

COGNITIVE DEFICIT, POSITIVE AND NEGATIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

I.Memedi¹, L.Miloseva²

¹Department of Psychiatry, Clinical Hospital Tetova, Republic of North Macedonia.

²Full Prof. of Medical Psychology, Psychopathology & Psychotherapy, Faculty of Medical Sciences, Goce Delcev University, Stip, North Macedonia. e-mail: lence.miloseva@ugd.edu.mk

Corresponding author: Imran Memedi, Department of Psychiatry, Clinical Hospital - Tetova, North Macedonia. E-mail:imran.memedi@unite.edu.mk. ORCID: 0000-0002-4175-5616

Medicus 2020, Vol. 25 (3): 399-404

ABSTRACT

Objective: The aim of the study was to introduce the relationship between positive and negative symptoms, cognitive deficit and antipsychotic treatment in acute schizophrenic patients.

Methods: The study included 21 acute schizophrenic patients who were selected from the Psychiatric Hospital in Skopje, and were diagnosed according to the ICD-10. All patients were receiving antipsychotic medication treatment at the time of testing and during the time they were clinically stable. At the beginning of the treatment all subjects received higher dose of neuroleptics, and before they left the hospital they were given lower drug doses. The Positive and Negative Syndrome Scale (PANSS) was used to assess the severity of positive and negative symptoms respectively. The Schizophrenia Cognition Rating Scale (SCoRS) was used to assess the cognitive function before and after the neuroleptic treatment. Statistical analysis of the results obtained in the research was conducted with SPSS 20.0 for Windows package program. The results were analyzed by applying Wilcoxon Signed Ranks Test and Pearson correlation coefficient.

Results: The results indicated that the acute schizophrenic patients had higher global rating score in the SCoRS assessment (M=53.667, SD=8.345) in the first weeks after psychosis onset. After 6-8 weeks treatment with antipsychotic medications, they had lower global rating score in the SCoRS assessment (M=41.952, SD=6.951). There was a positive relationship between the total SCoRS score and the dose of neuroleptics ($Z=-3.925$, sig.=0.000, $p<.001$). The high degree of positive and negative symptoms was a strong predictor of higher cognitive deficits in schizophrenic patients. The positive relationship was observed between the high dose of therapy, PANSS-Positive and SCoRS level ($r=.552$, $p<.01$) and PANSS-Negative and SCoRS level ($r=.607$, $p<.01$). In addition, there was a positive relationship between the low dose of therapy, PANSS-Positive and SCoRS level ($r=.342$, $p<.05$) and PANSS-Negative and SCoRS level ($r=.432$, $p<.01$).

Conclusions: During our work, we found that the regular and continued use of antipsychotic medications in schizophrenic disorders and good co-operation with the patients during the therapy could be important for better cognitive function of the person.

Keyword: cognitive deficit, positive and negative symptoms, schizophrenia, treatment.

INTRODUCTION

Psychotic disorders are a heterogeneous group of diseases that also include schizophrenia which is described in literature as a severe chronic and progressive psychotic disorder. Schizophrenia is an endogenous mental disorder with a chronic course, characterized by dysfunction in many domains, such as: perceptions, thinking, emotions and cognition [1].

The scientific and clinical public is oriented toward early detection, treatment and rehabilitation, with a special focus on treatment in the community, however over the past 20 years with the advancement of science, schizophrenia has been studied in the direction of a neurodevelopmental and a neurodegenerative process. In the acute phase, schizophrenia is manifested by subtle behavioral changes, changes in the neuromotor and the cognitive sphere [2]. Due to the heterogeneity of the symptomatology manifestation in the early phase of schizophrenia, along with the predominance of positive and negative symptoms, cognitive deficit is also monitored, therefore early detection and treatment play a major role in reducing the difficulties of the person's functioning, but already in the chronic phase the disease is dominated by negative symptoms and cognitive dysfunction, which of course leaves sequels from a personal and behavioral aspect of the schizophrenic person.

Modern approaches to schizophrenia focus on symptomatic and functional remission in order to improve the overall functionality and quality of life in patients with schizophrenia. At the same time, the psychopharmacological treatment, the psychotherapeutic and social therapeutic interventions are directed towards this approach, which is an imperative in order to prevent a bad prognosis, i.e. to achieve long remissions, to reduce the positive and negative symptoms, as well as the cognitive impairment, which is a fundamental prerequisite for partial to complete recovery and achievement of a satisfactory quality of life [3].

From a clinical perspective, schizophrenia is usually manifested with a gradual and slow onset, very rarely abruptly within a few days or weeks and mostly in early adolescence or at young age, but may also occur later in life, and is more common in females. The clinical presentation is focused on the subjective and objective syndromes, symptoms or signs of schizophrenia, i.e. the manifestation of the disorder is heterogeneous and is best described by the so-called pentagonal model of symptoms

that includes positive, negative, cognitive, affective, and aggressive-hostile symptoms [4, 5]. The positive or psychotic symptoms in schizophrenia refer to painful ideas - delusions, illogical speech and hallucinations, and the negative symptoms include: decreased motivation, lethargy, numbness of emotional expression and poorer speech [6]. From pathophysiological aspects, the positive symptoms originate from the hyperactivity of the dopaminergic neurotransmitter system in the mesolimbic brain structures (hyperdopaminergia), and therefore respond therapeutically well to classical antipsychotics [7]. The negative symptoms arise from the hyperactivity of the serotonergic neurotransmitter system and the hypoactivity of the dopaminergic system in the frontal cortex (hypodopaminergia).

In recent years there has been a growing belief that neurocognitive deficit is a functional component of schizophrenia rather than a result of symptoms or treatment consequences. This deficiency is most commonly associated with dysfunction of the prefrontal cortex, the sensory and associative cortex, the motor cortex, and the basal ganglia [8]. The impairment of the cognitive functions is observed early in patients, initially it acts as an impairment of a milder degree, and the intensity may worsen over the course of the disease. Cognitive dysfunction in schizophrenia is manifested through the speed of information processing, attention, memory, thinking, the learning process, problem solving and social cognition, it is considered an important and basic feature in almost all patients with schizophrenia which appears as early as in the first episode of schizophrenia, but is also found in the premorbid phase, and in the more advanced phase the cognitive deficit is already constant and cannot be reduced to secondary, rather it is inherent to the disease [9, 10]. The influence of psychotic symptoms on cognitive dysfunction shows moderate correlations, with the possibility to reflect on certain domains of cognition such as the ability to solve problems, where the cognitive process has the main role through the poor speech expression [11, 12]. Neurocognitive tests show that only 30% of patients with schizophrenia have satisfactory cognitive functioning [13].

AIM OF STUDY

- To evaluate the level of positive and negative symptoms among patients with schizophrenic disorder.
- To determine the degree of cognitive deficit in patients

in the acute phase of schizophrenia using certain psychological scales.

- To investigate the relationship between cognitive deficit, positive and negative symptoms and treatment with neuroleptics in patients in the acute phase of schizophrenia.

MATERIAL AND METHODS

This average study according to its design included 21 respondents of both genders, from 20 to 40 years of age, who received hospital treatment at the Psychiatric Hospital Skopje-Skopje, diagnosed with schizophrenia according to the diagnostic criteria of the ICD-10 classification in the period from January to June 2020. All patients were monitored in a period of 3 to 5 weeks after hospitalization. The criteria for inclusion of the respondents were as follows: male and female, 18 to 60 years of age, schizophrenia (according to ICD-10), patients in the first episode of schizophrenia without prior antipsychotic therapy, while the criteria for exclusion of the respondents were as follows: younger than 18 years of age, diagnosis of comorbid psychiatric disorder, use of more than one antipsychotic. Initially all patients were treated with high doses of neuroleptics, and before they leave the hospital they received lower doses of each of the medications indicated above.

The examination was monitored through the following structured test and clinical procedure:

Standardized psychiatric clinical interview.

Non-standardized questionnaire for socio-demographic and clinical data designed for the needs of the research.

Psychiatric rating scales for clinical assessment of the expression of the symptomatology: the Positive and Negative Syndrome Scale - PANSS for schizophrenia assessment and the Schizophrenia Cognition Rating Scale - ScoRS.

The Positive and Negative Syndrome Scale - PANSS for schizophrenia assessment consists of three subscales [14]. The positive scale contains 7 items (madness, cognitive disorganization, hallucinatory behavior, anxiety, grandness, suspicion and hostility), which same as all the other items in this scale, are scored from 1 (absent) to 7 (extreme). The negative scale also contains 7 items (flat affect, emotional withdrawal, impairment of emotional reasoning, social withdrawal, difficulty in abstract thinking, lack of spontaneity, stereotypical thinking). The

maximum score on this scale is 49 points. The General Psychopathology Scale contains 16 items and presents the structure of the clinical presentation. Cronbach's Alpha for the 28 of 30 items were .756, which represents a good correlation between items.

The Schizophrenia Cognition Rating Scale - ScoRS is a scale for assessing the cognitive impairment and the extent of its effect on the everyday functioning in patients with schizophrenia [15]. The scale itself consists of 20 items that cover the following cognitive domains: memory (4 items), learning (2 items), attention (3 items), working memory (2 items), reasoning and problem solving (3 items), motor skills (2 items), language (1 item) and social skills (3 items). Each item is ranked from 1 (absent deviation) to 4 (expressed deviation), whereby higher scores reflect a greater degree of disorder. The time frame for the cognitive deficit should not be shorter than two weeks, with retesting performed 3-4 weeks after the commencement of the drug treatment. The statistical validity of the scales expressed with Cronbach is within the range from 0.743 to 0.782.

The statistical analysis was performed with the SPSS software package (Statistical Package for the Social Science, version 20), by applying the Wilcoxon Signed Ranks Tests and the Pearson correlation coefficient. The values of $p < 0.01$ and $p < 0.05$ were considered statistically significant and important.

RESULTS

In the study was designed as a prospective, we included 21 (M:F=12:9) acute schizophrenic patients with an average age of 31.34 years, within the range from 20 to 40 years of age, and a standard deviation of 6.43. With respect to marital status, most of the participants were unmarried (62.25 percent), while 37.75 percent were married at the time of the study. 14.7 percent had low level of studies, medium educational level was 81.1 percent of the sample, and only 4.2 percent had high educational level.

From Table 1 and Figure 1 we can see that the average value of the total score on the Positive and Negative Syndrome Scale for schizophrenia assessment is $M=130.286$ with a minimum and maximum value ranging from 77 to 175, of the negative symptoms $M=31.143$ with minimum and maximum values from 10 to 43, of the positive symptoms $M=32.476$ with minimum and maximum values from 20 to 40, and on the scale for general psychopathology $M=67.143$ with minimum and maximum values from 39 to 97.

Table 1. Means and standard deviations of PANSS measures in the study participants

Descriptive Statistic	PANSS-Positive	PANSS-Negative	PANSS-General psychopathology	PANSS-Total score
Mean	31.143	32.476	67.143	130.286
Standard Deviation	9.096	6.022	14.482	25.285
Minimum	10	20	39	77
Maximum	43	40	97	175
Count	21	21	21	21

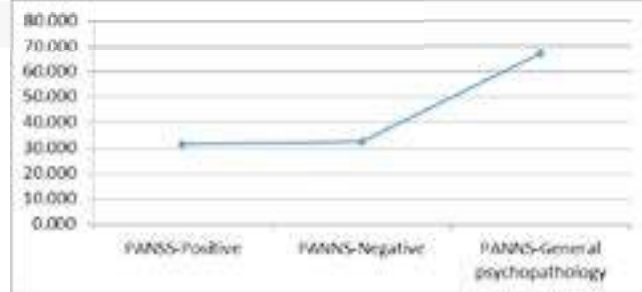


Figure 1. The level of PANSS subscales among participants

Table 2 and Table 3 show the mean values of the Schizophrenia Cognition Rating Scale and its domains in patients when they were receiving high and low doses of neuroleptic therapy. It is evident that at the beginning of the treatment the cognitive deficit is more expressed compared to the end of the hospital treatment, i.e. in the period when the patients left the hospital.

Table 2. Means and standard deviations of cognitive measures in patients with schizophrenia who used high doses of antipsychotic medications

	SCoRS (maximal drug use)	Memory	Learning	Attention	Working memory	Problem solving	Processing speed	Social cognition	Language	Global rating
Mean	53.66	10.52	5.42	8.19	5.66	7.85	4.95	8.23	2.66	3.90
SD	8.34	1.96	1.12	1.69	1.19	2.05	0.92	2.04	0.79	0.62
Minimum	38	7	3	4	4	3	3	4	1	3
Maximum	71	14	7	11	9	11	6	12	4	5
Count	21	21	21	21	21	21	21	21	21	21

Table 3. Means and standard deviations of cognitive measures in patients with schizophrenia who used low doses of antipsychotic medications

	SCoRS (minimal drug use)	Memory	Learning	Attention	Working memory	Problem solving	Processing speed	Social cognition	Language	Global rating
Mean	41.95	8.19	4.57	6.43	4.33	5.95	3.90	6.48	2.05	6.48
SD	6.95	1.50	1.08	1.36	1.39	1.77	0.89	2.16	0.59	0.60
Minimum	29	6	3	3	2	2	2	3	1	5
Maximum	54	10	7	9	7	9	6	12	3	7
Count	21	21	21	21	21	21	21	21	21	21

Figure 2 shows the values of the domains of the Schizophrenia Cognition Rating Scale at the beginning and the end of the treatment. By using the Wilcoxon signed-rank test, we found that a statistically significant correlation is present between the total SCoRS score and the dose of neuroleptic therapy ($Z=-3.925$, $sig.= 0.000$, $p<.001$).

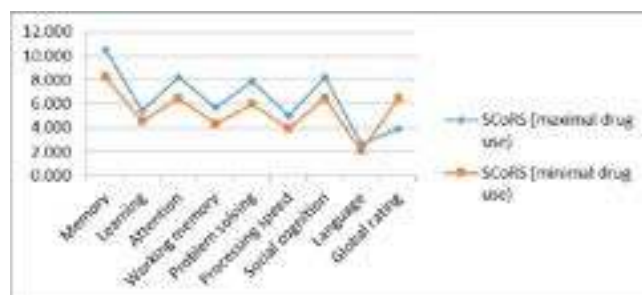


Figure 2. SCoRS global rating measures among schizophrenic patients

In Table 4 we can see that there is a statistically significant correlation between the high dose of therapy, the positive psychopathology of the disease and the total score of the ScoRS ($r=.552, p<.01$), as well as the negative symptomatology level ($r=.607, p<.01$). In addition, in Table 5 we can observe a positive correlation between the low dose of therapy, the positive psychopathology of the disease and the total score of the ScoRS ($r=.342, p<.05$) and the negative symptomatology and the total score of ScoRS ($r=.432, p<.01$).

Table 4. Correlation between the ScoRS (Maximal drug use) global rating and symptoms scales

Pearson Correlation	ScoRS (Maximal drug use)	PANSS-Positive	PANSS-Negative	PANSS-General psychopathology
ScoRS (Maximal drug use)	1			
PANSS-Positive	.557**	1		
PANSS-Negative	.607**	.666**	1	
PANSS-General psychopathology	.318	.060	.181	1

** . Correlation is significant at the 0.01 level (2-tailed).

Table 5. Correlation between ScoRS (Minimal drug use) global rating and symptoms scale

Pearson Correlation	ScoRS (Minimal drug use)	PANSS-Positive	PANSS-Negative	PANSS-General psychopathology
ScoRS (Minimal drug use)	1			
PANSS-Positive	.342*	1		
PANSS-Negative	.432**	.324*	1	
PANSS-General	-.204	-.447*	-.325	1

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Research shows that patients with schizophrenia suffer from a wide range of a cognitive deficits, which usually occur over a certain period of time, before and after the onset of the disorder, and this further determines the outcome of the mental condition. The cognitive deficits include changes in memory, attention, learning, performance function, abstract thinking, and language. It

should be noted that 75% of patients with schizophrenia suffer from cognitive symptoms as a result of the disease. Our obtained results confirm that positive and negative symptoms affect the cognitive functioning of the examined group of schizophrenic subjects.

Patients with schizophrenia suffer from a wide range of cognitive deficits, which usually occur within a specific period of time after the onset of the disorder, depending on the severity of the mental condition. Cognitive impairments include deficits in memory, attention, learning, performance function, abstraction, and language. It should be noted that up to 75% of patients with schizophrenia suffer from cognitive symptoms as a result of the disease. The most common cognitive symptom that leads to temporary or permanent damage to mental processes is the reduced ability to concentrate, which has a great impact on the process of acquiring new knowledge, it affects the form of the cognitive process, attention, speech, behavior, etc. The results of our research show that a cognitive deficit was present in the examined subjects at the beginning of the disease, but the application of an appropriate neuroleptic therapy leads to improved cognitive functioning in schizophrenic subjects in the acute phase of the disease.

Therefore, patients with schizophrenia need timely commenced antipsychotic therapy and psychosocial therapeutic interventions, in order to be able to affect the natural course of the disease. Simultaneously, the longer period that is required to achieve a satisfactory improvement of the patient's mental condition results in an extension of each subsequent deterioration from a mental aspect. At the same time, patients who show a poor response to neuroleptic therapy have residual psychotic symptoms that reduce the person's functional capacities [21, 22]. Therefore, it is believed that timely application of therapy (pharmacological, psychosocial and psychotherapeutic interventions) can reduce psychotic symptoms, reduce the regressive course of schizophrenia and prevent the development of therapeutic resistance.

Acknowledgments

The authors would like to express their gratitude to all participants who took part in this study.

Disclosure statement

None of the authors report any conflict of interest with this research.

REFERENCES

1. Galletly, C., Suetani, S., Dark, F. Medication discontinuation in first episode psychosis: thinking about the offset of psychotic disorder. *Australian Journal of Psychiatry* 2018; 52(9):819-824.
2. Nuechterlein, K.H., Barch, D.M., Gold, J.M., Green, M.F. Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research* 2004; 72:29-39.
3. McGurk, S.R., Reichenberg, A., Feo, C., Prestia, D. The course and correlates of everyday functioning in schizophrenia. *Schizophrenia Research Cognition* 2014; 1:47-52.
4. Green, M.F., Kern, R.S., Heaton, R.K. Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophrenia Research* 2004; 72:41-51.
5. Voruganti, L.N., Heslegrave, R.J., Awad, A.G. Neurocognitive correlates of positive and negative syndromes in schizophrenia. *Canadian Journal of Psychiatry* 1997; 42:1066-1071.
6. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. DC: American Psychiatric Association, 2013.
7. Heinrichs, R.W., Zakzanis, K.K. Neurocognitive deficit in schizophrenia: A quantitative review of the evidence. *Neuropsychology* 1998; 12:426-445.
8. Schaefer, J., Giangrande, E., Weinberger, D.R., Dickinson, D. The global cognitive impairment in schizophrenia: Consistent over decades and around the world. *Schizophrenia Research* 2014; 150:42-50.
9. Sharma, T., Antonova, L. Cognitive function in schizophrenia: Deficits, functional consequences and future treatment. *Psychiatric Clinics of North America* 2003; 26:25-40.
10. Green, M.F., Kern, R.S. Braff, D.L. Neurocognitive deficits and functional outcome in schizophrenia. *Schizophrenia Research* 2000; 26:119-136.
11. Dickerson, F., Boronow, J.J., Ringel, N. Social functioning and neurocognitive deficits in outpatients with schizophrenia. *Schizophrenia Bulletin* 1999; 23:19-28.
12. Pentilla, M., Hirvonen, N., Isohanni, M. . Duration of untreated psychosis as predictor of long term outcome in schizophrenia: systematic review and meta-analysis. *British Journal of Psychiatry* 2014; 205(2):88-94.
13. Vita, A., Deste, G., Barfati, S. Interview-based assessment of cognition in schizophrenia: applicability of the Schizophrenia Cognition Rating Scale (ScoRS) in different phases of illness and settings of care. *Schizophrenia Research* 2013; 146:217-223.
14. Kay, S.R., Fiszbein, A., Opler, L. *Positive and Negative Syndrome Scale (PANSS): Rating Manual Social and Behavioral Sciences Documents*. San Rafael: CA, 1987.
15. Keefe, R.S., Poe, M., Walker, T.M., Kang, J.W. The Schizophrenia Cognition Rating Scale: an interview-based assessment and its relationship to cognition, real-world functioning, and functional capacity. *American Journal of Psychiatry* 2006; 163:426-432.
16. Addington, J., Saeedi, H. The course of cognitive functioning in first episode psychosis: Changes over time and impact on outcome. *Schizophrenia Research* 2005; 78:35-43.
17. Saykin, A.J., Gur, R.C., Gur, R.E. Neuropsychological function in neuroleptic naïve patients with first-episode schizophrenia. *Journal of Neuropsychological Sciences* 2004; 1:88-99.
18. Bechard-Evans, L., Iyer, S., Lepage, M. Investigating cognitive deficits and symptomatology across pre-morbid adjustment patterns in first episode psychosis. *Psychological Medicine* 2010; 40:749-759.
19. Harvey, P.D., Keefe, R.S.E. Cognitive impairment in schizophrenia and implications of atypical neuroleptic treatment. *CNS Spectr* 1997; 2:1-11.
20. Keefe, R.S., Davis, V.G., Hilt, D. Reliability, validity and treatment sensitivity of the Schizophrenia Cognition Rating Scale. *European Neuropsychopharmacology* 2015; 25:1760184.
21. Torrey, E.F. Studies of individuals with schizophrenia treated with antipsychotic medication: A review. *Schizophrenia Research* 2002; 58:108-115.
22. Bedard, M.A., Scherer, H., Stip, E. Procedural learning in schizophrenia: further consideration on the deleterious effect of neuroleptics. *Brain Cognition* 2000; 41:31-39.