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## Genetic Identification of Sleep Vulnerabilities Inherited with Substance Use

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### ABSTRACT:

The overlap between substance use and sleep deficits is one of the most common clinical concerns in treatment. Substance use may affect sleep in general or manifest as specific sleep deficits. Here, we test the genetic overlap between substance use behaviors and sleep/activity measures, derive genetic clusters between these domains, and test processes of causality vs. pleiotropy, in the largest public samples of substance use behaviors and sleep/activity phenotypes/endophenotypes to date. We found 31 genetic correlations between substance use and sleep/activity measures that survived Bonferroni correction. Several of the discovered genetic correlations include novel relationships between substance use behaviors and objective measures of sleep/activity, while numerous of the genetic correlations confirm past work on substance use behaviors and subjective sleep measures. We found two broad genetic clusters that underly a pattern of coinheritance that characterizes the overlap of substance use and sleep. Genes associated with tobacco use severity shared overlap with elements of sleep health (sleep duration, sleep efficiency, and chronotype). Substance consumption and problematic substance use behaviors (use disorders and problematic use) clustered strongly with problematic measures of sleep as well as measures of activity. Latent causal variable analyses determined that pleiotropy likely underlies a majority of the associations between substance use and sleep/activity measures, with the caveat of one significant result which implied genetic causality for opiate use disorder on self-reported long sleep duration. Overall, these combined results imply a strong shared genetic relationship between the domains of substance use behaviors and sleep/activity measures.

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