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TITLE: Differential shared genetic influences of anxiety with problematic alcohol use compared to alcohol consumption.

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ABSTRACT:
Anxiety disorders and alcohol use disorders are common psychiatric disorders. Comorbidity of the two disorders can have tremendous effects on treatment on one or both of the disorders, as well as an individual's social, economic and physical well-being. We estimated genome-wide genetic correlations of anxiety and alcohol use with linkage disequilibrium score regression (LDSC), and found strong and positive correlations with problem use, but not with most consumption measures. Sex-stratified genome-wide genetic correlation analysis found strong positive correlations between males and females for all traits but suggested genetic correlation between alcohol use and anxiety might differ for males and females. Analyses of partitioned heritability using cell type and brain

region-specific expression annotations revealed distinct patterns between problematic alcohol use (PAU) and consumption, with consumption traits demonstrating more significant, positive enrichment correlations with anxiety disorders than PAU traits. Partitioning the genetic covariance between traits also identified the amygdala, caudate basal ganglia and frontal cortex as contributing significantly to positive genetic covariance between anxiety and PAU phenotypes. Finally, estimates of local genetic covariance demonstrated divergent genetic covariance profiles of PAU and consumption with anxiety phenotypes, and localized 12 specific regions that likely contribute to both anxiety and alcohol use. This study also serves as a framework for an approach to be used in future analyses of the genetics of comorbid disorders.

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