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Update from the Psychiatric Genomics Consortium: Alcohol

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Alcohol dependence is a leading contributor to the global burden of disease. The risk for alcohol dependence is about 50% heritable, but it is a complex genetic disorder to which many loci contribute. It is a heterogeneous disorder, which contributes to the challenge of identifying genetic variants that affect risk.

The Substance Use Disorder working group of the Psychiatric Genomics Consortium (PGC-SUD) has carried out the largest GWAS to date on alcohol dependence (defined by DSM-IV). This involved collaboration among many groups worldwide: 14 case-control studies, 9 family-based studies, and summary statistics from 5 others, for a total of 14,904 cases and 37,944 controls. We carried out meta-analyses separately by ancestry (46,568 European; 6,280 African), and then combined the results.

We identified two genome-wide significant variants within the same gene, rs1229984 in those of European descent ($p = 9.8 \times 10^{-13}$) and rs2066702 in those of African descent ($p = 2.2 \times 10^{-9}$). Both are coding variants that affect the rate at which alcohol dehydrogenase 1B oxidizes ethanol to acetaldehyde. Another variant reached significance in the African-American sample, but was not replicated. There are significant genetic correlations with 17 phenotypes, notably other substance use and psychiatric disorders, such as schizophrenia and depression. The genetics of alcohol dependence only partially overlap with those of alcohol consumption.

Much larger samples will be required to identify additional loci, and we are exploring ways to greatly enlarge our sample. We are also exploring related phenotypes, such as criterion count and maximum drinks, and comorbidity with other psychiatric traits.