M29. PHENOTYPIC TRAITS OF BIPOLAR DISORDER PREDICTED BY SCHIZOPHRENIA ASSOCIATED SNPS IN ROMANIAN BIPOLAR I PATIENTS. PRELIMINARY RESULTS

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Background Bipolar disorder (BP) and schizophrenia (SCZ) are heritable psychiatric disorders. Genome-wide research suggests that the molecular basis of BP and SCZ overlaps (Cross Disorder PGC Group, Lancet, 2013). The objective of our work was to investigate whether polygenic risk scores (PRS) based on SCZ-associated SNPs in the PGC sample (2012) might predict phenotypic traits in BP-I Romanian patients [presence of psychosis and incongruent psychosis, age of onset (AO), family history for major affective disorders (BP, Mdd-UP, schizoaffective) and SCZ, number of manic/mixed episodes].

Methods 439 BP-I cases and 283 controls were genome-wide genotyped on Illumina SNP-assays at the Institute of Human Genetics, Bonn. After QC 19 cases and 3 controls were excluded. There were 531,182 common SNPs between the Romanian and the SCZ sample. PRS profiles were constructed for ten P-values of association with SCZ using PLINK 1.07, but only three thresholds were analysed yet ($P \leq 0.05$; $P \leq 0.01$; $P = 0.10$). The association of SCZ-PRS with phenotypic traits of BP-I was examined with logistic and multinomial regression (SPSS software, v.17).

Results Presence of incongruent psychosis was significantly predicted by PRS_0.05 in the early onset group ($AO \leq 21$) ($P = 0.039$), in familial cases ($P = 0.034$), and in the total sample ($P = 0.05$). PRS_0.01 significantly predicted the presence of incongruent psychosis ($P = 0.025$) and of psychosis ($P = 0.039$) in familial cases and early AO cases, while in the total sample there was a trend to significance ($P=0.11$) for both incongruent psychosis and psychosis. Incongruent psychosis and psychosis were not predicted by PRS_0.10 in the total sample.

PRS_0.05 and PRS_0.01 tended to predict the AO when AO was classified into 3-AO-groups (early=$AO \leq 21$; intermediate AO = 22-34; late = AO >34) in the total sample ($P = 0.098$ for PRS_0.05; $P = 0.09$ for PRS_0.01). PRS_0.10 significantly predicted the 3-AO group division ($P = 0.048$) in the total sample.

Family history for major affective disorders and SCZ tended to be predicted in the total sample by PRS_0.01 ($P=0.09$) and PRS_0.10 ($P = 0.07$), while PRS_0.05 tended to differentiate familial from sporadic cases ($P = 0.08$) only in the early onset group.

PRS_0.05 tended to correlate with the number of manic/mixed episodes in the early AO group ($P = 0.08$).

Discussion The SCZ-PRS significantly discriminated between cases and controls at all P-values ($P < 0.000$) in our sample.

The best prediction of the five phenotypic traits investigated was found in the familial and the early AO patient group showing that they are genetically more homogeneous.

In the total sample, AO and incongruent psychosis were the best predicted phenotypic traits. The best association between SCZ-PRS_p0.05 and incongruent psychosis was shown by the female sex ($P = 0.007$) in the total sample. The PRS_0.05 predicted

most phenotypic traits in the total sample and in subgroups. The fact that only SNPs with a certain degree of association with SCZ ($P \leq 0.05$; $P \leq 0.01$) could predict the incongruent psychosis in BP-I indicates specificity of these SNPs.
No phenotypic trait was predicted by the three PRS profiles analysed in sporadic cases. Our results have only a suggestive value due to the reduced sample size. The present analysis will be repeated in an extended sample with several P-values for PRS.
Disclosure: Nothing to Disclose.