Where (section, paragraph #)?	Yes, Methods Section 1
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?	
a. If yes, is the number rejected and reasons for rejection described? Where (section, paragraph #)?	

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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.?

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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

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