## M28. POLYGENIC RISK FOR BIP, MDD, AND SCZ IN ANDALUSIAN MULTIPLEX FAMILIES

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**Background** Recent large-scale genome-wide association studies (GWAS) have successfully identified common genetic variations contributing to the risk for psychiatric disorders, such as major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SCZ). It has been suggested that familial cases of psychiatric disorders are not only driven by rare variants but also by an accumulation of common genetic risk variants.

In the Andalusian Bipolar Family Study (ABiFStudy), 100 multiplex families with bipolar I disorder, bipolar II disorder, recurrent MDD, and single episode MDD cases have been recruited. The objectives of the current study were to assess the patterns of common polygenic variation for BIP, MDD, and SCZ and their association with neuropsychological measures in the affected and unaffected members of the families.

**Methods** Genome-wide genotyping was carried out in 395 members of 33 families including 244 affected individuals using the Illumina Infinium PsychArray BeadChip (PsychChip). Genotype data was imputed using the 1000 Genomes Phase 3 reference panel. The polygenic risk score (PRS) for SCZ was calculated using the 2014 PGC SCZ2 data set. The PRS for MDD was calculated based on the latest freeze of the PGC MDD working group. PRS for BD will be calculated using the latest freeze of the PGC BD working group, after exclusion of family members included in the PGC data and results will be presented at the conference. Analyses were conducted via linear mixed polygenic models taking family structure into account, using the R package GenABEL. Covariates in the analyses were gender, age at the interview, and assessment batch.

**Results** Preliminary analyses revealed no significant associations between BD or MDD diagnosis and either MDD or SCZ PRS. Stratification into disease subgroups affected the results but simultaneously decreased power. The age at onset was nominally associated with the SCZ PRS in MDD cases. Accordingly, inclusion of the age at onset had a significant effect on the models.

**Discussion** We found no evidence for an accumulation of common risk variants for MDD or SCZ in members affected with either MDD or BD in comparison to healthy family members. This could either indicate that disease in these families is caused by rare variants or that all family members carry a high load of risk variants. Ongoing

sequencing studies in the families will complement these results. Moreover, comparisons with healthy, unrelated Spanish controls will be used to examine whether healthy family members show an increased genetic risk for psychiatric diseases.
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