



THE GENETICS OF ALCOHOL DEPENDENCE: HERITABILITY AND GENOME WIDE ASSOCIATION ANALYSES

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BACKGROUND

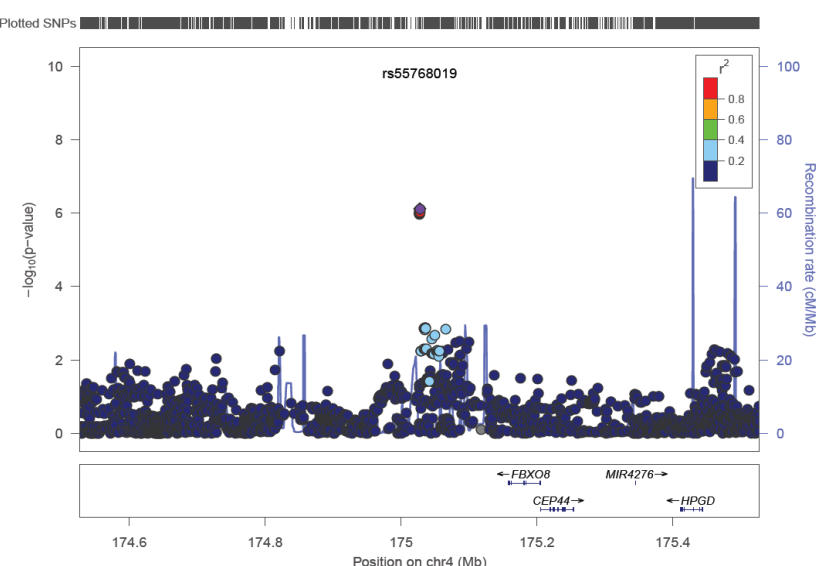
- **Alcohol dependence (AD)** is a complex psychiatric disorder in which individuals are physically or psychologically dependent upon drinking alcohol.
- **Lifetime prevalence** of alcohol dependence is 22% for men and 6.5% for women in the general population.
- **Aims** to identify genes associated with the AD using data from the Netherlands Twin Register (NTR) and the Netherlands Study of Depression and Anxiety (NESDA).

METHODS

- Presence of AD ascertained via the Alcohol Use Disorders Identification Test (AUDIT).
- Cut-off points of AUDIT for case-control status in men ≥ 9 and women ≥ 6 (Boschloo et al, 2010).
- Twin based heritability estimated using structural equation modeling in 7,694 MZ and DZ twin pairs.
- Estimate trait heritability by using GCTA (Yang et al., 2010).
- GWAS SNP effect concordance analysis (SECA) (Nyholt et al, 2014)

FIGURE 1:

Regional association plots for the top signal around 4q31.1

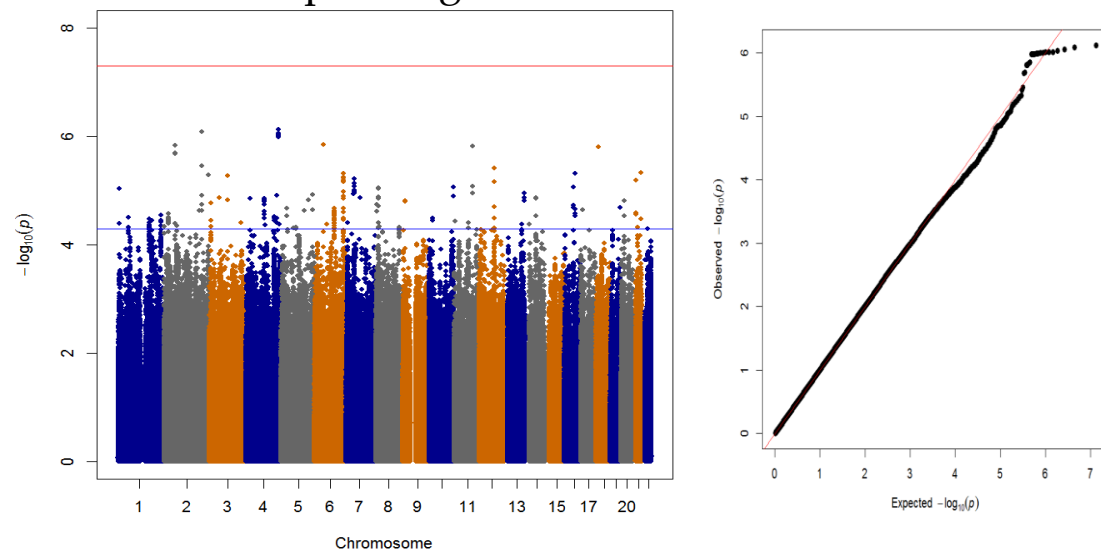


RESULTS

- Twin based heritability estimate of AD is 60% (55%-69%).
- GCTA shows that common SNPs jointly capture 33% (SE=0.12, $p = 0.002$) of this heritability.
- Top GWAS signals in 4q31.1, 2p16.1, 6q25.1, 7p14.1 with the strongest association for rs55768019 ($P=7.58 \times 10^{-7}$) (Fig. 1)
- Concordance of SNPs effects between our study and Gelernter et al, 2014 (permuted $P=9.99 \times 10^{-4}$ (95% CI: 5.12×10^{-5} -0.0056).

FIGURE 2:

Manhattan plot of genome-wide association SNPs



CONCLUSIONS

- First GWAS of AD using the AUDIT measure found consistent results with previous genetic studies using DSM diagnosis.
- Concordance in heritability estimates and direction of SNPs effect and overlap with top hits from previous GWAS.
- The questionnaire based AUDIT may provide a useful, cost-effective alternative to DSM diagnosis when phenotyping large population-based cohorts or biobanks.