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Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study. For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

Experimental design

1.	Sample size	
	Describe how sample size was determined.	N=495 (Discovery) - This was established based on the brain tissue on hand and the money available for sequencing. However, we have previously shown that developmental changes in brain expression require much smaller sample sizes; previous eQTL analyses and power calculation by GTEx suggested that this sample size was well-powered for eQTLs; previous analyses and power calculations suggested this sample size was well-powered for case-control expression differences.
2.	Data exclusions	
	Describe any data exclusions.	We only included samples from the two main ethnicities in our brain collection - Caucasian and African American.
3.	Replication	
	Describe the measures taken to verify the reproducibility of the experimental findings.	We have downloaded and uniformly processed and quantified data from the CommonMind Consortium and the GTEx project. We also report replication p-values and statistics for expression features differentially expressed in schizophrenia and also for eQTLs identified in the DLPFC
4.	Randomization	
	Describe how samples/organisms/participants were allocated into experimental groups.	This was an observational study from postmortem human brain tissue and thus subjects were not randomized into outcome groups. Subjects were diagnosed using medical records and next-of-kin interviews as described in the paper.
5.	Blinding	
	Describe whether the investigators were blinded to group allocation during data collection and/or analysis.	Investigators were not blinded to group allocation since the study was observational

Note: all in vivo studies must report how sample size was determined and whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a Confirmed

The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)

A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly

A statement indicating how many times each experiment was replicated

 \square The statistical test(s) used and whether they are one- or two-sided

A description of any assumptions or corrections, such as an adjustment for multiple comparisons

- Test values indicating whether an effect is present

A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)

|| Clearly defined error bars in <u>all</u> relevant figure captions (with explicit mention of central tendency and variation)

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this	
study.	

TopHat2 (v2.0.4 and v2.0.9), R/Bioconductor (limma, GenomicRanges, MatrixEQTL, sva, clusterProfiler, derfinder, derfinderPlot, minfi, crlmm), featureCounts (v1.4.3-p1), StringTie (v 1.1.2), regtools (v0.1.0), CuffMerge (v 2.2.1), plink (v1.9), bwtool. More information is availabe at our GitHub repository: https://github.com/LieberInstitute/brainseq_phase1

No unique materials were used - sequencing data will be made available as described below

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a third party.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

10. Eukaryotic cell lines

- a. State the source of each eukaryotic cell line used.
- b. Describe the method of cell line authentication used.
- c. Report whether the cell lines were tested for mycoplasma contamination.
- d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

No antibodies were used

No eukaryotic cell lines were used

No eukaryotic cell lines were used No eukaryotic cell lines were used

No eukarvotic cell lines were used

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide all relevant details on animals and/or animal-derived materials used in the study.

No animals were used

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

These 495 samples were from postmortem donors which are not considered human subjects - however, demographic data on these donors is available in Table S1. Briefly, this overall cohort was 65.9% Male and 48.7% Caucasian with an average age of 37.0 (including 50 prenatal samples). 175/495 subjects were patients diagnosed with schizophrenia.