

## **M52. ASSOCIATION OF COMT, DRD2, MTHFR, MIR-137, DNMT3B POLYMORPHISMS WITH COGNITIVE FUNCTIONING AND SYMPTOM SEVERITY OF SCHIZOPHRENIA PATIENTS**

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**Background** Schizophrenia is a complex disorder with a high heterogeneity of its clinical implications. A lot of studies analyzing polymorphisms of potential schizophrenia candidate genes give inconsistent results. It may be related to ethnic factor, differences in sample size, but also with inhomogeneity of samples regarding clinical characteristics. In an attempt to receive more reproducible results we made thorough sample selection to homogeneous groups according to the dominant manifestation of schizophrenia symptoms, cognitive defects and other disease aspects.

**Methods** Five gene polymorphisms: rs1801133 of MTHFR, rs4680 of COMT, rs1625579 of Mir-137, rs2424913 of DNMT3b were analyzed for 142 schizophrenia patients and 91 controls (Belarusian population) by RFLP and TaqMan probes. Symptom severity was evaluated with the help of PANSS rating criteria, cognitive functioning - by using WTSC. Chi square, Mann-Whitney, Kruskal-Wallis tests were used for the association of gene loci with schizophrenia, severity of symptoms and cognitive functioning of patients.

### **Results**

Analysis of the data revealed:

- 1) No direct association of any investigated loci with risk of developing schizophrenia.
- 2) There is an association of MTHFR and Mir-137 loci with total index of positive items of PANSS as well as of Mir-137 with general psychopathology and overall performance of all subscales for all patients (males and females). Remarkably, we have found an association of Mir-137 with total index of negative items and overall performance of all subscales for females only.
- 3) There is an association of COMT rs4680 with total index of negative items, general psychopathology and overall performance of all subscales. Such result is observed only for males.
- 4) There is an association of COMT rs4680 with variables of WTSC: percentage of nonperseverative errors, the number of cards used within the test, the number of completed categories, the number of trials to complete the first category.
- 5) There is an association of DNMT3b locus with total index of general psychopathology symptoms and overall performance of all subscales only for females.

### **Discussion**

We conclude:

- Both rs1801133 of MTHFR and rs1625579 of Mir-137 are involved in the mechanism of formation of positive syndrome for all patients, but the effects are observed only in the combined sample (males + females).
- COMT rs4680 is involved in the formation of the negative syndrome and general psychopathology symptoms for all patients, but for males is much stronger. A significant impact on the negative syndrome formation among females is observed for rs1625579 of Mir-137.

- Rs4680 of COMT and rs1625579 of Mir-137 are associated with the wide range of pathological processes in schizophrenia for all patients, but the effect of the COMT gene is stronger for males, and Mir-137 gene - for females. Moreover, rs2424913 of DNMT3b shows a significant influence on the general psychopathology symptoms and overall symptomology of disease pattern for females.
- COMT is associated with cognitive functioning of patients with schizophrenia. The obtained results indicate that investigated factors have gender-specific impacts on symptoms and syndromes and confirm the differences in the mechanisms of pathogenesis of schizophrenia between males and females.

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