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Differences in association of the genes with cognitive function and symptom severity of Belarusian schizophrenia patients

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Motivation and Aim: Cognitive and symptom impairments of schizophrenia patients are the base of their individual disability. Patients are treated using antipsychotic therapy but in majority of the cases the prescription process is conducted in trial and error way. The analysis of the genes that may be involved in cognitive and symptomatic changes in patients could result into better schizophrenia therapy progress.

Methods and Algorithms: Our sample consisted of 150 Belarusian individuals diagnosed with schizophrenia (age 46.8 ± 9.4; 54 % females) assessed using the PANSS (symptom severity), the WCST and Stroop test (cognitive functioning). The *MIR137* rs1625579, *COMT* rs4680, *DRD2* rs1800497, *MTHFR* rs1801133, *DNMT3B* rs2424913 polymorphisms of schizophrenia patients were analyzed using RFLP and TaqMan assay. Our outcome of interest was the association of gene polymorphisms with symptom severity and cognitive parameters analyzed using univariate ANOVAs. All statistical analyses were conducted in R v.4.3.2.

Results: *MTHFR* rs1801133 was associated with positive symptom severity ($p = 0.02$), *COMT* rs4680 ($p = 0.03$) and *MIR137* rs1625579 ($p = 0.03$) – with general symptom severity for both males and females. *MIR137* rs1625579 ($p = 0.02$) and *DNMT3b* rs2424913 ($p = 0.002$) were associated with negative and general symptom severity respectively for females only. Overall, the number of minor alleles across the five SNPs of interest was correlated with negative symptom severity ($r = 0.20$, $p = 0.09$) only for males. Furthermore, there were sex-specific differences in the combined *DNMT3B C/C* genotype and *COMT* G-allele ($p = 0.0001$). Males with the *DNMT3B C/C* genotype and *COMT* G-allele (N = 13) showed greater negative symptom severity (M = 27.2 ± 6.7) in comparison to female patients with the same genotypes (N = 18, M = 15.6 ± 5.6). For cognitive function, we found the association of *COMT* rs4680 with a number of variables of WCST (categories completed, nonperseverative errors, total errors) and Stroop test (total errors) but mostly for females only. Furthermore, female patients with A2/A2 (*DRD2/ANKK1*) and A-allele **(***COMT)* demonstrated a lower number (2.97) of WCST categories completed compared to A1-allele (*DRD2/ANKK1*) and A-allele (*COMT*) (4.94; $p = 0.03$). Females with T-allele (*MTHFR*) and T-allele (*DNMT3B*) have made twice as many Stroop test total errors in comparison with C/C (*MTHFR*) and T-allele (*DNMT3B*) ($p = 0.08$).

Conclusion: We found that genetic predictors involved in symptom severity and cognitive functioning of schizophrenia patients may have an impact on psychopathology of the disease in a different way for males and females.

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