The Psychiatric Genomics Consortium's Substance Use Disorders Group: Progress and Challenges

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The Substance Use Disorders Working Group of the Psychiatric Genomics Consortium (PGC-SUD) was established in 2014 with funding from the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The goal of the PGC-SUD, which includes > 80 researchers from 10 countries, is to conduct genomewide association studies of cannabis, opioids, cocaine, tobacco and alcohol-related phenotypes, including diagnostic indices, heavy use and novel measures (e.g. injection drug use). Additional goals include downstream analyses of GWAS findings using a variety of bioinformatics utilities and an examination of the extent to which loci identified for substance use and misuse correspond with discoveries for other psychiatric disorders and behavioral traits. Phenotypic expertise of PGC-SUD members is complemented by the modular ricopili pipeline developed by the PGC, which allows for harmonized processing and quality control of genomic data. The flagship analysis of the PGC-SUD group, comprised of 13,500 alcohol dependent cases and 32, 321 controls, identified rs1229984 in *ADH1B*. In a subset of the data that includes unrelated subjects, genomewide SNPs explained 11% of the variance in AUD. This heritable variation was correlated with the heritability of cigarette smoking, educational attainment and major depressive disorder. Further ongoing analyses will (a) aim to considerably expand the discovery sample size, (b) test whether polygenic risk scores derived from the discovery cohort predicts alcohol-related traits (AUDIT, CAGE scores) in independent samples as well as within a developmental context and (c) functionally annotate heritable variation and identify networks and pathways that may be enriched. A similar pipeline is also being applied to the immediate analysis of cannabis, nicotine, opioid and cocaine related data.