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Do deficits of working memory and executive functions in adolescent schizophrenic patients are more severe than in adult schizophrenic patients?

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Summary

Aim. The aim of the study was to compare working memory and executive function capacity in early-onset schizophrenic subjects with later-onset patients, who became ill in adulthood, in the first years of disease and also to assess the level of possible cognitive dysfunctions in the two groups of schizophrenic patients in partial remission of psychopathological symptoms.

Method. 25 adolescent schizophrenic patients, aged 15-18 (M-17) years during partial remission of symptoms (PANSS-77) and 25 adult schizophrenic patients, aged 20-37 (M-26,9) years, during partial remission of symptoms (PANSS M-56). The control group consisted of 25 healthy adolescents, aged 15-18 (M-17) years and 25 healthy adults, aged 21-39 (M- 26,8) years.

Results and conclusions. In schizophrenic patients with various types of illness onset (early vs. later) the significant dysfunctions of working memory and executive function, compared to healthy controls, were found. In the first years of disease there were no differences in the level of memory working and executive functions impairment in patients with early-onset compared to patients with onset of the illness in adulthood.

Key words: schizophrenia, early-onset, working memory, executive functions

Introduction

In people with schizophrenia numerous structural and functional disorders of the brain are observed, which are relevant in the development of specific cognitive deficits, currently recognized as one of the most important symptoms of this disease. Cognitive disorders in schizophrenia concern various cognitive functions. A recent meta-analysis of the results of various neuropsychological studies in schizophrenic patients confirms the presence in this disease of characteristic cognitive deficits, especially indicates disturbances in the processes of working memory, executive functions, memory and

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learning, attention and speed of information processing [1]. Studies on the specificity of cognitive impairment in schizophrenia led to identify working memory disorders as the most important deficit in this disease [2]. Multiannual neuropsychological research have shown in majority of patients with schizophrenia significant disorders of various aspects of working memory, compared to healthy subjects and people with other mental illnesses [3-6]. It was considered that the indicator of neuropsychological dysfunction of the prefrontal cortex are the impairments of working memory and executive functions [7]. For testing these cognitive processes Wisconsin Card Sorting Test (WCST) is one of the most frequently used [8]. Studies concerning cognitive impairment in schizophrenia suggest a link between the age of the onset of the illness and severity of cognitive deficits. They indicate significantly higher incidence of cognitive dysfunction in patients with early-onset disease compared with those with the onset in adulthood [9]. The differences found in the two periods of onset of the illness concern primarily disorders of attention, working memory, abstract thinking ability, memory and learning [10]. On the basis of researches it was also assumed that cognitive dysfunctions in the first episode of the disease are less severe than in chronic schizophrenia [11]. This may indicate a progressive character of cognitive impairments. The very severity of the cognitive deficits seen in the first episode of schizophrenia can be an indicator of further prognosis about the course of psychosis and treatment [12]. The observed in some patients with a first episode occurrence of a similar pattern of cognitive dysfunction as in patients with chronic psychosis, may suggest a faster progression in them, which in turn is associated with poorer psychosocial functioning [13-15]. Contemporary research of Jabben et al [16] showed a significant association between the severity of cognitive impairment and poorer psychosocial functioning in two groups of patients - from the spectrum of schizophrenia and bipolar disorder. However, the strength of this relationship was more significant in patients from schizophrenia spectrum in whom also more severe and more generalized cognitive dysfunctions were found, compared to patients with bipolar disorder.

Based on studies it can be assumed that people with early onset schizophrenia may have significantly more severe cognitive dysfunctions compared to those with the onset of the disease in adulthood. However, some reports indicate no differences in the severity of cognitive deficits in both onset-times, even after several years of the disease [17-18]. Therefore, the aim of this study was to compare the efficiency of working memory and executive functions in adolescents with schizophrenia and adults with schizophrenia in the initial years of the disease, and to determine the extent potential deficits in the assessed processes in both groups of patients during the partial remission of symptoms.

Participants of the study

Group of adolescents with schizophrenia consisted of 25 patients (10 girls, 15 boys) aged 15-18 years (M-17), with the onset of schizophrenia at the age of 12-16 (M-14, 9), with the duration of illness from 0.5 to 5 years (M-2, 1), the number of hospitalizations of 0 to 6 (usually 1-3, M-2), with education level measured in years from 8 to

11 (M-9,8). Schizophrenia was diagnosed according to ICD-10 criteria. Assessment of psychopathological symptoms and neuropsychological testing was performed in patients during at least partial remission of symptoms of schizophrenia. Intensity of psychopathological symptoms was assessed with PANSS scale (PANSS total M-77, 63-96) All patients with schizophrenia were taking antipsychotic medications, atypical neuroleptics. People with schizophrenia, who were qualified to the study, were not treated because of neurological disease, severe somatic diseases, were not dependent on psychoactive substances. Participation in the study was voluntary. Participants as well as their parents, after learning about the purpose and character of the study, expressed written consent to conduct the study. The subjects were informed that at any time may withdraw from the study without giving reasons and without bearing any consequences because of it.

The group of adult patients with schizophrenia consisted of 25 patients (11 females, 14 males) aged 20-37 (M-26,9), onset of the illness at the age of 19-32 years (M-23,6), the duration of illness from 1 to 8 years (M-3,4) and the number of hospitalizations of 1 to 5 (usually 1-3, M-2), with education level measured in years from 12 to 20 years (M-15,2). Schizophrenia was diagnosed according to ICD-10 criteria. Assessment of psychopathological symptoms and neuropsychological testing was performed in patients during partial remission of psychopathological symptoms (PANSS total M-56, 49-62). All patients with schizophrenia were taking antipsychotic medications, atypical neuroleptics. People with schizophrenia who were qualified to the study were not treated due to neurological diseases, severe somatic diseases, were not dependent on psychoactive substances. Participants of the research, after learning about the purpose and character of the study, expressed written consent to conduct the study. The subjects were informed that at any time may withdraw from the study without giving reasons and without bearing any consequences because of it.

The control group of healthy individuals in adolescence consisted of 25 patients (10 girls, 15 boys) aged 15-18 years (M-17), with education level measured in years from 8 to 11 (M-9,8). Healthy subjects, who were qualified to the control group, were not treated due to mental illness, neurological disorders, severe somatic diseases, were not dependent on psychoactive substances. They also had no first-degree relatives with schizophrenia or other mental disorders. Participation in the study was voluntary. Participants of the research as well as their parents, after learning about the purpose and character of the study, expressed written consent to conduct the study. The subjects were informed that at any time may withdraw from the study without giving reasons and without bearing any consequence because of it.

The control group of healthy adults consisted of 25 subjects (16 females, 9 males) aged 21-39 years (M-26,8), with education level measured in years from 13 to 20 (M-16,5). Healthy subjects, who were qualified to the control group, were not treated due to mental illness, neurological disorders, severe somatic diseases, were not dependent on psychoactive substances. They also had no first-degree relatives with schizophrenia or other mental disorders. Participation in the study was voluntary. Participants of the research, after learning about the purpose and character of the study, expressed written consent to conduct the study. The subjects were informed that at any time may wit-

hdraw from the study without giving reasons and without bearing any consequences because of it.

Method

Psychometric assessment of psychopathological symptoms intensification was carried out using the PANSS scale [19]. For the neuropsychological evaluation two computer versions of tests designed to evaluate different aspects of working memory and executive functions were used: Wisconsin Card Sorting Test (WCST) in Heaton version [20]. In the assessment of the test results into consideration were taken: the percentage of all errors, percentage of perseverative errors, percentage of non-perseverative errors, percentage of responses in line with the concept of logic, the number of correctly achieved categories, the number of cards needed to arrange I category and the Visual Working Memory N-back Test [21]. In the study, the version with 1-back numbers was used. The subject had to memorize the number currently exposed on the computer screen and the number presented before. The task was to press the key number, which was presented before the currently displayed. In this test, the percentage of correct responses was calculated as well as the percentage of incorrect responses and the time of reaction.

In the statistical analyzes to compare the statistical significance of differences between the studied groups tests for four independent groups were applied: one-way analysis of variance followed by a comparison of mediums by post-hoc Duncan's test. Statistical calculations was carried out using the computer software STATISTICA 7

Results

Both clinical groups – adolescents and adults with schizophrenia - achieved significantly worse results in four WCST test parameters compared to their matched groups of healthy subjects. They made significantly more of all errors, perseverative and non-perseverative errors, obtained a significantly lower response rate in line with the concept of logic, and a group of adult patients also used a larger number of cards to the first category arrangement, compared to healthy subjects. The results of these two groups of people with schizophrenia did not differ only from the results of healthy individuals in terms of the number of achieved categories, and in the group of ill adults also did not differ significantly in intensity of non-perseverative errors. Adolescents suffering from schizophrenia obtained the same results in all parameters of WCST test, except for the first category arrangement trial, as compared to adult patients with schizophrenia. They used a much smaller number of cards to the first category arrangement than the ill adults. Whereas the control groups did not differ between each other in the performance of this test. Tabłe 1 and Table 2 *on next pages*.

Table 1. **WCST test results in clinical groups, adolescents with schizophrenia (EOS) and adult patients with schizophrenia (AOS) in comparison with control groups and between groups - mean values (M), lower-upper quartile, standard deviation (SD)**

Research groups and their size		WCST test parameters					
		Perseverative errors	Non-perseverative errors	Total errors	% of conceptual answers	Number of categories achieved	Trial to complete first category
Clinical groups	EOS N = 25	M = 11.68** 9–14; SD 6	M = 10.60* 7–12; SD = 4.8	M = 22.28** 16–27; SD = 9.1	M = 72.52** 67–81; SD = 12.9	M = 5.72 6–6; SD = 0.7	M = 14.16 11–14; SD = 4.8
	AOS N = 25	M = 13.88*** 9–18; SD = 6	M = 11.88 7–15; SD = 6.3	M = 25.76*** 19–29; SD = 10.4	M = 68.72** 57–77; SD = 12.8	M = 5.68 6–6; SD = 0.9	M = 24.32 ***(#) 12–28; SD = 16
Control groups	For EOS N = 25	M = 7.56 6–8; SD = 1.7	M = 7.08 5–9; SD = 2.6	M = 14.64 12–17; SD = 3.3	M = 83.08 82–86; SD = 4.2	M = 6.00 6–6; SD = 0.0	M = 12.16 11–13; SD = 2.1
	For AOS N = 25	M = 8.32 6–9; SD = 3.5	M = 9.48 6–11; SD = 4.4	M = 17.80 13–19; SD = 7.3	M = 78.92 75–85; SD = 10.2	M = 5.88 6–6; SD = 0.0	M = 12.88 11–12; SD = 4.1

EOS – adolescents with schizophrenia; AOS – adults with schizophrenia; Control group for EOS – healthy adolescents;
Control group for AOS – healthy adults
Ducan's Test (post-hoc)
Comparisons concern EOS group and group of healthy peers– *$p < 0.05$; ** $p < 0.01$; ***$p < 0.001$
Comparisons concern AOS group and group of healthy adults– **$p < 0.01$; ***$p < 0.001$
Comparisons concern EOS group and AOS group – # $p < 0.01$
Comparisons between control groups: healthy adolescents and adults – statistically insignificant results

Table 2. **N-back test results in clinical groups, adolescents with schizophrenia (EOS) and adult patients with schizophrenia (AOS) in comparison with control groups and between groups - mean values (M), lower-upper quartile, standard deviation (SD)**

Research groups and their size		N-back test parameters		
		% of correct reactions	% of error reactions	Time of reaction
Clinical groups	EOS	M = 77.60 ***	M = 22.40***	M = 664.76**
	N = 25	60–100; SD = 24.9	0–40; SD = 24.9	346–862; SD = 331
	AOS	M = 72.32**	M = 27.68**	M = 903.80(#)
	N = 25	56–96; SD = 25.5	4–44; SD = 25.5	670–1088; SD = 283.8
Control groups	For EOS	M = 99.68	M = 0.32	M = 407.80
	N = 25	100–100; SD = 1.6	0–0; SD = 1.6	256–508; SD = 189.6
	For AOS	M = 89.92	M = 10.08	M = 804.24^
	N = 25	88–100; SD = 13.4	0–12; SD = 13.4	552–1090; SD = 318.7

EOS – adolescents with schizophrenia, AOS – adults with schizophrenia, Control group for EOS – healthy adolescents;
Control group for AOS – health adults
Duncan's Test (post-hoc)
Comparisons concern EOS group and group of healthy peers – ** $p < 0.01$; ***$p < 0.001$
Comparisons concern AOS group and group of healthy adults – ** $p < 0.01$
Comparisons concern EOS group and AOS group– # $p < 0.01$
Comparisons concern control groups: healthy adolescents and adults – ^ $p < 0.001$

Both clinical groups – adolescents and adults with schizophrenia - achieved significantly worse results in the N-back test in comparison with the matched groups of healthy individuals. They obtained significantly fewer correct responses and had significantly more incorrect responses than the healthy individuals, and a group of ill adolescents additionally had a much longer reaction time compared to healthy peers. Adolescents suffering from schizophrenia obtained the same results in two parameters of the N-back test as adults with schizophrenia. The exception was the response time, where they received a much faster response time than ill adults. Whereas in the control groups, healthy adolescents also had faster reaction times than healthy adults, and this was the only parameter in the tests differentiating these groups from each other .

Discussion of results

In the study it was indicated that despite significant reduction of psychotic symptoms, especially in adults with schizophrenia, the ill persons from both clinical groups achieved significantly worse results in tests compared to healthy subjects. This confirms the results of many previous studies which present severe cognitive deficits in schizophrenic patients in all stages of disease, also during remission [22-25]. The ill participants from both clinical groups in comparison with healthy subjects scored

significantly worse in WCST test. A higher rate of perseverative errors committed by them shows weakening of cognitive processes flexibility and the presence of stereotyped response, while a large number of non-perseverative errors - a disturbance in attention, especially in the group of adolescents The received by them lower rate of logical conception signifies substantial difficulties in formulating logical concepts. However, in this test, the sick and healthy persons achieved the same number of categories This result may suggest that, despite the poorer working memory function of patients suffering from schizophrenia, with different times of illness onset, in the period of partial remission of psychopathological symptoms they may have similar efficiency of thinking as healthy persons. However, the ability to use real-time information in both groups of patients with schizophrenia is significantly weakened in comparison with healthy subjects. It is also worth noting that the patients from the two groups were treated with new generation neuroleptics This can be an essential cause for such good results in terms of efficiency of thinking of the ill persons, as it is believed that these drugs improve cognitive functions [26].

This would indicate that selective deficits in working memory do not have to be related to disorganized thinking in schizophrenic patients in the period of partial remission, especially when in the treatment the medications are applied taking into account the improvement of cognitive function. This conclusion is confirmed by, for example, the study of Beninger et al [27], conducted among persons with schizophrenia treated with typical neuroleptics and the atypical ones. Although all of them obtained in the study significantly worse results than healthy controls, the performance in most of the WCST parameters in atypical neuroleptic-treated patients was significantly better than in those treated with typical neuroleptics. Similar results were obtained by Polish researchers comparing the impact of various neuroleptic drugs - risperidone, olanzapine, and phenothiazines - on cognitive functioning. They found that patients treated with atypical neuroleptics received significantly better results in the WCST than patients treated with drugs from the group of phenothiazines. And some of them, receiving systematically risperidone or olanzapine, obtained WCST results such as healthy individuals [28-29].

In the test for assessing simple visual working memory - N-back Test - patients with schizophrenia in both clinical groups in comparison with healthy subjects achieved significantly worse results, especially made more incorrect responses and were characterized by longer time of performing the tasks. However, the adolescent patient had significantly faster response time than adult patients, their results ranged between adult patients and healthy peers. Yet, performance of this test by the two groups of patients shows a visual working memory disorders, as well as a much weakened visual-spatial processes. In various studies using the N-back test it was found that its performance by schizophrenic patients was significantly worse in comparison with healthy subjects. Patients committed more errors in it and had a longer reaction time, which was associated with abnormal function of dorsolateral prefrontal cortex [30-31].

In the she study it was also showed that there were no significant difference in the severity of memory impairment and executive functions in adolescents with schizophrenia with early onset compared to patients with schizophrenia with onset during

adulthood. And even the ill youth obtained significantly better results in two parameters of the applied tests. These results are consistent with few works suggesting that cognitive impairment in patients with early onset are qualitatively and quantitatively similar to those disclosed by patients with the later onset of illness [17, 32]. In both studied groups the duration of the disease was relatively short, patients had comparable, small number of hospitalizations (usually 1-3), and all were treated with atypical neuroleptics. However, these groups differed in the intensity of psychopathological symptoms during the period of the study. Adolescents suffering from schizophrenia had significantly greater severity of psychopathological symptoms compared to adult patients, and still have not received worse outcomes in tests, and got even better in the individual parameters. In the WCST test they used much smaller number of cards to order the first category and in the N-back test had significantly faster response time compared with ill adults. However, the faster response time may be the result of age, as also the group of healthy peers performed the test more quickly than healthy adults and this was the only parameter in the tests differentiating the control groups from each other. These results are not consistent with previous statements about the large increase in cognitive impairment in patients with early-onset compared to those with onset in adulthood [9-10]. The data obtained can obviously only suggest that in the early years of schizophrenia may not be a difference in the severity of impairment of working memory and executive functions between people with early onset of the disease and those with the onset in adulthood. We cannot however exclude the possibility that, with the duration of the disease, particularly in those with early onset, can occur deterioration and cognitive disorganization. Some studies have shown deterioration in cognitive function efficiency after many years from the onset in patients with a greater number of previously experienced psychotic episodes [33]. But also the already mentioned works pointed to the lack of decrease of cognitive deficits in the average period of 9-10 years of disease in early-onset patients [17]. For example, in the reports from the 15-year long term follow-up, there was no difference in the severity of cognitive impairment among people with the onset in adolescence and adulthood, but significantly worse results were observed in patients with very early onset in childhood. Attention was also paid to the relationship between the severity of cognitive impairment and the length of duration of untreated psychosis and the type of getting ill. The longer the time of not treating psychosis and the so called deceitful conduct (type I by Crow), the greater the severity of cognitive dysfunction and worse psychosocial functioning [34].

It seems that there is a need to continue research on the specificity of cognitive impairment in schizophrenia, as they can help in finding answers to the following questions: Do cognitive dysfunctions are truly more severe in patients with early-onset compared to onset in adulthood? Do in patients with early-onset cognitive processes deteriorate with the duration of the disease? What factors are responsible for their stabilization or progression? Finding answers to the above problems will allow for better adjusted treatment, beginning from pharmacotherapy to cognitive functions training and psychotherapeutic treatment of patients with schizophrenia.

Conclusions

1. In patients with schizophrenia, regardless of the onset of the illness, in the period of partial remission problems with memory and executive functions occur.
2. No differences were found in the severity of memory impairment and executive functions in patients with early-onset compared to those with the onset in adulthood, in the initial years of the illness, which suggests that early onset of schizophrenia is not necessarily connected with more severe cognitive impairment.
3. Applying new generation of treatment with neuroleptics may have a significant impact on better cognitive functioning in patients regardless of the period of the onset.

Practical aspects

The results of the quoted and own research suggest the need for a comprehensive diagnosis of cognitive impairment in patients with schizophrenia, particularly in the early episodes, which will help in the selection of optimal treatment programs tailored to the needs of patients, ranging from pharmacotherapy to the psychotherapeutic treatment. They also point to the need for the inclusion of cognitive function training as an integral part of therapy of each patient with severe cognitive impairment. Early intervention, even already in the prodromal period, in which cognitive impairment occur, can reduce the negative consequences of the disease for the future psychosocial functioning of patients.

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