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Large genome-wide association study of cannabis abuse and dependence: an update from the PGC Substance Use Disorders working group

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While previous genome-wide association studies (GWAS) have had some success identifying genome-wide significant loci for CUD, the goal of the current study is to drastically increase CUD sample size and thus improve power to replicate previous findings, discover new loci, and assess genetic correlations with other traits of interest. In the largest GWAS meta-analysis to date of DSM-IV cannabis abuse and/or dependence cases and unexposed controls (7,507 cases and 22,472 controls of European ancestry (EA)), we found no genome-wide significant hits, but two genes were significantly associated in gene-based tests (p < 2.65e-6): *NR1H2* and *NAPSA,* previously associated with several metabolic traits, as well as with alcohol intake frequency. We found significant positive genetic correlations with cannabis initiation, smoking initiation, schizophrenia, and risk-taking. Although not significant, we saw a negative genetic correlation with educational attainment (similar to Demontis et al. (*bioRxiv* preprint)) which was contradictory to the largest study of cannabis use which reported a positive correlation (r_g = 0.299), thus underscoring key differences between cannabis use and CUD. We anticipate improved power via an expanded meta-analysis with iPSYCH and deCODE (projected N_{case} ~ 15,000; $N_{controls}$ ~ 300,000; 67% power to detect common variants (MAF ≥ 0.25) with GRR = 1.08). Importantly, we also have a large sample of African ancestry (total N ~ 12,800) with results forthcoming. This research is an important next step in better understanding the genetic etiology of CUD, including in non-European samples, which are currently understudied in complex disease genetics.