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Polygenic Risk Scores and Their Predictive Power in Early-Onset Cannabis Use Disorders

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Introduction

As cannabis use becomes more socially accepted and legalized in many regions, concerns over early-onset cannabis use disorders (CUD) have intensified, particularly among adolescents and young adults. While environmental and social factors are undeniably influential, emerging evidence highlights the significant role of genetic predisposition in determining an individual's susceptibility to developing CUD. Polygenic Risk Scores (PRS), which aggregate the effects of numerous genetic variants associated with a disorder, are becoming powerful tools in predicting psychiatric and substance use disorders. This paper explores the predictive power of PRS in identifying early-onset cannabis use disorders and the implications for early intervention and prevention strategies [1-4].

Description

Polygenic Risk Scores are calculated by summing the effects of multiple single-nucleotide polymorphisms (SNPs) identified through genome-wide association studies (GWAS). These scores estimate an individual's genetic liability to certain traits or disorders. In the context of psychiatric conditions and substance use, PRS have shown promise in predicting disorders such as schizophrenia, depression, and now, cannabis use disorder [5,6].

Cannabis use disorder is characterized by the continued use of cannabis despite significant psychological, physical, or social impairments. Early-onset CUD, typically developing during adolescence or early adulthood, is associated with more severe clinical outcomes, including increased risk for cognitive impairment, mental health disorders, and long-term substance dependence. Identifying individuals at high genetic risk before the onset of symptoms could open the door to preventative strategies tailored to genetic susceptibility [7,8].

Recent GWAS have identified multiple genetic loci associated with cannabis use, including variants near genes involved in neurotransmitter signaling, reward processing, and neurodevelopment. These findings provide the foundation for developing PRS specific to cannabis use and addiction risk [9,10].

Discussion

The application of PRS in predicting early-onset CUD is gaining momentum in psychiatric genetics. Studies have shown that individuals with higher PRS for cannabis use are significantly more likely to engage in early and frequent cannabis consumption. Moreover, these individuals are also more vulnerable to developing dependency symptoms and comorbid psychiatric conditions, such as anxiety, depression, or psychosis.

One key advantage of PRS is their potential to identify at-risk individuals even before cannabis use begins. For example, adolescents with high genetic risk scores may benefit from targeted interventions that include education, behavioral therapy, and family support. This preemptive approach aligns with the growing emphasis on precision medicine and personalized mental health care.

However, the predictive power of PRS is not absolute. While a high PRS may indicate elevated risk, it does not guarantee the development of a disorder. The expression of genetic risk is moderated by environmental influences, such as peer pressure, parental supervision, trauma, and socioeconomic status. Thus, PRS must be interpreted within the broader context of gene-environment interactions.

Another limitation is the current underrepresentation of diverse populations in GWAS data. Most PRS models are derived from European-ancestry cohorts, which can limit their applicability and predictive accuracy in other ethnic groups. Expanding research to include more genetically diverse populations is critical for the equitable application of PRS in global health contexts.

Despite these challenges, the integration of PRS into clinical and public health settings holds promise. By combining genetic data with behavioral and environmental assessments, clinicians can create nuanced risk profiles to guide early intervention efforts. Additionally, schools, youth health programs, and community mental health services could benefit from incorporating genetic insights into their prevention models.

Conclusion

Polygenic Risk Scores offer a valuable lens through which to view early-onset cannabis use disorders, providing insight into the genetic architecture that contributes to addiction vulnerability. While PRS alone cannot determine outcomes, they serve as an important component in a multi-factorial risk framework. Their predictive power, when coupled with environmental data, allows for more targeted and proactive approaches to prevention, especially in adolescents. As research advances, and as PRS models become more refined and inclusive, these tools could revolutionize early addiction screening and personalized care strategies. Ultimately, harnessing genetic data responsibly and

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ethically will be essential in addressing the rising challenge of cannabis use disorders in a changing sociocultural landscape.

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Page 2 of 2