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TITLE: Genomic analysis of ~1.5 million people uncovers genes associated with externalizing

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ABSTRACT:

Externalizing refers to behaviors and disorders related to self-regulation, such as substance use disorders, childhood behavior problems, and risky sexual behavior, which have profound individual and societal costs. Previous twin-family studies have indicated that there is a strong heritable component shared across behaviors and disorders

characterized by behavioral undercontrol. In this project, we apply multivariate genomic structural equation modeling to study the underlying genetic liability that influences a spectrum of externalizing disorders and behaviors. Our results identify 579 independent loci associated with externalizing liability. The identified genes are largely expressed in the brain and involved in neurodevelopment. The polygenic risk score explained 10% of the variance in externalizing in independent samples and was also significantly associated with a wide range of behaviors and disorders on the externalizing spectrum, including multiple substance use and psychiatric disorders, childhood and adult antisocial behavior, risky sexual behaviors, and suicide attempts; economic and social correlates of externalizing, including criminal justice system involvement and employment history; and a wide range of biomedical outcomes related to behavioral undercontrol, including HIV infection, diabetes and obesity, cirrhosis of liver, and lung cancer. These analyses demonstrate the wide-reaching effects of a genetic liability for externalizing.

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