Multivariate Genetics Architecture of DSM-5 Alcohol Use Disorder

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Aims: Alcoholism is a multifactorial disorder influenced by multiple gene loci, each with small effect. Recent studies (Kendler et al., 2012, Palmer et al., 2015b) suggest shared genetic influences across symptoms of the Diagnostic and Statistical Manual of Mental Disorder's alcohol dependence (AD) symptoms, but these have been limited to DSM-IV symptoms. We aimed to test the assumption of genetic homogeneity across the 11 symptoms of DSM-5 alcohol use disorder (AUD).

Methods: Data from 2596 alcohol using individuals of European ancestry from the Study of Addiction: Genetics and Environment were used to examine the genomewide SNP-heritability (h^2_{SNP}) and SNP-covariance ($r_{G\text{-}SNP}$) between 11 DSM-5 AUD symptoms. Phenotypic relationships between symptoms were examined to confirm an underlying liability of AUD and the SNP-heritability of the observed latent trait and the co-heritability among AUD symptoms was assessed using Genomic-Relatedness-Matrix-Restricted-Maximum-Likelihood. Genetic covariance among symptoms was examined using factor analysis.

Results: Phenotypic relationships confirmed a unidimensional underlying liability to AUD. Factor and parallel analyses of the observed genetic variance/covariance provided evidence of genetic homogeneity (i.e., a single genetic factor was supported). Additive genetic effects on DSM-5 AUD symptoms varied from 0.10 to 0.37 and largely overlapped ($r_{G\text{-}SNP}$ across symptoms ranged from 0.49 – 0.92). The additive genetic effect on DSM-5 AUD as a latent trait, severity score, or problem use measure were 0.36 (SE=0.13), 0.22 (SE=0.13), and 0.14 (SE=0.21), respectively.

Conclusions: Common genetic variants influence DSM-5 AUD symptoms. Despite evidence for a common AUD factor, the evidence of only partially overlapping genetic effects across AUD symptoms further substantiates the need to simultaneously model common and symptom-specific genetic effects in molecular genetic studies in order to best characterize the genetic liability.