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SAFE Glen Cove Coalition: NIDA Research Findings Show Shared Genetic Markers Underlying Substance Use Disorders

A recent research study conducted by researchers at the Washington University in St. Louis, along with more than 150 coauthors from around the world have identified genes commonly inherited across addiction disorders, regardless of the substance being used. There has been limited knowledge of the molecular genetic underpinnings of addiction until now as most clinical trials and behavioral studies have focused on individual substances, rather than addiction more broadly. The study was supported by the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute of Mental Health (NIMH), the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Institute on Aging.

By combing through genomic data of over 1 million people, this research may help reveal new treatment targets across multiple substance use disorders, including for people diagnosed with more than one. The findings also reinforce the role of the dopamine system in addiction, by showing that the combination of genes underlying addiction disorders was also associated with regulation of dopamine signaling.

In 2021, more than 46 million people in the United States aged 12 or older had at least one substance use disorder, and only 6.3% had received treatment. Moreover, people who use drugs are facing an increasingly dangerous drug supply, now often tainted with fentanyl. Approximately 107,000 people died of drug overdoses in 2021, and 37% of these deaths involved simultaneous exposure to both opioids and stimulant drugs. Drug use and addiction represent a public health crisis, characterized by high social, emotional, and financial costs to families, communities, and society.

Substance use disorders are heritable and influenced by complex interactions among multiple genes and environmental factors. In recent decades, a method called genome-wide association, has emerged to try to identify specific genes involved in certain disorders. This method involves searching entire genomes for regions of genetic variation, called single-nucleotide polymorphisms (SNPs), that associate with the same disease, disorder, condition, or behavior among multiple people.

In this study, researchers used this method to pinpoint areas in the genome associated with general addiction risk, as well as the risk of specific substance use disorders – namely, alcohol, nicotine, cannabis, and opioid use disorders – in a sample of 1,025,550 individuals with genes indicating European ancestry and 92,630 individuals with genes indicating African ancestry.

Using genomics, researchers can create a data-driven foundation to prioritize existing medications for further study and improve chances of discovering new treatments. To do this accurately, it's critical that the genetic evidence we gather includes globally representative populations and that we have members of communities historically underrepresented in biomedical research leading and contributing to these kinds of studies. Researchers discovered various molecular patterns underlying addiction, including 19 independent SNPs significantly associated with general addiction risk and 47 SNPs for specific substance disorders among the European ancestry sample. The strongest gene signals consistent across the various disorders mapped to areas in the genome known to control regulation of dopamine signaling, suggesting that genetic variation in dopamine signaling regulation, rather than in dopamine signaling itself, is central to addiction risk.

Compared to other genetic predictors, the genomic pattern identified here was also a more sensitive predictor of having two or more substance use disorders at once. The genomic pattern linked to general addiction risk also predicted higher risk of mental and physical illness, including psychiatric disorders, suicidal behavior, respiratory disease, heart disease, and chronic pain conditions. In children aged 9 or 10 years without any experience of substance use, these genes correlated with parental substance use and externalizing behavior. Compared to other genetic predictors, the genomic pattern identified here was also a more sensitive predictor of having two or more substance use disorders at once. Genomic analysis in the African ancestry sample revealed one SNP associated with general addiction risk and one substance-specific SNP for risk of alcohol use disorder. The findings underscore ongoing disparities in data inclusion of globally representative populations that must be addressed in order to ensure data robustness and accuracy.

This study validates previous findings of alcohol-specific risk variants, and of shared genetic risk variants across different substance use disorders provides insight into some of the mechanisms that underlie these disorders and the relationships with other mental health conditions. Together the findings of alcohol-specific risk variants and common addiction-related variants provide support for individualized prevention and treatment. Continued genomic studies will further illuminate factors that may protect or predispose a person to substance use disorders – knowledge that can be used to expand preventative services and develop personalized interventions that are tailored to an individual's unique biology, environment, and lived experience to provide the most benefits.

The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world's research on the health aspects of drug use and addiction. The Institute carries out a large variety of programs to inform policy, improve practice, and advance addiction science. For more information about NIDA and its programs, visit <u>www.nida.nih.gov</u>.

The SAFE Glen Cove Coalition is conducting an opioid prevention awareness campaign entitled. "Keeping Glen Cove SAFE," to educate and update the community regarding opioid use and its consequences. To learn more about the SAFE Glen Cove Coalition please follow us on www.facebook.com/safeglencovecoalition or visit SAFE's website to learn more about the Opioid Epidemic at www.safeglencove.org.