Name: Alex Miller Email: alexmill@iu.edu

Genome-Wide Association Meta-Analysis of Early Onset Cannabis Use

Alex P. Miller[1], Jared V. Balbona[2], Emma C. Johnson[2], and Arpana Agrawal[2]

[1]Department of Psychiatry, Indiana University School of Medicine;
[2]Department of Psychiatry, Washington University School of Medicine

Early onset cannabis use is associated with increased risk for developing cannabis use disorder (CUD) as well as other psychiatric disorders and problems (e.g., early school dropout) during both childhood and adulthood and recent estimates suggest that more than 13% of adolescents report lifetime use of cannabis prior to age 16. Genetic influences may play a considerable role in early onset cannabis use. Twin research has demonstrated that age at first cannabis use is significantly heritable (h2 = 0.38) and genetically correlated with but separable from liability conferring risk for lifetime cannabis use and CUD. While recent large-scale genome-wide association studies (GWAS) have further highlighted shared, but distinct, genetic architectures between lifetime cannabis use and CUD (rg = 0.50), including differential genetic relations with other traits (e.g., educational attainment, psychiatric disorders and symptoms), similar efforts leveraging advances in large-scale genomic approaches to better understand the genetic architecture of early onset cannabis use have fallen behind (max N = 24,953). We proposed to conduct multi-ancestral GWAS meta-analyses of early onset cannabis use employing multiple analytic frameworks, including linear and time-to-event mixed models, and using data from over 200,000 individuals including 169,681 UK Biobank participants (median age of first cannabis use = 20). Forthcoming analyses, including functional enrichment, gene-based, and polygenic score models will explore shared and divergent genetic risk factors underlying early onset cannabis use, lifetime cannabis use, and CUD as well as other substance use and psychiatric disorders and traits.