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Association of Polygenic Liability for Cannabis Initiation and EEG Connectivity in Adolescence and Young Adulthood

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Differences in the connectivity of functional brain networks among individuals who use and abuse cannabis, point to dysfunctional neural communication and related cognitive impairments. We examined how polygenic risk scores (PRS), derived from a recent GWAS of cannabis initiation conducted by Paskan et al. (meta-analysis of the International Cannabis Consortium + UK Biobank), relate to longitudinal measures of interhemispheric and intrahemispheric EEG connectivity (theta, alpha, and beta frequencies) in adolescent and young adult offspring from the Collaborative Study on the Genetics of Alcoholism (COGA) between ages 12 and 31. Findings indicate that cannabis initiation PRS (p -threshold < 0.001) was associated with increased tempo-parietal and centro-parietal interhemispheric alpha connectivity and fronto-parietal intrahemispheric alpha connectivity in males from ages 20–31, and with increased fronto-central, tempo-parietal, centro-parietal interhemispheric alpha connectivity in females. All *betas* ranged from 0.02–0.06, p -values ranged from 10^{-6} – 10^{-12} . Individuals with higher cannabis initiation PRS also demonstrated performance deficits on neuropsychological tasks, were more likely to have used cannabis, and were at higher risk for DSM-5 cannabis use disorder. We conclude that measures of neural connectivity, together with neurocognitive performance and substance use behavior, can be used to further understanding of how genetic risk variants from large GWAS may influence brain function. In addition, these data indicate the importance of examining sex and developmental effects. Understanding of neural mechanisms linking genetic variants emerging from GWAS to risk for substance abuse may help to identify specific points in development when neurocognitive prevention/intervention efforts may be most effective.