BrainSeq Phase II: schizophrenia-associated expression differences between
the hippocampus and the dorsolateral prefrontal cortex

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INTRODUCTION

We previously identified widespread genetic, developmental, and schizophrenia-associated changes in polyadenylated RNAs in the dorsolateral prefrontal cortex (DLPFC), but the landscape of hippocampal (HIPPO) expression using RNA sequencing is less well-explored. We performed Brain-seq using tissue samples across 511 individuals (148 with schizophrenia) in a discovery cohort, and applied the GenotypeTissueExpression (GTEX) network of the Genecode v25 reference transcriptomes, including genes, exons and splice junctions. Within and across brain regions, we modeled age-related changes in controls using linear splines, integrated genetic data to perform expression-quantitative trait loci (eQTL) analysis, and performed differential expression analyses controlling for observed and latent confounders.

METHODS

Focus on being conservative: established processing methods, strict cutoffs, using replication when possible, adjust for RNA quality degradation confounding, avoid potential batch effects and take into account correlation at the individual level.

- Region-specific for adult or prenatal
  - Smaller expression changes in regions with a higher number of eQTLs
  - Smaller expression changes in regions with a higher number of eQTLs

- Development
  - Region-specific for adult or prenatal
  - Smaller expression changes in regions with a higher number of eQTLs
  - Smaller expression changes in regions with a higher number of eQTLs

- Case-control
  - Region-specific for adult or prenatal
  - Smaller expression changes in regions with a higher number of eQTLs
  - Smaller expression changes in regions with a higher number of eQTLs

RNA DEGREGATION ADJUSTMENT: qSVA

- 48 DE genes at FDR <5% in hippocampus, 24 in DLPFC (FDR <5%) suggesting regional homogeneity of the molecular correlates of schizophrenia diagnosis
- DLPFC results agree with BrainSeq Phase I

SCZD vs NON-PSYCHIATRIC CONTROLS

- 48 DE genes at FDR <5% in hippocampus, 24 in DLPFC (FDR <5%) suggesting regional homogeneity of the molecular correlates of schizophrenia diagnosis
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- We are hiring! Multiple positions open

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