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Exploring the genetic overlap of suicide-related behaviors and substance use disorders

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ABSTRACT:

Suicide-related behaviors are heterogeneous and transdiagnostic, and may demonstrate varying levels of genetic overlap with different substance use disorders (SUDs). We used linkage disequilibrium score regression and genomic structural equation models to examine the genetic relationships between several SUDs and suicide-related behaviors. Our analyses incorporated summary statistics from the largest genome-wide association studies (GWAS) of problematic alcohol use (PAU), the Fagerström Test for Nicotine Dependence (FTND), cannabis use disorder (CUD), and opioid use disorder (OUD; N s ranging from 46,213-435,563) and GWAS of ever self-harmed, suicide attempt, and suicide death (N s ranging from 18,223-117,733). We also accounted for genetic liability to depression ($N=500,199$) and risk tolerance ($N=315,894$). Ever self-harmed correlated most strongly with CUD ($r_g=0.60$) and suicide death correlated most strongly with OUD ($r_g=0.53$). Suicide attempt correlated similarly with all SUDs. Simultaneously correlating a common SUD factor with each specific suicide indicator while controlling for depression and risk tolerance revealed significant, positive genetic correlations between all SUDs and suicide-related behaviors ($r_g=0.26-0.46$). Our findings suggest that genetic and behavioral contributions to suicide death may somewhat differ from non-lethal suicide-related behaviors. Additionally, we identify a general level of genetic overlap between SUDs and suicide-related behaviors which is independent of depression and risk tolerance.

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