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Neuropsychological disorders in patients with schizophrenia and depression

Neuropsihološki poremećaji obolelih od shizofrenije i depresije

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Abstract

Background/Aim. Neuropsychological deficits among persons with psychotic disorders are identified clinically but also through many investigations. Comparison of patients with schizophrenia and depressive patients with healthy persons showed that both groups of patients are significantly impaired on the cognitive level compared to healthy persons. The aim of this study was to compare the neuropsychological functioning between patients with schizophrenia and depressive patients with psychotic symptoms (DPS) in remission, as well as between these two groups of patients and healthy persons. **Methods**. The study included 90 right-handed persons divided into three groups: 30 inpatients with schizophrenia, 30 inpatients with DPS, and 30 healthy persons. For examining neuropsychological functions of all participants, the following tests were applied: Wechsler's Individual Test of Intelligence (with subtests: Information, Digit Span, Arithmetic, Similarities, Picture Completion, Block Design, Digit Symbol), Mini-Mental State Examination, Trail Making Test, Rey-Osterrieth Complex Figure test, Hooper Visual Organization Test, phonemic, i.e., verbal fluency task, Rey Auditory Verbal Learning Test, and Wisconsin Card Sorting Test. **Results**. In the group of patients with schizophrenia, dysexecutive syndrome and reduced attention were singled out in several domains as basic deficits. Disturbances in abstract thinking and verbal fluency appeared together with dysexecutive syndrome, while attention disorders cause secondary damage to short-term memory, recognition in verbal modality, and information processing speed. In the neuropsychological profile of the DPS group, mild disturbances in the domain of visual search speed and information processing speed were noted. Impaired attention negatively affected the proper carrying out of other neuropsychological functions, while this phenomenon specifically impacted executive functions, visual gnosis, and processing speed among the DPS group. **Conclusion**. Neuropsychological disorders of patients with schizophrenia manifest in a larger number of cognitive domains and are more severe than those of the DPS group. In the DPS group, mild neurocognitive disorders were registered. Lack of motivation and effort during testing contributes to cognitive disturbances in the DPS group.

Key words:
depression; cognition disorders; neuropsychological tests; schizophrenia.

Apstrakt

Uvod/Cilj. Neuropsihološki deficiti osoba obolelih od psihotičnih poremećaja identifikuju se klinički, ali i mnogim istraživanjima. Poređenje obolelih od shizofrenije i depresije sa zdravim osobama pokazalo je da su obe grupe bolesnika značajno oštećene na kognitivnom planu, u odnosu na zdrave osobe. Cilj rada bio je da se uporedi neuropsihološko funkcionisanje između obolelih od shizofrenije i obolelih od depresije sa simptomima psihoze (DPS) u remisiji, kao i između ove dve grupe bolesnika i zdravih osoba. **Metode**. Ispitivanjem je obuhvaćeno 90 desnorukih osoba, svrstanih u tri grupe: 30 hospitalizovanih osoba obolelih od shizofrenije, 30 hospitalizovanih osoba obolelih od DPS i 30 zdravih osoba. Za ispitivanje neuropsihološke funkcije svih učesnika primenjeni su sledeći testovi: Vekslerov individualni test inteligencije (sa subtestovima: Informacije, Brojevi, Aritmetika, Sličnosti, Dopune, Kocka mozaik, Šifra), Kratko ispitivanje mentalnog statusa, Test trasiranja puta, Rej-Osteritov test složene figure, Huperov test vizuelne organizacije, zadatak fonemske, tj. verbalne fluentnosti, Rejov test auditivnog verbalnog učenja, Viskonsin test sortiranja karata. **Rezultati**. U grupi obolelih od shizofrenije kao bazični deficiti izdvojili su se disegzekutivni sindrom i redukovana pažnja u nekoliko domena. U sklopu disegzekutivnog sindoma nastale su i teškoće na planu apstraktnog mišljenja i verbalne fluentnosti, dok su smetnje pažnje sekundarno oštetile kratkoročnu memoriju, prepoznavanje u verbalnom modalitetu i brzinu obrade informacija. U neuropsihološkom profilu

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DPS grupe uočeni su blagi poremećaji u domenu brzine vizuelnog pretraživanja i brzine obrade informacija. Narušena pažnja negativno je uticala na pravilno odvijanje ostalih neuropsiholoških funkcija, dok je fenomen posebno uticao na egzekutivne funkcije, vizuelnu gnoziju i brzinu obrade informacija kod DPS grupe. **Zaključak**. Neuropsihološki poremećaji obolelih od shizofrenije ispoljavaju se u većem broju kognitivnih domena i težeg su stepena nego u grupi DPS. U grupi DPS registrovani su neurokognitivni poremećaji u umerenom stepenu. Nedostatak motivisanosti i uloženog napora tokom testiranja doprinosi kognitivnim smetnjama u DPS grupi.

Ključne reči:
depresija; saznanje, poremećaji; testovi, neuropsihološki; shizofrenija.

Introduction

Psychotic disorders are often connected with cognitive deficits. These deficits are registered through numerous studies that deal with the cognitive functioning of patients with schizophrenia (SCH) and patients with depression (DP) [1, 2]. More than 30 years ago, neurodevelopmental hypotheses [3, 4] emerged as an explanation for this phenomenon among patients with SCH, which was supported in later examinations [5, 6]. According to this concept, SCH is a neurodevelopmental disorder where abnormalities of the nervous system do not predominate until they interact with brain development processes, particularly in the frontal plane. Regarding depression, a model called the diathesis-stress model [7, 8] was presented. It explains that longer or repeated stress among adults, based on a hyperactive stress response system (due to early trauma), leads to a continuous increase of neuropeptide neurotransmitters, which is the basis for depression and anxiety.

Both groups of patients, with SCH and depression, were significantly more damaged compared to the group of healthy persons (HP) [9]. In addition, SCH is associated with a wide range of cognitive disorders (CDs), while according to meta-analytic studies, CDs among psychotic DP are mildly present [10].

It was demonstrated that the most prominent disorder among patients with SCH is information processing speed [11]. This deficit is conjoined with impaired immediate verbal memory already during the first episode of SCH [12]. Generally, patients with SCH display more severe disorders in all cognitive domains compared with DP [13].

Compared with the control group of HP, DP show weaker functioning of working, verbal, and visual memory, and disturbed information processing speed [14, 15]. Compared to the patients with SCH, those with post-acute depression show better functioning in the domain of verbal memory, fluency, and selective attention [16].

On cognitive levels, disturbed information processing speed is common among both disorders. Reductions in prefrontal cortex gray matter, which may be related to cognitive impairment, have also been reported in both disorders [17].

On the other hand, the results of the research, where they compared the cognitive functioning of patients with SCH and DP, are somewhat heterogeneous [18] because the severity of the clinical picture and stage of the disease have a significant impact on neuropsychological functioning. Here is a high probability of occurrence of neuropsychological disorders among those with psychotic disorders [19].

The aim of this study was to determine whether there are differences in cognitive functioning between patients with SCH and those with depression with psychotic symptoms (DPS) in the remission phase. Moreover, the aim was to determine the presence of differences between both patient groups and the HP on the level of cognitive functioning.

Methods

The study included three groups of right-handed subjects only because nobody was left-handed. Furthermore, determining the dominant hemisphere is more precise among the right-handed population because the vast majority of them have their left hemisphere as dominant for speech (at around 95–99% of cases). Among the left-handed population, the left hemisphere is dominant in a lesser number of cases (60–70%), and bilateral representation of speech is more common among the left-handed than the right-handed subjects [20].

The first group comprised 30 patients with SCH, the second 30 patients with DPS, and the third 30 HP. Both groups of patients were hospitalized in the Psychiatry Clinic of the University Clinical Center of Serbia. For this investigation, Ethics Committee Approval was obtained from the University Clinical Center of Serbia (No. 420/2, from 26 December 2024). Patients gave their written consent for hospitalization upon arriving at the clinic, and they confirmed weekly their written consent for applying diagnostic and therapeutic procedures.

Patients were diagnosed according to the International Classification of Diseases, 10th revision (ICD-10) criteria and were tested during clinical remission. Remission was confirmed by applying the Positive and Negative Syndrome Scale (PANSS) in the group of patients with SCH and the Hamilton Rating Scale for Depression (HRSD) in the group of DP, where the average score ± standard deviation was 51.32 ± 2.51 and 5.20 ± 2.10, respectively.

Neuropsychological testing was carried out in the scope of relevant diagnostic procedures. Exclusion criteria implied the presence of organic psycho-syndromes, neurological illnesses, substance or alcohol abuse, and disorders such as head trauma, brain insult, and epilepsy. Inclusion criteria constituted persons who never had organic psycho-syndromes, neurological illnesses or disorders (head injuries, epilepsy), and those who did not suffer from alcohol or substance abuse.

The applied neuropsychological battery comprised the following tests: Wechsler's Individual Test of Intelligence

(WITI), which is a version of the Wechsler Adult Intelligence Scale in Serbian language standardized on the Serbian population [21] (subtests: Information, Digit Span, Arithmetic, Similarities, Picture Completion, Block Design, Digit Symbol), Mini-Mental State Examination (MMSE) [22], Trail Making Test (TMT) [23], Rey-Osterrieth Complex Figure (ROCF) test [24], Hooper Visual Organization Test (HVOT) [25], phonemic, i.e., verbal fluency (VF) task [26] (adapted Benton Controlled Oral Word Association Test and given with three letters: s, k, l), Rey Auditory Verbal Learning Test (RAVLT) [27], and Wisconsin Card Sorting Test (WCST) [28].

WITI is a composite test consisting of six verbal and five non-verbal subtests. The test evaluates the current intellectual status of adults and adolescents. Verbal, non-verbal, and total intelligence quotients are derived from test scores. Subtest Information examines general knowledge that most people should have. Digit Span is a test of attention span and immediate memory, i.e., short-term memory. Subtest Arithmetic examines the ability to calculate and concentrate, while results are also influenced by immediate memory and calculi (arithmetic operations in the narrow sense). Subtest Similarities examines abstract thinking, i.e., finding a mutual category of objects. The Picture Completion subtest investigates visual gnosis and is based on visual perception, visual organization, and conclusions, as well as on long-term memory. Block Design subtest is a test of constructional and visuospatial abilities, i.e., it examines constructional praxis in three dimensions. The Digit Symbol subtest is an attention and processing speed test. Manual proficiency, sharpness of vision, and visual-motor coordination are significant as well.

MMSE is dedicated to evaluating cognitive falls. The test is a composite of many simple tasks.

TMT consists of two parts, A and B. Part A evaluates mostly attention, i.e., concentration, visual perception, and visual search speed. Besides the aforementioned, part B evaluates complex visual search speed, which is part of executive functions.

RAVLT in verbal modality (VM) examines learning, recognizing, and recalling. In the scope of all these functions, immediate memory, learning strategy, creation of learning curve, proactive and retroactive interference, tendencies towards confabulation, and retention evaluation are being determined.

In the first part of ROCF, constructional praxis in two dimensions is being examined. In the second part of the test, learning and postponed memory, as well as evoking in visual modality, are being examined.

HVOT examines visual-perceptive analysis and conceptual reorganization of fragmented objects. Achievements on this test mostly depend on visual-spatial organization, visual gnosis, and conceptual abilities.

Achievements in VF depend on the ability to formulate a specific strategy for remembering words and intact divergent thinking that allows finding more correct answers to the same task.

WCST is the most famous test for revealing perseveration and mental rigidity. Success on this test depends on perception organization, experience with adequately remembered material, and other aspects of thinking.

Data processing was conducted using standard statistical procedures in SPSS (Version 16.0.1). Group differences were analyzed using Analysis of Variance (ANOVA), which is appropriate for this sample size given that the central limit theorem supports the approximation of normality in the sampling distribution of the mean, even with imperfectly distributed original data sources [29]. The value of $p \leq 0.05$ is considered statistically significant

Results

The study included a total of 90 respondents divided into three groups: patients with SCH, DPS, and HP. Each group (n = 30) had an equal number of men and women. They were similar in terms of age ($p > 0.05$), education level ($p > 0.05$), and gender (Chi-square = 1.97, $p > 0.05$) (Table 1). Education level was determined according to the number of years and months of schooling.

On all applied WITI subtests, significant differences between groups were noted (Table 2). Achievements on subtests Information ($p < 0.01$), Similarities ($p < 0.01$), Picture Completion ($p < 0.01$), and Digit Symbol ($p < 0.01$) are significantly lower in both patient groups compared to the control group, while patients with SCH had significantly lower values compared to patients with DPS. These subtests are indicators of the level of general knowledge, abstract thinking, visual gnosis, and information processing speed. Subtests Digit Span ($p < 0.01$) and Arithmetic ($p < 0.01$), which represent attention span, short-term memory, and concentration, differ significantly between the group with SCH and the other two groups. On the subtest Block Design that examines construction praxis in three dimensions, the achievements of the two patient groups are significantly lower compared to the control group ($p < 0.01$).

Significant differences between groups were registered on the MMSE, by which the general cognitive level was examined. Patients with SCH had significantly lower achievements compared to the other two groups ($p < 0.01$) (Table 3). The time needed to complete the task, visual search speed – TMT A ($p < 0.01$), was significantly prolonged in both patient groups compared with the HP group, while patients with SCH required significantly more time for this task compared with the DPS group. Complex visual search speed –

Table 1

Main demographic characteristics of respondents of all groups

Parameter	Groups			F test	*p*-value
	SCH	DPS	HP		
Age	42.398 ± 7.248	43.38 ± 8.76	41.73 ± 6.54	0.50	> 0.05
Education level	13.178 ± 2.035	13.59 ± 2.32	13.57 ± 2.52	0.42	> 0.05

SCH – schizophrenia; DPS – depression with psychotic symptoms; HP – healthy persons.
Values are given as mean ± standard deviation.

Table 2

Achievements of respondents of all groups on Wechsler's Individual Test of Intelligence (WITI) subtests

Subtests	Groups			F test	*p*-value
	SCH	DPS	HP		
Information	12.97 ± 6.72	16.57 ± 2.01	19.38 ± 6.60	10.25	< 0.01
Digit Span	13.07 ± 3.49	15.70 ± 3.16	16.77 ± 3.73	13.45	< 0.01
Arithmetic	10.49 ± 2.85	12.76 ± 2.32	12.90 ± 2.77	10.77	< 0.01
Similarities	11.58 ± 4.08	14.60 ± 5.59	17.52 ± 3.03	13.93	< 0.01
Picture Completion	11.09 ± 2.99	12.83 ± 2.91	14.65 ± 1.84	14.45	< 0.01
Block Design	18.41 ± 7.73	23.20 ± 14.11	30.17 ± 2.00	10.46	< 0.01
Digit Symbol	23.78 ± 11.62	29.00 ± 1.77	39.38 ± 2.50	11.31	< 0.01

Values are given as mean ± standard deviation.
For abbreviations, see Table 1.

Table 3

Achievements of respondents of all groups on neuropsychological tests

Tests	Groups			F test	*p*-value
	SCH	DPS	HP		
MMSE	26.28 ± 1.80	27.93 ± 1.19	28.08 ± 1.24	7.36	< 0.01
TMT A	70.00 ± 10.60	62.17 ± 24.22	52.41 ± 16.31	14.22	< 0.01
TMT B	137.73 ± 34.13	128.07 ± 19.36	114.41 ± 57.25	3.65	< 0.01
ROCF C	27.24 ± 2.83	28.24 ± 3.91	28.75 ± 5.91	1.53	> 0.05
ROCF 40'	12.06 ± 2.94	13.15 ± 4.32	15.41 ± 8.21	3.69	< 0.05
HVOT	21.19 ± 4.00	20.65 ± 4.12	21.55 ± 2.38	0.69	> 0.05
VF s	9.83 ± 5.50	10.83 ± 1.63	11.60 ± 1.80	3.47	< 0.05
VF k	12.07 ± 1.40	11.00 ± 4.200	12.80 ± 1.02	6.39	< 0.05
VF l	8.93 ± 1.40	8.07 ± 3.10	8.90 ± 1.31	2.25	> 0.05
RAVLT t	44.05 ± 4.24	43.52 ± 7.88	46.50 ± 7.77	2.48	> 0.05
RAVLT e	7.58 ± 1.73	7.86 ± 2.60	7.90 ± 1.08	0.43	> 0.05
RAVLT r	11.39 ± 1.36	11.93 ± 1.10	12.52 ± 2.18	3.50	< 0.05
WCST ca	3.23 ± 1.61	4.73 ± 1.20	5.01 ± 1.06	4.15	< 0.05
WCST fms	2.34 ± 1.39	1.36 ± 0.91	1.27 ± 0.52	14.99	< 0.01
WCST per	53.10 ± 24.15	42.48 ± 21.46	30.37 ± 26.97	10.25	< 0.01

MMSE – Mini-Mental State Examination; TMT A – Trail Making Test (TMT) that evaluates attention, i.e., concentration, visual perception, and visual search speed; TMT B – TMT that evaluates complex visual search speed in addition; ROCF C – copying of the Ray-Osterrieth Complex Figure (ROCF); ROCF 40' – postponed visual memorizing of the ROCF; HVOT – Hooper Visual Organization Test; VF s – verbal fluency: overall number of collective nouns that begin with letter s; VF k – verbal fluency: overall number of collective nouns that begin with letter k; VF l – verbal fluency: overall number of collective nouns that begin with letter l; RAVLT t – total number of repeated words in five attempts in the Rey Auditory Verbal Learning Test (RAVLT); RAVLT e – number of repeated words after 30 min (evocation) in the RAVLT; RAVLT r – number of correctly recognized words (recognition) in the RAVLT; WCST ca – categories achieved in the Wisconsin Card Sorting Test (WCST); WCST fms – failures to maintain set in the WCST; WCST per – perseverative responses in the WCST. For other abbreviations, see Table 1.
Values are given as mean ± standard deviation.

TMT B ($p < 0.01$), drastically differentiated the group with SCH from the HP group. Both patient groups had significantly lower achievements on VF s and VF k in the domain of highly frequent words compared to the HP group ($p < 0.05$). Examining executive functions showed significant differences between groups. Both groups of patients had drastically lower working memory – WCST ca ($p < 0.05$), as well as drastically increased number of perseverative answers – WCST per ($p < 0.01$), compared to the control group of HP. On the other hand, the SCH group had significantly lower WCST ca and WCST per compared to the DPS group. Visual memory – ROCF 40' ($p < 0.05$), the ability to recognize previously learned material – RAVLT r ($p < 0.05$), that reflect the learning capacity, as well as prolonged attention – WCST fms ($p < 0.01$), were drastically lower in the SCH group compared to the other two groups.

Discussion

Significant differences in the achievement of most of the applied tests were identified among the SCH group in clinical remission. Results show that the most noticeable deficits in this group include information processing speed, level of general knowledge, abstract thinking, visual gnosis, and constructional praxis in three dimensions because their achievements are significantly lower compared with the control group on tests that evaluate these functions. To the same degree, the following examined attention modalities were

disrupted: attention span, concentration, prolonged attention, visual and complex visual search speed, followed by one or a couple of peculiarities in the scope of complex mental, motor, or perceptual activity. Disruptions of short-term memory and a tendency for perseveration are also significant among SCH patients. To a mild degree, working memory (the capacity of learned content in VM and phonemic/VF, i.e., verbal divergent thinking that leads in different ways towards a goal) was reduced.

In the active phase of illness, the presence of incoherent speech was observed among a certain number of patients with SCH included in the investigation. Although this characteristic does not imply a disorder of language functions, such as aphasia, difficulties of VF may be, to some extent, the consequence of a lack of coherence, i.e., a lack of structure in the discourse.

However, although the cognitive level is significantly lower in this group, from the clinical point of view and the perspective of everyday functioning, these patients do not have drastic CDs because their MMSE score is in normal ranges. This is also supported by the preserved capacity of verbal learning and remembrance, constructional praxis in two dimensions, mental rotation, and phonemic/VF in the domain of low-frequency words.

Differences in neuropsychological profiles between the two groups of patients are worse for patients with SCH in terms of levels of general knowledge, abstract thinking, visual gnosis, short-term memory, and recognition in VM, as well as in executive functions.

Furthermore, several attention modalities are reduced in the SCH group compared with the DPS group: simple attention (span), concentration, information processing speed, visual search speed, and prolonged attention.

By analyzing neuropsychological disturbances in the SCH group, dysexecutive syndrome (disrupted working memory and increased number of perseverative answers) and reduced attention in a couple of domains (simple, prolonged attention, concentration, and visual search speed) were noted as basic deficits. As part of dysexecutive syndrome, difficulties in abstract thinking and VF occur as well. On the other hand, attention disorders secondarily disrupt short-term memory, recognition on VM, and information processing speed.

Two groups of patients function similarly in the domain of constructional praxis in three dimensions – complex conceptual memory, visual memory, and VF.

Mild CDs were registered in the DPS group. Their achievements were significantly lower on a smaller number of tests compared to the HP group. Besides that, their results are either drastically better or similar to those of the SCH group.

General cognitive level, short-term memory, simple attention (attention span), and concentration among DPS patients are preserved. Moreover, complex visual search speed, visual memory, and recognition in VM are being carried out without difficulties. Their executive functions (working memory, perseverative answers), information processing speed, and visual search speed are damaged to a mild degree compared to the SCH group. This pattern of achievement is applied to abstract thinking as well as visual gnosis and the level of general knowledge.

In the neuropsychological profile of patients with DPS, mild disturbances in the domain of attention, visual search speed, and information processing speed are being singled out. In general, disrupted attention negatively influences the proper carrying out of other neuropsychological functions, while among the depression group, this phenomenon specifically influences executive functions, visual gnosis, and processing speed.

Besides the fact that the patients with DPS were investigated in the remission phase, during testing, they did not put enough effort into working on tests, and their motivation for this kind of examination oscillated, with the tendency to get discouraged when faced with more difficult challenges. More precisely, psychogenic factors contributed to lower achievements in this group. This was specifically brought to light on the tasks that examined general knowledge because these tasks included searching and recalling information stored in long-term memory.

Neuropsychological disturbances that were registered among the groups of patients with SCH and DPS are in harmony with previous investigations [30] and can be considered permanent [31, 32], keeping in mind that these difficulties were registered in remission, i.e., when symptoms of mental disorders were gone. Given that the research included middle-aged people, the possibility of a further deterioration of neuropsychological functions as a cause of aging cannot be ruled out, which leads to a longer duration of the disease. To check this assumption, longitudinal studies that would enable tracking of cognitive flows of these mental disorders are necessary.

Given that this is a cross-sectional study represents a certain limitation to our investigation. That being said, the patients are not retested in later stages of treatment after discharge. Therefore, conclusions on potential variations over time in their cognitive profiles cannot be made. In order to come to a more precise conclusion, longitudinal monitoring in terms of retesting is necessary.

Conclusion

Neuropsychological disturbances of patients with schizophrenia are being demonstrated in a more significant number of cognitive domains and are at higher levels compared to patients with depression.

Among the patients with schizophrenia in clinical remission, dysexecutive syndrome, disrupted information processing speed, and disrupted attention in a couple of domains were noted. Executive difficulties were followed by compromised abstract thinking and disrupted verbal fluency. As a consequence, attention difficulties reduce short-term memory, recognition in visual memory, and information processing speed.

Among the patients with depression with psychotic symptoms in clinical remission, neurocognitive disorders of a mild degree were registered. Disrupted visual search

speed and information processing speed secondarily disrupt executive functions and visual gnosis. Lack of motivation and effort during testing contributes to cognitive deficits.

The results of this investigation can serve as a basis for planning neuropsychological rehabilitation of patients with schizophrenia and patients with depression with psychotic symptoms in clinical remission in terms of designing principal, general, and special methods of treatment of cognitive dysfunctions. Special methods can apply an individualized approach to every patient according to their neuropsychological deficits.

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