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Conserved Co-expression Signatures of Chronic Alcohol Consumption across Species

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Transcriptomic, epigenetic, and chromatic interaction studies of brain structures implicated in alcohol behaviors have shed some light on the underlying biology, but additional information is needed to overcome the lack of tissue specific data. Consilience of alcohol biology across experimental systems may help to prioritize genes and biological processes, in so much as response to ethanol is mediated by perturbations in conserved pathways. We utilized postmortem brain samples from humans (n=50 [30 AUD cases]; pre-frontal cortex (PFC), nucleus accumbens (NAc), and central nucleus of the amygdala (CEA)), primates (PFC [n=30], CEA and [n=30], NAc core [n=23]), and mice (NAc from 68 mice bred for high drinking in the dark; PFC, NAc, CeA, and bed nucleus of striatum from 103 mice assigned to different groups to study chronic intermittent alcohol) via publicly available RNA-sequencing data. Differential and Whole Genome Co-expression analyses of human, monkey, and mouse RNA-seq samples vary across model systems and differ by tissues and behavior outcome. We identified 30 highly conserved co-expression networks across species and 57 unique hub genes, several of which are involved in substance use and related traits, such as impulsivity, stress, and motivation.
Gene networks were enriched for certain brain cell types (e.g., Myelinating Oligodendrocytes, adjusted $p=3.72E^{-108)}$. The top 2.5% of these gene networks revealed 57 unique hub genes, several of which are involved in substance use and related traits. Molecular signature overlap between the brains of individuals with AUD and models of alcohol use depend on species, brain region, animal trait and method.