Measures of consumption versus disordered substance use: evidence of different genetic architectures

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Indices of lifetime use and substance consumption (e.g., cigarettes per day, lifetime cannabis use) have enabled the collection of very large (up to 1 million) samples and led to meaningful discoveries. Despite smaller sample sizes (current largest GWAS of alcohol use disorders (AUD): N_case = 45,995), findings from recent GWAS of substance use disorders indicate very different genetic architectures when compared with corresponding results for substance use/consumption. This symposium presentation will outline a series of findings from the Psychiatric Genomics Consortium’s Substance Use Disorders group and other large efforts. Three key take-home messages will be substantiated. First, findings from two large GWAS of substance use and use disorders will document that genetic correlations between substance use disorders and other major psychiatric illness are indicative of shared psychopathology. For instance, cannabis use disorder is genetically correlated with lower liability to educational attainment (r_g = -0.39) while cannabis use is related to a genetic predisposition to higher educational attainment (r_g = 0.34); results are similar for AUD vs. alcohol consumption. Second, using the example of alcohol and schizophrenia, we show that the genetic covariance between AUD and schizophrenia is enriched for biologically meaningful annotations while the covariance with alcohol consumption is less so. Finally, using opioids and nicotine, both highly addictive substances, as contrasts, our analyses will document the importance of considering the addictive potential of a substance and the resulting likelihood of transitioning to problematic use as important factors when comparing the genetic etiology of substance use and use disorder.