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D3 receptor gene polymorphism and the results of Trial Making Test in patients with schizophrenia

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Summary

Cognitive deficits are a major problem in clinical psychiatry and their presence adversely affects the course of the disease and adaptation of schizophrenic patients. Intensity of these deficits in the groups of patients varies, and their origin and relation to brain structure abnormalities in schizophrenia is not fully understood. The authors studied 34 hospitalized patients with schizophrenia paranoid psychosis in its acute phase. They analyzed the relationship between some polymorphisms of histamine H1, serotonin, dopamine D2, D3 receptor genes and the results of Trail Making Test. It has been shown that patients with schizophrenia with Ser/Ser polymorphism of D3 receptor gene present lower levels of functioning in the visual-spatial operational memory and switching than those with Ser/Gly polymorphism of this gene.

Key words: schizophrenia, polymorphism of dopamine receptors

Introduction

Varied and unsatisfactory response to treatment is a serious problem for clinical psychiatry. Seeking the genesis of this problem by means of genetic research includes, among other things, analysis between polymorphisms of receptor genes and various data on clinical picture and course of schizophrenia. The research concerns primarily dopaminergic and serotonin receptor because these neurotransmitter systems seem to play a significant role in pathogenesis and in the response to medication in schizophrenia [5,8]. It has been proved there are relations between the polymorphism of 5HT2A receptor gene and clinical response to atypical drugs [1,2,8]. His 452 Tyr and T102 C polymorphisms affect a clinical response in patients treated with olanzapine. Thus, if the response stands for the reduction of 30 percent of symptoms in PANSS scale after six weeks of treatment, then the patients with this polymorphism produce better clinical response [7]. The relations have been observed between the polymorphism of receptors and some side effects including weight gain [3]. Cognitive dysfunctions seem to be a crucial aspect of schizophrenia, the increase of which usually leads to a worse prognosis and response to treatment [4,10]. Rybakowski et al. stated that there is a link between the polymorphism of dopamine receptor and the results of the Wisconsin Test. It seemed noteworthy to examine associations of other polymorphisms of selected receptors or neurotransmittive transporters with cognitive functions in patients with schizophrenia.

Objective

The objective of this study was to examine associations of polymorphisms of selected neurotransmittive receptor genes with cognitive functions in patients with paranoid schizophrenia. The following genes and their polymorphisms were examined: H1 histamine receptor - polymorphism 17 T/C, serotonin transporter SERT - short-long polymorphism, dopamine receptor DRD3 - Ser/Gly polymorphism, DAT dopamine transporter - VNTR polymorphism, 5HT2 serotonin receptor - T102C polymorphism, and D2 dopamine receptor - 141 Ins/Del polymorphism.

Methods

There were 99 test participants with paranoid schizophrenia (according to ICD-10 criteria), treated at the Department of Psychiatry, Medical University of Lublin. 34 patients were examined with the Trial Making Test. This popular neuropsychological test of cognitive functions is comprised of 2 parts: part A - tests the speed of psychomotor reaction, whereas part B tests switching processes and visual-spatial operational memory. An average age was 26,1 and the average age of the first occurence: 22,1. Twenty-three men and eleven women underwent the test. Since it was taken in an acute phase of the illness, at the beginning of treatment

only 34 patients' results have been analyzed. The test was approved by Bioethics Committee. After a written consent had been obtained, the patients were drawn peripheral blood from the cubital vein. DNA extraction and genotyping was performed at Department of Medical Genetics, Medical University of Lublin. PCR-RFLP technique was applied in a molecular analysis.

Results

The results were analyzed statistically using the U-Mann Whitney's test. No statistically significant differences were observed in the applicable neuropsychological test for H1 histamine receptor gene - polymorphism 17C/T, serotonin transporter SERT gene - short-long polymorphism, DAT dopamine transporter gene - VNTR polymorphism, 5HT2 serotonin receptor - T102C polymorphism, and D2 dopamine receptor - 141 Ins/Del polymorphism. While an interesting correlation was observed in relation to the dopamine D3 receptor related with polymorphism Ser/Ser and Gly/Ser. In the test group polymorphism Ser/Ser was found in 11 subjects and polymorphism Ser/Gly occurred in 17 patients. If in Part A of the test there were no differences between patients of polymorphisms Ser/Gly and Ser/Ser (results, respectively: 43,65 sec. and 59,45.- s, $p = 0{,}121$), in Part B of the test the difference was found between the patients with polymorphism Ser/Ser /132,64 pp/ and patients with polymorphism Ser/Gly /72.71 pp/ for $p = 0{,}018$. Patients with polymorphism Ser/Ser were characterized by lower levels of functioning of the visual-spatial working memory and switching than those with polymorphism Ser/Gly.

Discussion

Cognitive deficits play an important role in the picture and course of schizophrenia. Their occurence is usually combined with a worse response to medication and worse psychosocial adaptation of patients. The origin of these deficits is not clear, it is shown that there is a correlation between their presence and intensity and structural changes in the brains of patients with schizophrenia. It is even been assumed that patients with schizophrenia without cognitive deficits may be afflicted with another variant of the disorder [10]. Rybakowski et al. [9] have shown that there is a relationship between polymorphisms of certain genes and neuropsychological testing results, mainly concerning the prefrontal cortex. At the same time the results of other studies indicate a relationship between some polymorphisms of genes for receptors of the neurotransmitter systems and clinical response in schizophrenia. Thus, Lan et al. [6] showed that the polymorphism Ser/Gly of the D3 receptor is associated with better response to risperidone treatment. In our study we showed that this polymorphism is also associated with better functioning of visual-spatial operational memory, and the switching processes. Patients with Ser/Ser polymorphism of the receptor gene would obtain definitely worse results in this respect than patients with Ser/Gly polymorphism. Interestingly, in our results we compared patients' neuropsychological functioning among one another and we have shown differences between patients, associated with different polymorphisms. A relatively small group of patients and the fact that only one neuropsychological test has been used bring certain constraints to this work. The constraints resulted from the fact that we studied patients hospitalized in the acute period of illness, at the beginning of treatment. Their psychological state was connected with such cooperation which allowed for the tests. It would be interesting to confirm the existence of the described associations in a greater number of patients, and to examine these persons using neuroimaging techniques. Finding links between genotype variants, neuropsychological changes and deviations in brain structure could prove an important step towards the possible identification of various types of schizophrenia in terms of its course and origin.

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