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THE CONNECTION BETWEEN THE CLINICAL SYMPTOMS AND THE COGNITIVE LEVEL IN SCHIZOPHRENIA (I)

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Abstract:

"Schizophrenia is a chronic affection, with a long, ceaseless, intermittent or remitting evolution, whose clinical, complex and polymorphic expression has as central criterion the autistic dissociation of the personality".

Schizophrenia is the most severe and disabling psychosis, with poor growth potential. Other features of schizophrenia identified in literature are: eclecticism, multifactoriality, the multidimensional aspects and the high variability among cultures and regions. Conclusively, schizophrenia is considered a major public health problem due to the early installation, extended development and severe semeiology, which produce pain to both patients and their families and to the environment. Cognitive deficits correlate well with the clinical symptoms and both the severity and duration of an untreated disease have impact on the functioning level. The deficits of the neuro-cognitive domains such as attention, working memory, language skills, and executive functioning tend to be moderate, with higher deficits detected in the learning process and verbal memory.

Key-words: schizophrenia, cognitive impairment symptoms

Rezumat:

Introducere: „Schizofrenia este o afecțiune cronică, cu evoluție îndelungată continuă, intermitentă sau remitentă, a cărei expresivitate clinică polimorfă are drept element central disocierea autistă a personalității”. Schizofrenia este psihoza cea mai severă și invalidantă, cu potențial de dezvoltare sărac. Alte caracteristici ale schizofreniei identificate în literatura de specialitate sunt: heterogenitatea, multifactorialitatea, multidimensionalitatea și variabilitatea ridicată între culturi și regiuni. În concluzie, schizofrenia este considerată o problemă majoră de sănătate publică, datorită instalării precoce, evoluției prelungite, severității simptomatologiei care produce suferință atât pacienților și familiei, cât celor din mediul înconjurător.

Deficitele cognitive se corelează bine cu simptomele clinice, și atât severitatea, cât și durata bolii netratate au impact asupra nivelului de funcționare. Deficitele domeniilor neurocognitive, cum ar fi: atenția, memoria de lucru, competențele lingvistice și funcționarea executivă tind să fie moderate, cu deficite mai pronunțate constatate în procesul de învățare și memorie verbală.

Cuvinte-cheie: schizofrenie, deficite cognitive, simptome pozitive

INTRODUCTION

Schizophrenia (Bleuler, 1911), synonymous with Dementia praecox (Kraepelin, 1896), (25, 26, 31, 32) is a name of a group of mental illnesses. The manifestation of major psychopathological symptoms such as hallucinations, delusions, formal thought disorder, affective disorders, conduct disorders, personality disorganization, cognitive impairment is characteristic in schizophrenia.

It is difficult to formulate a definition of schizophrenia because of its complexity and of the divergences between psychiatrists.

Despite the difficulties encountered regarding the development of an unique and clear definition of the disease, that are due to the very different manifestations of the symptoms and different clinical forms, psychiatrists have also tried synthesizing such developments. A broad definition of the disease that can be considered comprehensive, belongs to H. Ey: “Schizophrenia is a set of disorders dominated by discrepancy, ideative and verbal incoherence, ambivalence, autism, delusions, poorly systematized hallucinations, profound affective disturbances meaning detachment, alienation of ones feelings, problems that tend to move towards deficit and personality dissociation” (32).

Schizophrenia as a chronic affection, with a long, ceaseless, intermittent or remitting evolution, whose clinical, complex and polymorphic expression has as central criterion the autistic dissociation of the personality (32).

Ionescu elieves that schizophrenia is a central, nozographic entity accredited with striking dark psychopathological significance (21).

Prelipceanu believes schizophrenia to be “the most severe and disabling psychosis, a chronic disease with poorly evolutionary potential (progressive depletion of the psychic life)” (32, 33).

According to ICD 10, schizophrenic disorders are generally characterized by fundamental and specific distortions of thought, perception and the inappropriate or hackneyed affects. The clear field of consciousness and intellectual capacity are usually preserved although certain cognitive deficits can appear in time. The disorder involves the basic functions that give a person the feeling of uniqueness, identity and autonomy. The main features of schizophrenia identified in literature are eclecticism, multifactoriality, multidimensional aspects (38).

FEATURES OF SCHIZOPHRENIA

The general clinical features of schizophrenia are positive and negative symptoms.

Psychopathologically, schizophrenia is characterized by a large polymorphism of its symptoms.

The disorders of perception, especially the qualitative ones, are frequent and of particular importance in the diagnosis of schizophrenia. Out of the qualitative disorders of perception, in schizophrenia, delusions and hallucinations are reoccurring (25).

Attention is a sphere of the psychism, secondly modified to autism, psychomotor inhibition, dissociation of mental functions. Lack of spontaneity, introversion, autism, detachment from reality put their mark on the proper functioning of attention (33).

Memory disorders are of hypomnesic type and are due to the disinterest in the surrounding events, the tendency of detaching reality. However, hypermnesic manifestations can occur in manic schizoaffective forms, in the hebephrenic form of schizophrenia or even the paranoid form. In schizophrenia, qualitative memory disorders can occur. They are due to some imaginative productions, some delirious insights and sometimes to the derealisation experience. Sometimes, the patient evokes false memories (pseudo-amnesiae), other times experiences confabulations, false recognition. In the confusional forms of schizophrenia lacunose amnesiae may appear, which are characteristic to any confusional state.

Both the thinking process and the content of thoughts can be affected in schizophrenia. The added thinking processes seems to come out from a general difficulty to focus and eliminate the irrelevant stimuli. In formal terms, schizophrenic thinking takes place most frequently slowly, with ideative flux stops, assuring the barrier to mutism. The ideative flux slowing with fading or mutism is present in simple catatonic, paranoid, undifferentiated forms of schizophrenia. In schizoaffective forms with manic decompensation, the ideative flux is fast, has accelerated progress, similar to that in manic syndromes.

Disorders of thought form are diverse and can be grouped into the following categories: ideation rhythm disorders, coherence, logic, formal structure of thought. Schizophrenic thought disorder content is part of the discrepancy, bizarre, impenetrability, autism. People with schizophrenia lack the vigor and clarity of thought, elements which are agglutinated by dissociation to inconsistency in its content. Out of the qualitative thought disorders, delusional ideas occur mainly to people with schizophrenia. There is no delusional thematic pathognomonic to schizophrenia, although some abnormal ideas are more common in psychiatric practice (8).

The same authors show that there may be a particularity and in this context, the delusional content and thematic should be interpreted according to the populational group the patient belongs to. The traditions, social and religious customs and specific connections of the community members will be taken into account (8).

Language, as a means of communication in general is a verbal expression of thought. In schizophrenia there are formal content changes of spoken and written language.

The discordance of the schizophrenic psychic life includes the affective sphere. If the schizophrenic's thinking is dissociated, his affectivity is modified, meaning over low emotional resonance, weak emotional modulation, emotional inversion or flattening.

The schizophrenic's will is frequently altered towards hypobulia or even aboulia, in the inhibited and especially catatonic forms.

In schizophrenia, the field of consciousness is clear, accompanying the numerous symptoms. The schizophrenic patient, although autistic, strange, ambivalent and discordant, is auto allopsychic oriented, temporally, he registers correctly in space and time. However, there are some particular situations, when the field of consciousness is altered: the onset dream states of hebephrenia or catatonia, in schizophrenic acute delirium forms, which occur mostly at the onset of disease, catatonic conditions associated with particular conditions of consciousness (catatonia type Stauder). Moreover, identity itself can be affected (34).

COGNITIVE DEFICITS IN SCHIZOPHRENIA

Over the years, many authors have questioned whether schizophrenia is characterized by authentic cognitive disorders. Traditionally, the denotive cognitive insufficiency was considered to be significant only in old, damaged schizophrenic patients. In the past 25 years, evidence was gathered to challenge this view, but recent studies have clearly demonstrated the presence of cognitive dysfunctions (28).

In accordance with the view that in schizophrenia any specific deficiency manifests itself in general cognitive functioning, administered a battery of neuropsychological tests in patients with schizophrenia and compared the results with those obtained from a healthy population. A proportion

of 27 % of patients with schizophrenia were classified as “normal” from the neuropsychological point of view (29).

This also indicates that significant cognitive disorders in schizophrenia are frequent.

The study also highlights that a percentage of the schizophrenic patients appear to remain cognitively intact. This suggests that the psychopathology underlying the cognitive deficits, often associated with schizophrenia, may be distinct from the one which causes some of the basic clinical characteristics. Studies, which proved symptomatic improvement after treatment with clozapine, but without any improvement accompanying the functioning cognition sphere (7, 12).

Heinrichs and Zakzanis conducted a comprehensive meta-analysis, analyzing a large number of studies concerning cognitive deficits in schizophrenia, involving comparisons of schizophrenic patients and free of disease individuals as control subjects. The greatest damage was found in the global verbal memory functioning (18).

Recently, there is a recurrence of cognitive factors as critical indicators of schizophrenia and their significance was underlined by several key studies published in the last twenty-five years. While historically the position of cognition in schizophrenia had growth or decline periods, it is now shown that cognitive deterioration is a basic independent domain (9, 23).

Cognitive neuroscience of schizophrenia has emerged as a link in the study of neurobiological changes and psychological processes and its development had a very important contribution to understanding the new results in schizophrenia (17).

The current status of research shows that brain changes correlate with psychological dysfunction and may have a causal relation. Therefore, a significant number of behavioral traits, functional limitations and psychological vulnerabilities can be explained on the basis of neurobiological deficits that underlie them. Cognitive neuroscience has emerged as one of “missing links” in understanding the phenomenology of schizophrenia. Schizophrenia is a disease with functional handicap-disability, which represents a major problem.

In the past, measures were focused only on clinical symptoms, but today it is recognized that social issues are an area of the same importance. To capture the quality of life of people affected by schizophrenia, it became necessary to take into account social, occupational and cognitive variables in defining the outcome. The reappearance of cognitive functions in the study of schizophrenia is seen as a turning point in the research progress. This offered various arguments and mechanisms to look beyond the cluster symptoms. Cognitive functions have become a link between impairment, disability, handicap, symptoms and neurobiological changes. It was also shown that cognitive disorders are actually the norm and often pre-dates the disease (24).

Cognitive deficits proved to be very important for many research areas of schizophrenia, such as:

- Understanding of psychopathology;
- Epidemiology (vulnerability indicators);
- Genetics (endophenotypes);
- Neuroimaging (including functional neuroimaging) and
- Psychopharmacology (these can be used as a evaluation parameter in therapeutic trials with new molecules or cognitive psychotherapy). Some areas of cognitive functioning are not affected by schizophrenia.

Current knowledge does not allow an exhaustive listing of cognitive deficits in schizophrenia. A lack of clear understanding of the neural and neuropsychological substrates makes the assessment difficult, if cognitive issues that appear are isolated deficits or if they reflect a higher depreciation in global level domains (3).

Association of cognitive deficits with other clinical symptoms.

The connection between different cognitive deficits and other (positive or negative) symptoms of schizophrenia represented an attraction point for research. Both the negative symptoms of schizophrenia as well as positive ones were associated with a functional outcome. Several studies have sought to compare the magnitude of the neurocognition and symptoms associations with the action, but the published results were contradictory (10, 11, 24, 36, 37).

Some cross studies regarding chronic schizophrenia suggested that the psychopathology may be more strongly correlated with community functioning than with cognition (19, 24, 36, 37).

The study of Perlick, Rosenheck examined the association of measures of the positive and negative symptoms PANSS Scale, Kay, Fiszbein and Opler, as well as that of neurocognition with community functioning (obtained with the quality of life Scale of Heinrichs-Carpenter, Heinrichs-Carpenter Quality of Life Scale) and the working days (13, 15, 19, 22, 30, 37).

The results suggested that: clinical symptoms and neurocognition have independent functioning associations; symptoms may even be more strongly associated with functioning than with neurocognition. A future examination of the connection between neurocognition, symptoms and functioning is needed. It is thought that it could potentially guide the development of pharmacology, rehabilitation treatments and the understanding of the complexity of illness.

Mohamed investigated the effects of positive, negative and disarrangement symptoms on specific cognitive deficits and found that only negative symptoms were correlated with reduced performance and this correlation was weak. In a longitudinal study of 42 patients with first episode schizophrenia, found that improvement in cognitive performance was associated with improvement of positive symptoms, but was not also associated with an improvement of the negative symptoms or beginning of medication. Changes in cognitive functioning were not correlated with the morphology of the brain, revealed by imaging through magnetic resonance (MRI) (20, 27).

Reduced performances in all cognitive areas were most strongly correlated with increased negative symptoms. Research has shown that deficits of the working memory, episodic memory and executive function are partially mediated with an increase in negative symptoms in schizophrenic patients. The negative symptoms mediate the working and episodic memory deficits, but have only partially mediated the deficits in the executive function (1, 35).

Bora, Yucel and Pantelis conducted a meta-analysis on a number of 31 studies that compared the performance of people with schizophrenia (1979 participants) with the performance of people with affective or schizoaffective psychosis (1314 participants). People with schizophrenia with more severe negative symptoms, younger age at the disease's onset may be more frequently affected in cognitive functioning than those with affective psychosis disorder / schizoaffective disorder (4).

In the first figure the connections between clinical and cognitive variables is presented schematically.

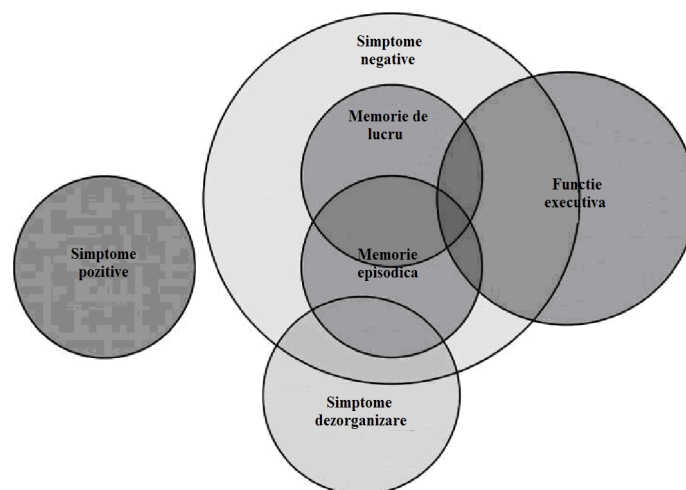


Fig. 1: *Connections between clinical and cognitive variables*

Research has found that cognitive deficits correlate well with clinical symptoms and both the severity and duration of untreated disease have impact on the functioning level (7). The deficits of the neurocognitive areas such as attention, working memory, language skills, and executive functioning tend to be moderate, with more pronounced deficits observed in learning and verbal memory (26).

All these neurocognitive areas are related to accommodation and social skills, with executive learning functions and verbal memory, which show greater variance in several areas, more than other neurocognitive variables (14).

Negative symptoms and neurocognitive areas, although related, are distinct and have differentiated ways of changes towards treatment (16). General psychopathological symptoms such as depression and anxiety can become important objectives such as treatment strategies developed for the compiling of the cognitive improvement of the functional performance to the real world (16). Cognitive functions are probably the best predictors of the adaptive outcome.

Currently, different data tend to assert that cognitive dysfunctions are basic disorders in schizophrenia and their severity is predictive as the disease develops.

It is also clear that disorders measured by cognitive tests, are neither consequences of positive or negative symptoms, nor related to motivation or global intellectual deficit, or anti-psychotic medication.

It is also known that the severity of cognitive symptoms is a better indicator of the functional and social outcome than the positive or negative symptom severity. Patients with more severe cognitive deficits during the first episode of the disease are more susceptible to presenting a chronic and severe form later. There is also support for the longitudinal correlation between cognitive skills and a basic, evolutionary, functional outcome (5, 14).

REFERENCES:

1. Addington, J., Saeedi, H. Addington, D. (2005). *The course of cognitive functioning in first episode psychosis: Changes over time and impact on outcome*, *Schizophrenia Research*, 78, 35-43.
2. Aleman, A., Hijman, R., Edward, H., et al (1999), *Memory impairment in schizophrenia: a meta-analysis*, *American Journal of Psychiatry*, 156, 1358-1366.
3. Bilder, R. M., Goodman, R. S., Robinson, D., et al (2000), *Neuropsychology of first-episode schizophrenia: initial characterization and clinical correlates*, *American Journal of Psychiatry*, 157, 549-559.
4. Bora, E., Yucel, M., Pantelis, C. (2009), *Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study*, *The British Journal of Psychiatry*, 195, 475-482.
5. Bora, E., Yucel, M., Pantelis, C. (2010), *Cognitive Impairment in Schizophrenia and Affective Psychoses: Implications for DSM-V Criteria and Beyond*, *Schizophrenia Bulletin*, 36 (1), 36-42.
6. Bowie, C.R., Harvey, P.D. (2005), *Cognition in schizophrenia: Impairments, determinants, and functional importance*, *Psychiatr Clin North Am*, 28, 613-33, 626.
7. Buchanan, R.W., Koepl, P., Breier, A. (1994), *Stability of neurological signs with clozapine treatment*, *Biol Psychiatry*, 36, 198-200.
8. Chiriță, V., Papari, A. (coord.) 2002, *Tratat de Psihiatrie*, Vol. I, Ed. Fundatiei „Andrei Șaguna“, Constanța.
9. Dias, V. V., Brissos, S., Frey, B. N., Andreazza, A. C., Cardoso, C., Kapczinski, F. (2009), *Cognitive function and serum levels of brain-derived neurotrophic factor in patients with bipolar disorder*, *Bipolar Disorder*, 11, 663-71.
10. Dickerson, F., Boronow, J. J., Ringel, N., Parente, F. (1996), *Neurocognitive deficits and social functioning in outpatients with schizophrenia*, *Schizophr Res*, 21, 75-83.
11. Dickinson, D., Coursey, R. D. (2002), *Independence and overlap among neurocognitive correlates of community functioning in schizophrenia*, *Schizophr Res.*, 56, 161-170.
12. Goldberg, T. E., Greenberg, R. D., Griffin, S. J., et al (1993), *The effect of clozapine on cognition and psychiatric symptoms in patients with schizophrenia*, *British Journal of Psychiatry*, 162, 43-48.
13. Green, M. F. (1996), *What are the functional consequences of neurocognitive deficits in schizophrenia?* *American Journal of Psychiatry*, 153, 321-330.
14. Green, M. F., Kern, R. S., Braff, D. L., Mintz, J. (2000), *Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"?*, *Schizophr Bull*, 26, 119-36.
15. Green, M. F., Olivier, B., Crawley, J. N., Penn, D. L., Silverstein, S. (2005), *Social cognition in schizophrenia: Recommendations from the measurement and treatment research to improve cognition in schizophrenia new approaches conference*, *Schizophr Bull*, 31, 882-7.
16. Green, M. F. (2007), *Cognition, drug treatment, and functional outcome in schizophrenia: A tale of two transitions*, *Am J Psychiatry*, 164, 992-994.
17. Grozăvescu, Raluca (2009), *Schizofrenia din perspectiva neurodezvoltării*, *Revista Română de Psihiatrie a copilului și adolescentului*, 3, 2.
18. Heinrichs, R. W., Zakzanis, K. K. (1998), *Neurocognitive deficit in schizophrenia: A quantitative review of the evidence*, *Neuropsychology*, 12, 426-445.

19. Heslegrave, R. J., Awad, A. G., Voruganti, L. N. (1997), *The influence of neurocognitive deficits and symptoms, quality of life in schizophrenia*, *J Psychiatry Neurosci*, 22, 235-243.
20. Hoff, A., Sakuma, M., Weineke, M., et al. (1999), *Longitudinal neuropsychological follow-up study of patients with first-episode schizophrenia*, *American Journal of Psychiatry*, 156, 1336-1341.
21. Ionescu, G. (1995), *Tratat de psihologie medicală și psihoterapie*, Ed. Asklepios, București.
22. Kay, S. R., Fiszbein, A., Opler, L. A. (1987), *The Positive and Negative Syndrome Scale (PANSS) for schizophrenia*, *Schizophr Bull*, 13, 261-276.
23. Kraus, M. S., Keefe, R. S. (2007), *Cognition as an outcome in schizophrenia*, *Br J Psychiatry*, 50, 46-51.
24. Kurtz, M. M., Moberg, P. J., Ragland, J. D., Gur, R. C., Gur, R. E. (2005), *Symptoms versus neurocognitive test performance as predictors of psychosocial status in schizophrenia: a 1- and 4-year prospective study*, *Schizophr Bull.*, 31, 167-174.
25. Manea, Mirela, Patrichi, B. E., Manea, T. (2007), *Psihiatrie – note de curs pentru studenții Facultății de Medicină Dentară*, Ed. Universitară „Carol Davila” București.
26. Manea, Mirela (2008), *Psihiatrie și psihopatologie pentru psihologi*, Ed. Titu Maiorescu.
27. Mohamed, S., Paulsen, J. S., O’Leary, D., et al. (1999), *Generalised cognitive deficits in schizophrenia, study of first-episode patients*, *Archives of General Psychiatry*, 56, 749-754.
28. Mohamed, S., Rosenheck, R., Swartz, M., Stroup, S., Lieberman, J. A., Keefe, R. S. E. (2008), *Relationship of Cognition and Psychopathology to Functional Impairment in Schizophrenia*, *Am J Psychiatry*, 165, 978-987.
29. Palmer, B. W., Heaton, R. K., Paulsen, J. S., et al. (1997), *Is it possible to be schizophrenic yet neuropsychologically normal?* *Neuropsychology*, 11, 437-44.
30. Perlick, D. A., Rosenheck, R. A., Kaczynski, R., Bingham, S., Collins, J. (2008), *Association of symptomatology and cognitive deficits to functional capacity in schizophrenia*, *Schizophr Res.*, 99, 192-199.
31. Predescu, V. (1989), *Psihiatrie*, Ed. Medicală, București.
32. Prelipceanu, D. (2003), *Psihiatrie. Note de curs*, Ed. Medicală, București.
33. Prelipceanu, D. (2011), *Psihiatrie Clinică*, Ed. Medicală, București.
34. Sandock, B., Sandock, Virginia (Ed.) (2004), *Comprehensive Textbook of Psychiatry*, vol. 1, Lippincott Williams & Wilkins.
35. Saykin, A. J., Shtasel, D. L., Gur, R. E., et al. (1994). *Neuropsychological deficits in neuroleptic naïve patients with first episode schizophrenia*, *Archives of Psychiatry*, 51, 124-131.
36. Velligan, D. I., Mahurin, R. K., Diamond, P. L., Hazleton, B. C., Eckert, S. L., Miller, A. L. (1997), *The functional significance of symptomatology and cognitive function in schizophrenia*, *Schizophrenia Research*, 25, 21-31.
37. Wegener, S., Redoblado-Hodge, M. A., Lucas, S., Fitzgerald, D., Harris, A., Brennan, J. (2005), *Relative contributions of psychiatric symptoms and neuropsychological functioning to quality of life in first-episode psychosis*, *Aust NZ J Psychiatry*, 39, 487-492.
38. *** WORLD HEALTH ORGANISATION – *The ICD-10 Classification of Mental and Behavioral Disorders: Clinical Description and Diagnostic Guidelines*, WHO, Geneva, 1992.