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Systematic identification of genetic loci associated with both cannabis use disorder and schizophrenia

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ABSTRACT: Recent genome-wide association studies (GWAS) have found modest but significant genetic correlations between schizophrenia (SCZ) and cannabis ever-use (Pasman et al., 2018), and between SCZ and cannabis use disorder (CUD; Johnson et al., 2020). No study has yet examined the specific genetic loci and biological pathways associated with both CUD and SCZ liability. Using the largest genome-wide datasets available (Ns 46,213 - 632,802), we applied ASSET, a cross-disorder method, to identify >100 independent genome-wide significant loci pleiotropic for CUD and SCZ. A previously identified chromosome 8 locus that contains the genes *EPHX2* and *CHRNA2* showed a particularly strong signal for both CUD and SCZ, suggesting that this may be a point of shared genetic vulnerability. As tobacco smoking is phenotypically and genetically correlated with both CUD and SCZ, we also plan to use LAVA to examine bivariate and local genetic correlations between CUD and SCZ after conditioning on tobacco smoking and other potential confounds (e.g., SES).

Johnson, Emma C., et al. "A large-scale genome-wide association study meta-analysis of cannabis use disorder." *The Lancet Psychiatry* 7.12 (2020): 1032-1045.

Pasman, Joëlle A., et al. "GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal effect of schizophrenia liability." *Nature neuroscience* 21.9 (2018): 1161-1170.

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