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Multivariate genome-wide assocation meta-analysis of 1 million subjects identifies loci underlying multiple substance use disorders

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Genetic liability to substance use disorders can be parsed into loci that confer general or substance-specific addiction risk. This is reflected in the large and significant genetic correlations across substance use disorders.

We report a multivariate genome-wide association meta-analysis that disaggregates general and substance-specific loci for published summary statistics of problematic alcohol use, problematic tobacco use, cannabis use disorder, and opioid use disorder in a sample of 1,025,550 individuals of European descent and 92,630 individuals of African descent. Nineteen independent SNPs were genome-wide significant for the general addiction risk factor, which showed high polygenicity. Across ancestries, PDE4B was significant, suggesting dopaminergic regulation via toll-like receptor 4. We demonstrate that polygenic risk scores from this GWAS predict individual substance use disorders, are more accurate then previous PRS, and are most effective at predicting polysubstance use disorder and opioid use disorder. We also demonstrate that these data can be used to develop data-driven exploration of potential compounds for drug repurposing.

By leveraging the genetic correlations across psychiatric disorders, we gained predictive power in biological discovery, prediction, and intervention exploration. Ever larger and more diverse Genome-wide association studies are needed to continue our exploration.