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Comparative Neuro-Transcriptomics of Alcohol Use and Dependence

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For over 100 years the scientific community has investigated the neurobiological basis for drug use. Yet, how results generalize to the human addiction is sparsely explored. The current study investigates one question through the lens of neurobiology: what animal organisms and/or specific alcohol behavioral models best recapitulate findings from human alcoholics? To address this question, we integrated gene expression findings (microarray, RNA-seq, CHIP-seq) of post-mortem brain tissues for 23 bioinformatic studies transcending five species: *homo sapiens*, *mus musculus*, *rattus norvegicus*, *drosophila melanogaster* and *danio rerio*. This study quantifies the degree to which species and specific behavioral mechanisms of alcohol use correspond to human alcoholics. After meta-analyzing results across species and gene expression studies, we identified substantial neuro-transcriptomic overlap with human alcoholics among mice (OR=1.99, 95% CI [1.81,2.20], Jaccard similarity (*J*): $M=0.0115$, $s.e=0.0010$, range: 0.0-0.0818) and rats (OR=1.47 [1.33, 1.63], $M=0.0099$, $s.e=0.0010$, range: 0.0-0.0631), but not fish (OR= 0.33 [0.23, 0.44], *J*: $M=0.0056$, $s.e=0.0011$, range: 0.0-0.0108, $s.e.=0.006$) nor fly models of alcohol use (OR=0.33, CI [0.20,0.54], *J*: $M=0.0082$, $s.e = 0.0011$, range: 0.0-0.0183). We discuss our results in the context of what behavioral models best intersect with findings from human alcoholics. Our study plans to incorporate these results within a genome-wide framework in humans to help decipher the genetic code underlying alcohol use and dependence. Ultimately, these analyses hope to bridge the translational space between human and animal genetics and assess the degree of overlap between humans and model organisms.