

HUNTING FOR GENES ASSOCIATED WITH CANNABIS USE INITIATION IN THE NETHERLANDS TWIN REGISTER

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BACKGROUND

- **Cannabis** is the most frequently used and abused illicit drug.
- 22.5% **lifetime prevalence** in Europeans aged 15-64.
- a risk factor for developing substance dependence.

AIMS & METHODS

- Estimate trait heritability based on **genetic relatedness** (Yang et al., 2010)
- Identify common and population specific SNPs associated with the trait by using **gee** (Carey, 2012) accessed from **Plink** (Purcell et al., 2007).
- Hunt for genes conferring susceptibility to initiate cannabis use by employing **the extended Simes test** (Li et al. 2011).
- Sample: 6744 individuals (mean age=39.09, SD=17.45; 61% females) from the **Netherlands Twin Register**.
- **GoNL** (Boomsma et al., 2014) reference panel used to impute unobserved genotypes.

FIGURE 1:

Region on chromosome 19 +/- 1000 kb around rs35917943

RESULTS

- Heritability on the observed scale estimated at 25% (SE=0.08, p = 0.0016).
- rs35917943 on chromosome 19 showed the strongest association signal (p=1.62E-7, Fig. 1)
- Top genes in the gene-based analysis (Fig. 2):
- * ZNF181 (p=3.7E-6)
- * MIR643 (p=3.03E-5, start position 52785049)

FIGURE 2:

Manhattan plot genomewide gene-based analysis



CONCLUSIONS

*A significant proportion of variance in liability to initiate cannabis use is explained collectively by the SNPs.



***** Several interesting candidate genes were suggested by gene-based analyses.

* Investigating these genes in replication samples and considering them jointly in pathway analyses shall provide additional insights into the etiology of the early stage of cannabis use.



