

Genome-wide polygenic scores for schizophrenia are associated with substance use during emerging adulthood

Travis T. Mallard, B.S.; K. Paige Harden, Ph.D.; & Kim Fromme, Ph.D

University of Texas at Austin

Background: Epidemiological research has demonstrated that comorbid substance use, although common in many psychiatric disorders, is particularly prevalent among individuals with schizophrenia (SCZ). Initially, this was hypothesized to represent self-medication efforts to alleviate distress engendered by the symptoms of SCZ. However, recent advances in neuroscience and genetics suggest that this comorbidity may, in part, reflect a shared genetic etiology.

Method: The present study employed genotyping and daily monitoring methods to assess the effect of genetic predisposition to SCZ on several substance use behaviors as they occur in daily life. We calculated a genome-wide polygenic score (GPS) for 318 unrelated non-Hispanic White participants using β -weights and p -values from summary statistics provided by the Psychiatric Genomics Consortium (PGC). Summary statistics were derived from the PGC's 2014 GWAS of SCZ with a sample size of 36,989 cases and 113,075 controls. We then examined the GPS for SCZ as a predictor of daily alcohol and drug use across 22,832 days of individual assessment.

Results: We did not observe any significant effect of GPS for SCZ on binge drinking ($\beta = 0.09$, OR = 1.10, $p > 0.05$). However, we did observe a significant association between GPS for SCZ and illicit drug use ($\beta = 0.35$, OR = 1.41, $p = 0.023$), as well as a significant association between GPS for SCZ and polysubstance use ($\beta = 0.46$, OR: 1.59, $p < 0.0005$). The association with polysubstance use is robust at several GPS p -value thresholds (e.g., using all SNPs, only using SNPs with a GWAS p -value $\leq .10$, etc.), and is similarly associated with a more conservative phenotype of polysubstance use (concurrent binge drinking and illicit drug use) at every level of analysis. Age, sex, and genomic principal components of ancestry were included as covariates in every model.

Conclusions: Genetic predisposition to SCZ was associated with illicit drug use and polysubstance use in a non-clinical sample of young adults. These results are the first, to our knowledge, to identify genome-wide factors that contribute to substance use at the event-level. In accordance with other behavioral and molecular genetic research, these results suggest that the high rates of comorbidity between SCZ and substance use may, in part, be due to a shared genetic architecture.

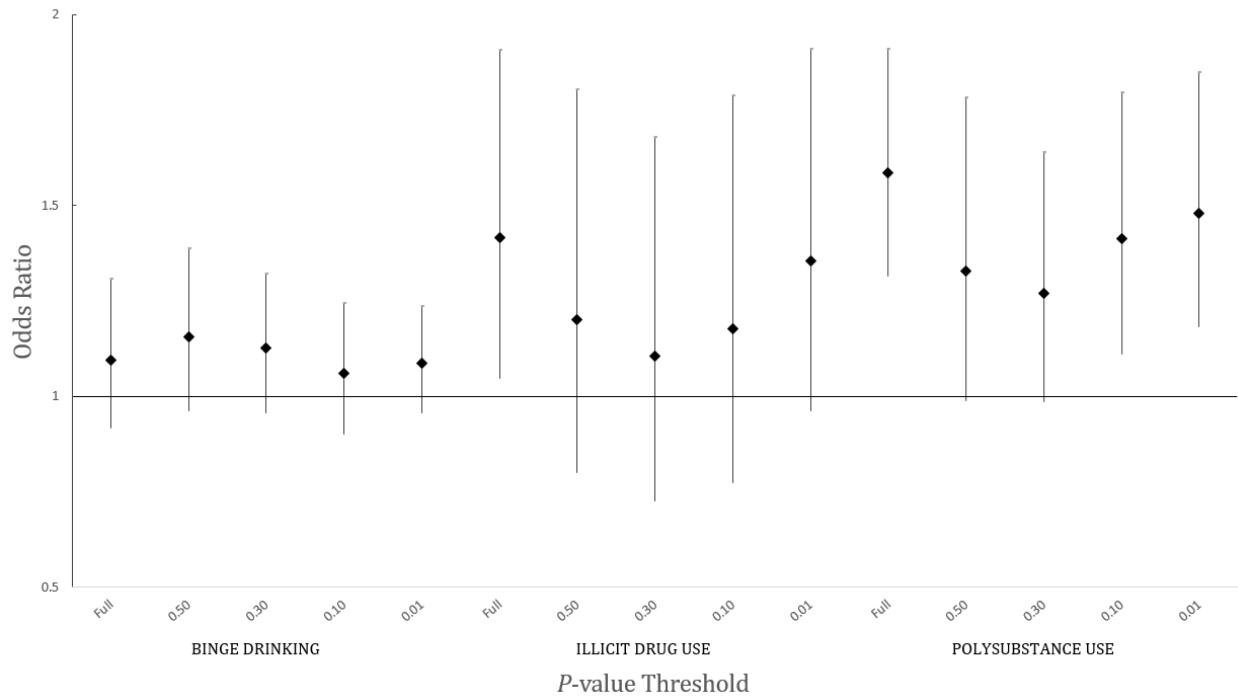


Figure 1. Odds ratios representing the effects of GPS for SCZ on binge drinking, illicit drug use, and polysubstance use. The GPS was tested at five thresholds (1.00, 0.50, 0.30, 0.10, and 0.01) for each phenotype.

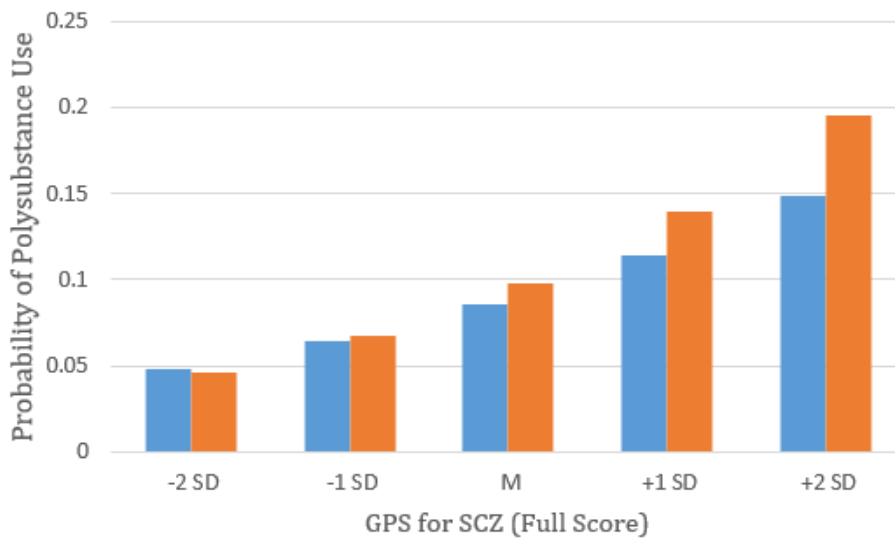


Figure 2. The effect of GPS for SCZ on the likelihood to engage in polysubstance use ($p < 0.0005$). The blue bars represent a liberal phenotype of polysubstance use (any concurrent drug and alcohol use) while the orange bars represent a more conservative phenotype of polysubstance use (concurrent drug use and binge drinking).