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Mapping genotype-expression associations in Heterogeneous Stock rat brains to advance behavioral genetics research

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Research into the genetic influences of impulsivity and reward motivated behavior relies heavily on outbred animal populations, including Heterogeneous Stock (HS) rats, for the genetic diversity necessary to identify genotype-trait associations. Many such associations have been detected, but it is not always clear which gene or other feature near the identified genomic location is functionally responsible for the association. Since these traits are in part mediated by gene expression, mapping the associations between genotype and gene expression in these animals will enable the discovery and deeper understanding of these trait associations. We therefore obtained genotypes and RNA-Seq gene expression for five brain regions from 88 HS rats and mapped expression quantitative trait loci (eQTLs) for each region. We identified cis-eQTLs in over 3,000 genes per brain region and validated their effect sizes using allele specific expression. Surprisingly, use of a linear mixed model had little impact on the eQTLs identified compared to a fixed effects model. We also used the genotype-expression associations found in this cohort to train an expression prediction model, enabling transcriptome-wide association studies on larger rat cohorts that lack expression data. This resource will enable new discoveries of the genetic influences of complex behavioral traits.