

Genome-wide association study implicates *CHRNA2* in cannabis use disorder

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Cannabis is the most frequently used illicit psychoactive substance worldwide. Life time use was reported among 35-40% of adults in Denmark and the United States. Cannabis use is increasing in with heritability estimates in the range of 51 – 70%.

Here we report the identification of a genome-wide significant locus at chromosome 8 (rs56372821; P-value = 9.31×10^{-12}), identified in a genome-wide association study (GWAS) of 2,387 individuals with cannabis use dependence (CUD) and 48,985 controls. The locus was replicated in an independent sample of 5,501 CUD cases and 301,041 controls from Iceland. Furthermore, a case only analysis suggested an impact of the locus on earlier age of first diagnosis.

The index SNP is a strong eQTL for *CHRNA2* which encodes the nicotinic acetylcholine receptor alpha-2 subunit. Analyses of the imputed genetic regulated gene expression found significant association of decreased *CHRNA2* expression in cerebellum with CUD. At the polygenic level analyses revealed a significant decrease in the risk of CUD with increased load of variants associated with increased cognitive performance.