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M81. GENETIC LIABILITY TO EXTERNALIZING PREDICTS ADOLESCENT NICOTINE AND CANNABIS USE AND AGE OF ONSET IN THE ADOLESCENT BRAIN COGNITIVE DEVELOPMENT (ABCD) STUDY

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tribute to susceptibility. However, pinpointing specific variants remains challenging. This study aimed to identify genetic association with this phenotype using a family-based approach.

Methods: Genetic and phenotypic data were collected from 392 individuals belonging to 135 Costa Rican nuclear families, each with at least one clinically diagnosed subject and at least one unaffected relative; family sizes ranged from 2 to 8 members, with 1 to 6 affected individuals per family. Genotypes were obtained using microarray containing approximately 56000 SNPs. Analyses were performed using the Family-Based Association Test (FBAT), which accounts for family structure and potential population stratification. Affected/unaffected status was used as a binary phenotype.

Results: This family-based analysis identified a significant association with a SNP on chromosome 1, as well as a marker on the X chromosome. Additional suggestive signals were observed on chromosome 20 and 10.

Discussion: This constitutes the first genome-wide association analysis for alcohol use disorder conducted in Costa Rica. Further functional studies and independent replications are needed to validate these findings and elucidate the underlying molecular mechanisms.

Disclosure: Nothing to disclose.

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M81. GENETIC LIABILITY TO EXTERNALIZING PREDICTS ADOLESCENT NICOTINE AND CANNABIS USE AND AGE OF ONSET IN THE ADOLESCENT BRAIN COGNITIVE DEVELOPMENT (ABCD) STUDY

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Background: Adolescent nicotine and cannabis use pose major public health risks, increasing vulnerability to long-term mental and physical health issues, including substance use disorders (SUD). Externalizing (EXT) refers to heritable traits and disorders characterized by impulsivity and behavioral disinhibition, including SUD. This study tests whether polygenic scores (PGS) for EXT predict early onset and increased likelihood of smoking behaviors during adolescence across diverse ancestry groups.

Methods: We analyzed youth- and parent-reported data from the Adolescent Brain Cognitive Development (ABCD) Study (Release 5.1; N=10,977). Multivariate logistic regres-

sion and Cox proportional hazards models assessed associations between EXT PGS and the onset of nicotine and cannabis use from ages 9-10 (baseline) through 14-15 years (year 3 follow-up; N=9,574). Models adjusted for key sociodemographic and prenatal confounders. Analyses were stratified by genetic ancestry: European (EUR; N=5,688), Admixed (ADM; N=2,901), and African (AFR; N=1,923). EXT PGS were computed via PRS-CSx. Ancestry-matched GWAS summary statistics were used for EUR (N=3.18M) and AFR (N=246K), while a meta-analytic combination of EUR and AFR summary statistics was used for ADM. We hypothesized that greater genetic liability for EXT would be associated with both increased use and earlier onset.

Results: In EUR, higher EXT PGS was associated with both increased odds and earlier onset of nicotine (OR=1.82, 95% CI: 1.60-2.07; HR=1.67, 95% CI: 1.46-1.90; both $p < .0001$) and cannabis use (OR=1.94, 95% CI: 1.63-2.30; HR=1.76, 95% CI: 1.50-2.08; both $p < .0001$). In ADM, EXT PGS was similarly associated with increased odds and earlier onset of nicotine (OR=1.29, 95% CI: 1.08-1.54; HR=1.29, 95% CI: 1.08-1.54; both $p=.004$) and cannabis use (OR=1.33, 95% CI: 1.05-1.70; $p=.02$), though the timing effect for cannabis onset was only marginal (HR=1.24, 95% CI: 0.99-1.54; $p=.06$). In AFR, EXT PGS was not significantly associated with either the odds or onset of nicotine (OR=1.04, $p=.76$; HR=1.18, $p=.17$) or cannabis (OR=1.23, $p=.45$; HR=1.15, $p=.30$) use.

Discussion: Findings suggest that genetic liability for EXT behaviors contributes to early smoking risk. The lack of significant associations in AFR ancestry groups may reflect reduced predictive power due to smaller sample sizes, underscoring the need to expand genetic research in underrepresented populations. These results support the utility of EXT PGS in identifying youth at elevated risk for early smoking behaviors, with implications for tailored prevention strategies.

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M82. SUBJECTIVE RESPONSE TO OPIOIDS PREDICTS RISK FOR OPIOID USE DISORDER

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Background: Opioids are commonly first encountered in medical settings; 59% of individuals with opioid use disorder (OUD) report initial exposure via prescription. While not all individuals prescribed opioids develop OUD, we lack scalable tools to predict who is at risk. The initial subjective