nature portfolio

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Last updated by author(s): Nov 11, 2021

Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on 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.*
☐	☒ 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 statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☐	☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data used for this analysis comes from the AD Knowledge Portal (adknowledgeportal.synapse.org) and the PsychENCODE Knowledge Portal (synapse.org/pec) and is hosted on the Sage Bionetworks' Synapse platform for access by qualified investigators. Data was generated from post-mortem tissue and has be de-identified according to the Synapse terms of use, and is available through the submission of an AD Knowledge Portal Data Use Certificate (https://adknowledgeportal.synapse.org/DataAccess/DataUseCertificates) or by application to the NIMH Repository and Genomics Resources (http://nimhgenetics.org), respectively. We also used publicly available data from GTEX (gtexportal.org).
Data analysis	eQTL discovery was performed with a linear mixed model using the mmQTL software developed in this work (https://github.com/jxzb1988/mmQTL and https://doi.org/10.5281/zenodo.5560014). All downstream analysis was performed with R v4.0.3.

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Analysis results are available at http://icahn.mssm.edu/brema

Field-specific reporting

Please select the one below that is the best 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/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We included samples with genotype and brain gene expression data from GTEx, PsychENCODE, and ROSMAP datasets. The sample size was based on the availability of the existing data. No statistical method was used to determine what sample size to use
Data exclusions	Samples with < 8 million well imputed SNPs (info < 0.3) were excluded from PsychENCODE. All other samples with both genotype and brain gene expression were retained.
Replication	We evaluated the replication of our eQTL analyses in independent datasets of 1) bulk brain tissue (Wang, et al), 2) granule cell layer of the dentate gyrus enriched for excitatory neurons (Jaffe, et al, 2020) and 3) purified microglia (Kosoy, et al. in prep). The genome-wide replication rate is consistent with the rest of the field.
Randomization	We performed analysis on existing data, so randomization of the experimental design does not apply
Blinding	We performed analysis on existing data, so blinding of the experimental design does not apply

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Data generated by Bendl, et al (in revision, https://doi.org/10.1101/2021.01.11.426303) was show in Figure 7 involves use of NeuN antibody. However no data was generated as part of the current study. We refer the reader to that work for experimental details.
Validation	*Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.*