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Cognitive aspects of schizophrenia / a narrative review

Kognitivni aspekti šizofrenije – narativni pregled

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ABSTRACT

Cognitive dysfunction has been recognized as a key aspect of schizophrenia evident even during remission of symptoms. During the previous decade, interest in cognitive deficits has increased due to the recognition of their key importance for the functional outcome and degree of social adaptation. Prominent cognitive deficits are disorders of memory, attention and executive functions that manifest themselves as a disorder of verbal fluency, problems with serial learning, difficulty in problem solving, and disturbance of executive functions. The observed cognitive deficit is attributed to the dysfunction of cortical-cerebellar-thalamic circuits. Social cognition is the ability to construct an image of relationships between oneself and others and the ability to use flexible mental constructs as a guide to social interactions. The data from previous studies strongly support the association of neurocognitive and sociocognitive deficits with the performance of independent functioning and quality of life, emphasizing the need for prevention and treatment of cognitive deficits.

Key words: schizophrenia; cognitive dysfunction; social cognition.

APSTRAKT

Kognitivna disfunkcija je prepoznata kao ključni aspekt šizofrenije, očigledan čak i tokom remisije simptoma. Tokom prethodne decenije povećano je interesovanje za kognitivne deficite zbog prepoznavanja njihovog ključnog značaja za funkcionalni ishod i stepen socijalne adaptacije. Izraženi kognitivni deficiti su poremećaji pamćenja, pažnje i izvršnih funkcija koji se manifestuju kao poremećaj verbalne fluentnosti, problemi sa serijskim učenjem, teškoće u rešavanju problema i poremećaj izvršnih funkcija. Uočeni kognitivni deficit se pripisuje disfunkciji kortikalno – cerebelarno - talamičkih kortikalnih kola. Socijalna kognicija je sposobnost da se konstruiše slika odnosa između sebe i drugih i sposobnost korišćenja fleksibilnih mentalnih konstrukata kao vodiča za društvene interakcije. Podaci iz prethodnih studija snažno podržavaju povezanost neurokognitivnih i sociokognitivnih deficita sa performansama samostalnog funkcionisanja i kvalitetom života, naglašavajući potrebu za prevencijom i lečenjem kognitivnih deficita.

Ključne reči: šizofrenija; kognitivna disfunkcija; socijalna kognicija.

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INTRODUCTION

Cognitive deficits have been recognized as a key feature of schizophrenia since the time of Krepelin[1]. Krepelin emphasized his concept of key characteristics of the disorder by the name he chose for it: it is a disease that begins at an early age ("precox") and has a relatively chronic course characterized by significant cognitive and social damage ("dementia")[1]. The neuropsychological theory begins with the assumption that psychotic disorders are a consequence of cerebral dysfunction and that clinical sympomatology has neurofunctional correlates, that is, it is possible to link a psychological deficit with a site of brain damage[2].

Cognitive processes are the fundamental basis of psychological, behavioral and interpersonal aspects of human interactions [3]. Cognition includes every mental process that can be described as an experience of knowing, observing, recognizing, reasoning, and concluding[3]. Within the cognitive functioning, two domains are taken into consideration: the domain of neurology and social cognitive domains. Conceptually, neuroscience includes the acquisition of general information and processing functions such as attention, memory, information processing speed, language, speech and executive functions[4].

Social cognition is the ability to construct an image of relationships between oneself and others and the ability to use flexible mental constructs as a guide to social interactions, with the aim of solving adaptive problems within complex social behavior[5]. The capacity for presenting one's own mental state and the mental state of another person is a key feature of social competence6. Social cognition is presented as a multidimensional construct which includes different subcomponents: 1) Theory of the mind (ToM), 2) Social perception, 3) Social knowledge, 4) The recognition of emotions, and 5) Attributional style[7,8]. Although these domains are generally accepted and represent a construct of social cognition, their boundaries can not be considered absolute and there is a significant overlap between them[8].

In patients with psychiatric disorders, cognitive errors of internal processes and their interference with external stimuli were observed i.e. the misrecognition of internal content as external content, early conclusions, intolerance towards ambiguity, attention and perception disturbances, delusional beliefs, errors of conclusion[9], have been observed. The processing of socially relevant information relies on neurocognitive capacities, and therefore it is not clear to which degree these two cognitive domains are independent, given the neuronal correlations of both cognitive constructs. The results of factor analysis suggest that neurocognition and social cognition are two separate fields of sensitivity in psychosis[10-12].

COGNITIVE DEFICITS IN SCHIZOPHRENIA

Cognitive dysfunction has been recognized as a key aspect of schizophrenia evident even during symptom remission[13,14]. During the previous decade, interest in cognitive deficits had been increased due to the recognition of their key importance for the functional outcome and degree of social adaptation15. Prominent cognitive deficits are disorders of memory, attention and executive functions that manifest themselves as a disorder of verbal fluency, problems with serial learning, issues with problem solving, and dysfunction of executive functions (problems with maintaining and focusing attention, concentration, prioritization, and modulating behavior in relation on social hints) [16,17]. The observed cognitive deficit is attributed to the dysfunction of cortical-cerebellar-thalamic circuits[18]. Attention deficit is considered to be the primary cognitive deficit in schizophrenia, also observed in the pre-morbid period[19]. Schizophrenia is a neurodevelopmental disorder, but the etiopathogenesis of cognitive deficits is still unknown. The assumption is that changes in the brain represent a cumulative effect of neurodevelopmental abnormalities, changes in neuroplasticity and changes in neural maturing[20]. Changes in the neuroplasticity of brain-mediated neurotrophic growth hormone (BDNF) hippocampal cells contribute to the formation of cognitive deficits[21].

Schizophrenia is to some extent characterized by cognitive heterogeneity, which is confirmed by the coexistence of a smaller group of schizophrenic patients with preserved cognitions[22,23]. The existence of a group of neuropsychologically normal individuals with schizophrenia is incompatible with the idea that the damage to neurocognition is the main feature of schizophrenia. Therefore, the existence of such a subgroup could have important implications for efforts to understand not only the neuropathology of this disorder, but also the etiological heterogeneity of this disorder and the possible implications for treatment[24]. In other words, if cognitive impairment is understood as a fundamental feature, then it should have occurred in every patient, and only the degree of its severity may vary[25].

Considering the existence of cognitive heterogeneity, stratification into four cognitive subgroups within schizophrenia is proposed; two extreme subgroups (one with a nearly normal cognitive profile and one with extremely worsened cognitive performance) and two transitional categories with moderate cognitive-domain dysfunctions[26]. Only a few studied the prevalence of otherwise normal neuropsychologically status of patients with schizophrenia, and the results of these studies were inconsistent and estimates of prevalence vary between 55 and 2%[22, 24]. However, Kremen and associates point out that even neuropsychologi-

cally normal patients have poorer neuropsychological performance compared to the expected or premorbid level of functioning[22].

Studies that did research of cognitive deficits in different stages of illness (first episode, repeated episodes, chronic stage) confirm the existence of cognitive deficits in all phases, including healthy relatives. Within the neurodevelopmental model, it is considered that these deficits exist even before the onset of full psychosis, while the persistence of deficits that is more prominent in chronic groups confirms current neurodevelopmental and neurodegenerative changes[27].

Magnetic resonance functional studies have documented that patients with schizophrenia have reduced blood flow and glucose utilization in a prefrontal cortex, a concept known as hypofrontality. Hypofrontalityis functionally expressed in the deficiencies of working memory and exquisite functions[28, 29]. Despite extensive literature on hypofrontality in schizophrenia, neuronal mechanisms that are at the core of this pathophysiological trait remain unknown. Possible causes include damaged synaptic association and neurotransmission resulting from neurodevelopmental and/or genetic factors. These disorders can, at least partially, explain the dysregulation of dopamine activity in the limbic striatum and mediodorzal thalamus, which have reciprocal relationships with the prefrontal cortex (cortical-cerebellar-thalamic circuits). The activity in this neural circuit is regulated by gabaergic neurons by producing synapses with glutamatergic pyramidal neurons in the prefrontal cortex[30]. Gabaergic interneurons containing parvalbumin as markers of these neurons are particularly relevant in schizophrenia studies[31]. In addition, this network activity is associated with EEG gamma rhythms and cognitive processing. Indeed, patients with schizophrenia show deficiency in gamma rhythms[32], which increases the possibility that dysfunction of gabergic neurons (especially parvalbumin-containing cells) is an important contributor to the dysfunction of the prefrontal cortex in the disease and the onset of cognitive deficits.

The relationship between cognitive abilities and positive and negative psychopathology in schizophrenia has been the subject of several authors' studies. There is a general consensus that positive psychotic symptoms are not associated with cognitive performance[33,34]. However, the relationship between negative symptoms and cognition is less clear. Individually, the authors of the studies recorded inconsistent conclusions as to the possible relationship between negative symptoms and cognitive abilities. The relationship between them is described by some authors[35-38], but not by all[39-41]. The results of meta-analytic studies have shown the existence of a small to moderate correlation[33,34]. Considering the complex relationship, models have been suggested in which it is proposed that negative symptoms and cognitive dysfunction have a common etiology[42].

Most of the social cognitive studies in schizophrenic patients were conducted in relation to the three most commonly investigated domains: Theory of the Mind (Tom), the emotional perception / recognition and attributional style[43], and therefore the research does not provide complete and consistent answers. Studies that dealt with ToM in schizophrenia have almost the same conclusions that people with schizophrenia show clear deficiencies in ToM in relation to healthy control subjects and patients with other psychiatric disorders[44,46]. Given that first-degree sufferers of schizophrenia also report disturbances in ToM, this finding suggests that ToM deficiency could be a potential endophenotype for schizophrenia[47]. By examining deficits through different stages of the disease, the existence of deficits throughout all stages of the disease was confirmed, and that the deficit at the onset of the disease was comparable to the deficit observed in the chronic stage of the disease[48]. However, studies still can not give a precise answer as to whether these deficits are "straight" or "trait" markers[49,50]. Also, meta-analytical studies of socio-cognitive deficits in schizophrenia confirm the existence of deficits[51] and emphasize the existence of a direct relationship between a sociocognitive deficit and a functional outcome[11, 52].

Although recent modeling studies suggest that social cognition is independent of negative symptoms[53,54], other studies show the association of negative symptoms with the results of social cognitive tests[55]. Relationships with positive symptoms are similarly inconsistent and unclear56. Somewhat higher consistency in literature was found for associations between attributive style and delusion or paranoid belief[57,58]. Deficiencies identified during the symptomatic remission period confirm the independence of the clinical condition deficit, while on the other hand there are findings confirming the deterioration of the performances during the acute disease[59] and indicate the partial correlation of the specific characteristics of the disease, such as the negative symptoms[60] and disorganization[61].

The data from previous studies strongly supports the correlation of neurocognitive and sociocognitive deficits with the performance of independent functioning and quality of life, emphasizing the need for the prevention and treatment of cognitive deficits[62,63]. Lam et al.[64] in the study of the relationship between neurology and social cognition in schizophrenia attempted to check the hypothesis that the theory of mind and empathy could mediate between neurocognitive abilities (executive function or perception)

and clinical symptomatology (negative, positive and general symptoms). In an attempt to clarify the relationship between neurocognitive abilities and negative or positive symptoms in schizophrenia, it has been found that ToM (Theory of Mind) is a complete intermediate[11]. In particular, the findings of the research indicate that impairments in perception or executive functioning worsen the interpretation and understanding of mental states or intentions of others. Such a deficit, according to Fet and associates, can condition the emergence of negative symptoms[11]. In other words, deficits in the organization, identification and interpretation of sensory information in presenting and understanding of the environment, as well as the skills of problem solving, influence the ability to detect social cues of "Faux pass" in interindividual interactions. On the other hand, there is a backward impact on social functioning, disabling pleasure in social interactions. In addition, the deficit of executive functions may predispose the emergence of positive symptoms by increasing ToM deficiency in schizophrenia[11]. In general, the conclusion would be that the lack of control and regulation of cognitive processes, such as work memory, reasoning, flexibility in solving tasks in people with schizophrenia, aggravates the ability to detect social indications and "Faux pas". This further leads to several psychopathological outcomes such as hallucinations, delusional beliefs, and bizarre behavior[64].

NEUROANATOMIC BASES OF COGNITIVE DEFICITS

In studies of diffuse structural abnormalities, the expansion of the third chamber and lateral chambers of the cerebrospinal fluid system is the most consistent of the abnormalities in schizophrenia65. Although this is a non-specific marker, ventricular enlargement is associated with impaired performances in neuropsychological tasks and possibly followed by negative symptoms[66]. Findings indicate that abnormalities during neurological development affect neuronal migration, survival and interconnection[67]. In functional neuroimaging studies, there was no localized center for hallucinations or delusional beliefs, but a contribution has been observed of the cortex, frontal areas, cingulate gyros, and subcortical structures[68].

From the standpoint of cognitive neuropsychology, the occurrence of auditory hallucinations is explained as a monitoring disorder internal speech[68]. The source of hallucinations themselves is not clear, but it is assumed that they are externalized thoughts due to the disturbance of internal speech monitoring mediated by normal premotor cortex, cerebellar cortex, lentiform cores, thalamus, hipocampus, temporal cortex[4]. Patients with schizophrenia and auditory verbal hallucinations have, according to measurements of magnetic resonance, reduced volume of the upper temporal gyrase and wider cerebral chambers, where those with more intense hallucinations have a lower volume of the upper temporal convolution[69]. Voxel MR volumetry shows that the reduction of the left Heshla gyrus is associated with hallucinations, while the reduction of the left temporal planum associated with delusionary ideas[70]. Functional tests link distortions of reality with activation in the temporal lobe and the frontal Cingular cortex[68]. However, other researchers document that wider areas of the brain can be active during auditory hallucinations, and that there is activation of the corresponding sensory areas in the onset of hallucinations in this modality[71].

In terms of neuroanatomical correlates of observed social cognitive deficits, Bas and associates consider social cognition to be associated with the shift of brain activity into the medial orbitofrontal cortex, amygdala, and right insula[72]. Studies by Eilman and associates have shown a decrease in amygdala activity compared with the control group, which is in line with the results of previous research[73]. It is believed that the amygdala and the orbitofrontal cortex have a significant contribution in the facial expression process, while the medial and orbitofrontal cortex are related to theTheory of mind. The front cingular gyrus is a key component that controls affective and cognitive functions. As part of the rostral limbic system, ACG modulates internal emotional responses, and is considered an integral component of various exquisite functions as well as an essential component of social cognition or mentalization[74]. A disorder in this region can be associated with social cognition and psychopathology in schizophrenia[75].

CONCLUSION

Cognitive impairment is the basic domain of schizophrenia dysfunction. Relatively stable and permanent cognitive deficiencies limit the functional recovery capacity. The premorbid existence of cognitive deficits in people who will later develop schizophrenia, as well as the presence of defects in close non-infected relatives suggests that cognitive deficits may be a marker of vulnerability to schizophrenia. Considering the complex relationship between symptomatology and cognitive deficits, and their impact on the degree of functionality, neurocognitive rehabilitation represents a significant focus of treatment.

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