M63. GENOME WIDE ASSOCIATION RESULTS OF ALCOHOLIC USE DISORDER PATIENTS AND HEALTHY CONTROLS

Swapnil Awasthi[1], Eva Friedel[1], Hans-Ulrich Wittchen[2], Andreas Heinz[1], Henrik Walter[1], Stephan Ripke[3]
[1]Charite Universitatsmedizien, [2]Universität Dresden, Dresden, Germany, [3]MGH

Background Recent genome wide association studies (GWAS) of alcoholic use disorder (AUD) have estimated a 40-60% variance explained by common genetic variants. Since GWAS require large sample sizes this study aims at combining genetics and imaging data to help finding genetics risk variants in smaller datasets (referred to as imaging genetics data). In this presentation we will focus on the genetic results of this study

Methods We had genotypic data of 115 cases of AUD according to DSM-IV-TR and 286 healthy controls. We used Ricopili pipeline for quality control (QC), principal component analysis (PCA), imputation, association analysis and polygenic risk scoring. Standard thresholds during QC were applied: call rate for individuals 98%, call rate for SNPs 98%, missing differences between cases and controls 2%, Hardy Weinberg Equilibrium for controls 10e-06, HWE for case 10e-10. We also checked for sex inconsistencies between reported sex and empirical sex as well as for related individuals between all the individuals by using identity by descent on a set of LD-pruned SNPs. After removing the related and overlapping individuals, PCA results were checked for hidden population stratification. Pre-phasing was done using Shapeit and imputation using Impute2 (using 1000 Genomes phase 1 as reference). We clumped GWAS summary statistics from the biggest currently available AUD dataset (n=16,087) and scored the individuals of our study. We also inspected for genetic correlation between Schizophrenia by using the largest available data sets from the Psychiatric Genomic Consortium (PGC).

Results All cases passed QC but four controls were excluded due to call rate. Out of 603,132 SNPs, 42% (253,361) were excluded, most of which were invariant (39%). PCA revealed slight population stratification without strong outliers; overlap testing could reveal one related and one completely overlapping case, of which one each was excluded from downstream analysis. After imputation 8,696,851 SNPs, 115 cases and 280 controls were chosen for the analysis. As expected, we did not find any genome wide significant SNPs. The QQ plots showed only slight inflation from expectation (lambda=1.054).

Polygenic risk score with four alcoholism phenotypes (two Discovery sample for alcohol dependent and ordinal trait and two SAGE sample with alcohol dependent and ordinal trait) (Gelernter J, et al, 2014) could not show significant separation of cases and controls in our study for any of the p-value thresholds. We also found no significant correlation with schizophrenia as the training dataset.

Discussion QC, imputation of this study was straightforward and as expected could not identify new genome wide significant SNPs. The genetic data is now ready to use to understand more about genetic aetiology of AUD using imaging genetics. Polygenic risk scoring with the biggest data available for AUD GWAS showed no signal, which might be due to low power of the training data (Gelernter J, et al, 2014). Newer and much more powerful PGC results will soon give more insight. As expected this study also showed no genetic association with schizophrenia.

Disclosure: Nothing to Disclose.