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COGNITIVE FUNCTIONS AND POLYMORPHISM OF THE *BDNF* GENE IN PATIENTS WITH SCHIZOPHRENIA AND HEALTHY INDIVIDUALS

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INTRODUCTION

Schizophrenia is a serious medical and social problem worldwide due to the chronic course, severe characteristic personality changes and a neurocognitive deficiency that worsens the quality of life and is the cause of a high percentage of patient's disability.

The contribution of genetic mechanisms has been proven in the variability of attention instability and long-term memory impairment.

Brain derived neurotrophic factor (BDNF) plays an important role in cell differentiation, survival, long-term potentiation, synaptic plasticity, learning and memory. Dysregulation of BDNF has been associated with the pathogenesis of schizophrenia, mood and anxiety disorders.

The aim of the research is to study cognitive functions in patients with schizophrenia and healthy persons and identify associations between cognitive function and polymorphism of *BDNF* gene.

MATERIALS AND METHODS

550 patients with schizophrenia

43.2% male

Age	39 [32; 48] years
Duration of disease	13.5 [7; 20] years
Age of onset	25 [20; 29] years

56.8% female

The control group consisted of **485** healthy persons.

Blood sample was obtained for DNA isolation and genotyping. Genotyping was carried out on polymorphic variant rs6265 of *BDNF* gene. Statistical analysis was performed using SPSS 20.0. Frequency distribution of the study sample was tested in accordance with **Hardy-Weinberg** equilibrium. The critical p-values of significance was **0.05**.

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– ***Cognitive functions***

Assessment of cognitive functions was carried out for all patients on the Brief Assessment of Cognition in Schizophrenia (**BACS**), in the adapted Russian version. A set of tasks on this scale («List learning», «Digit sequencing task», «Token motor task», «Verbal fluency», «Symbol coding», «Tower of London») allows you to evaluate the parameters, according to the sequence of the list: **verbal memory, working memory, motor speed, processing speed, attention and processing speed, executive functions**.

BACS subtests	Healthy persons	Patients with schizophrenia	p-value
Total time, min	35.8±7.798	44.45±10.446	<0.001
List Learning (Verbal Memory), score	41.33±9.027	35.58±11.818	
Digit Sequencing Task (Working Memory), score	21.76±3.689	17.03±4.797	
Token Motor Task (Motor Speed), score	66.74±16.784	38.04±17.732	
Verbal Fluency (Processing Speed), score	53.65±11.86	38.41±13.738	
Symbol Coding (Attention and Processing speed), score	56.6±12.169	37.77±14.787	
Tower of London Test (Executive Functions), score	18.04±3.055	14.72±4.332	

RESULTS

The prevalence of genotypes in both groups was consistent with **Hardy-Weinberg** equilibrium. Significant differences in the distribution of genotypes of rs6265 (*BDNF* gene) in patients with schizophrenia and healthy individuals were not found ($\chi2=1.999$, $p=0.368$). The distribution of C and T alleles in the patient and control groups also did not differ significantly ($\chi2=0.74$, $p=0.39$).

Assessment of **cognitive functions** was carried out in **160 patients with schizophrenia** and **106 healthy individuals** using the **BACS** scale. The indicators of cognitive function in patients with schizophrenia are **significantly worse** than in healthy controls.

Average scores for sub-tests were analyzed according to the carrier genotypes of polymorphism *BDNF* gene. In the study cohort of patients with schizophrenia, associations of genotypes of rs6265 were not identified with scores on the BACS scale, which characterizes cognitive functions ($p>0.05$).

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CONCLUSION

In the control group, **significant differences** were found between the average scores for several subtests of the **BACS** scale, depending on the carrier of **CC** and **CT** genotypes. Healthy individuals with the **CC** genotype had a **higher score** in the subscale "**Verbal Fluency**" (characterizing processing speed) compared with carriers of the **CT** genotype (53.66±9.544 and 46.94±11.402, **p=0.002**). The examined persons made some mistakes during the tests and their number was taken into account in the analysis of cognitive functions. Healthy people with genotype **CT** often make mistakes when performing subtest "**Symbol Coding**" (characterizing attention and processing speed) and make fewer mistakes in the test "**List Learning**" (characterizing verbal memory) compared to healthy carriers **CC** genotype (**p=0.024** and **p=0.049**)

The data obtained indicate that according to all BACS tests, the indicators of **cognitive function** in patients with schizophrenia are **significantly worse** than in healthy controls, which is comparable with the results of other studies. Thus, it has been shown that **neurocognitive deficit** among people with schizophrenia, according to various estimates. Also, associations of genotypes of polymorphism rs6265 of the ***BDNF* gene** were detected by performing subtests of the **BACS** scale, which characterize such cognitive functions as **verbal memory, processing speed, attention and processing speed**.

This work was supported by a RFBR grant #18-315-20019 "New approaches to the genetics of clinical polymorphism and neurocognitive deficits in schizophrenia".