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Does the liver or the brain control voluntary alcohol consumption: using the HRDP

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We have collected whole transcriptome data for several organs of a subset (30) of the Hybrid Rat Diversity Panel (HRDP) and have used quantitative genetics and Weighted Gene Co-expression Analysis (WGCNA) of brain and liver transcriptomes to investigate the predisposing factors for the variation in voluntary alcohol consumption. We found two QTLs for the trait of alcohol consumption and our criteria for linking the transcriptome data to the behavioral data was based on the correlation of the eigengene values for the co-expression modules with the behavior and the overlap of the genomic location of the behavioral QTL with the QTL for the co-expression module eigengene. When examining the brain data, we found a module that satisfied all criteria and the eigengene QTL overlapped the behavioral QTL on Ch. 12. The hub gene for this module was an lncRNA and we demonstrated a functional relationship of this lncRNA and alcohol consumption. However, we did not find any brain co-expression modules related to the behavioral QTL on Ch. 1. When we examined the co-expression modules derived from the liver transcriptome we identified a module which met all criteria and overlapped the alcohol consumption QTL on Ch. 1. This module explained 24% of the genetic variance in alcohol consumption. The transcripts included in the liver module brought attention to liver products influencing immune and inflammatory pathways and give credence to the hypothesis relating inflammatory systems in brain and periphery to voluntary alcohol consumption.

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