



NEUROPSYCHOLOGY AND SCHIZOPHRENIA: THE ROLE OF COGNITIVE DEFICITS IN SCHIZOPHRENIA'S DIAGNOSIS, THEIR EMERGENCE AS SYMPTOMS, AND THE COGNITIVE FIELDS AFFECTED

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Abstract:

Schizophrenia's (SZ) development results from various factors, including physical, genetic, psychological, and environmental contributions. Over the last decades, many neuropsychological studies have demonstrated cognitive deficits' superiority over psychopathological symptoms as determinants in the SZ diagnosis. However, efforts to accurately identify specific cognitive deficits under certain forms of functional impairment remain vague. According to the recent literature, SZ is universally recognized as a neurobiological disorder with solid neurocognitive content, usually accompanied by neurological deficits. Therefore, in the present review, we will try to identify the cognitive deficits observed in SZ patients and determine their impact on the suffering of SZ patients. Furthermore, we present an overview of the tests used to assess executive functions and elaborate on the factors that affect mental performance stability.

Keywords: cognitive deficits, neuropsychology, schizophrenia, speech, memory, attention, intelligence

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1. Introduction

Looking back, we notice that the brain was not always considered a vital organ of the individual. On the contrary, the brain was perceived as a useless organ for centuries. It took hundreds of years and the evolution of science to understand how it affects our behaviors. The philosopher Rene Descartes was one of the personalities who highlighted the brain's importance. He declared that the mind controls the body and vice versa; the body can control the mind and resist or even influence other human behaviors. This theory, called "dualism", began, and later evolved the scientific community's idea to focus on the brain's complex functions. Another important figure was Thomas Willis, who also coined "hemisphere" and "lobe" for the brain. By combining psychiatry with neurology, he focused on examining the behaviors and brains of people suffering from mental disorders and hysteria. Although the importance of the brain and its functions have been challenged, their theories formed the basis on which later ones relied, leading to the development of neuropsychology. Subsequently, Paul Broca's observations and methods gave neuropsychology the recognition and respect it deserves as a science.

Neuropsychology is the bridge between two branches, neurology, and psychology. It studies the relationship between the central nervous system's structural and functional organization as a science. Neuropsychology aims to understand cognitive and other functions in humans and how they regulate healthy and pathological behavior. Cognitive neuropsychology also belongs to the specializations of neuropsychology. This field seeks to understand the mind and brain by focusing on individuals who have suffered brain damage or neurological disease. However, neuropsychology is related to other disciplines, such as cognitive psychology and specializations. For this reason, it is worth noting that cognitive psychology investigates the cognitive mechanisms of five essential executive functions of the brain, i.e., memory, speech, attention, and intelligence visual-spatial ability of the brain.

The goal of these sciences is to understand the brain's functions and how they affect human behavior and personality. Research studies include healthy individuals and patients with mental disorders, including SZ. During its manifestation, patients experience speech and thinking disturbances, perception of reality, and cognitive deficits.

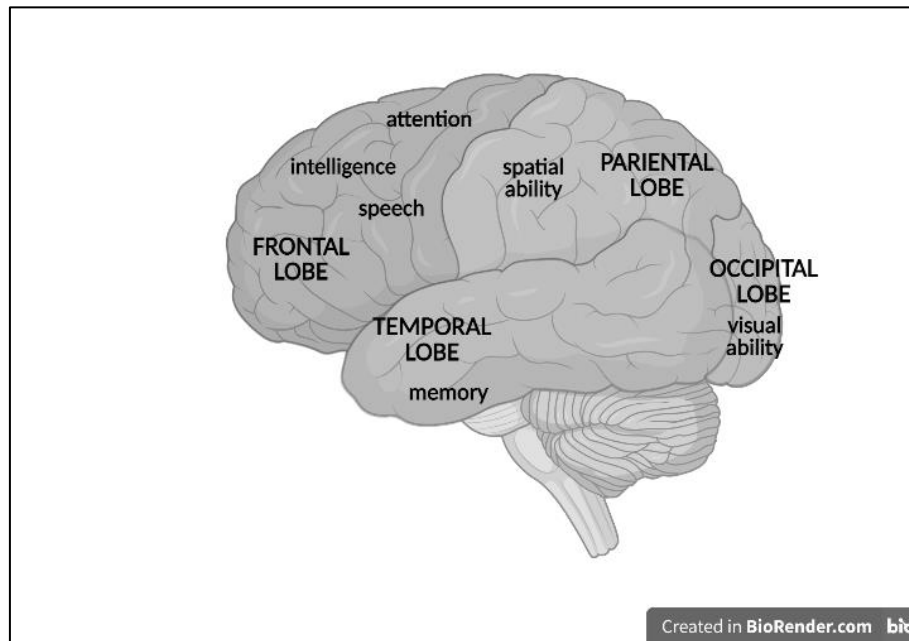


Figure 1: Lobes of the brain and the functions they control

2. Cognitive deficiencies and cognitive fields

Cognitive deficits are a vital part of SZ's features as they affect multiple areas of cognitive function. Research shows a wide range of cognitive deficits in patients with SZ (Bozikas et al., 2006). One of the most critical cognitive deficits is the reduction of executive functions (Bozikas, Kosmidis, Kiosseoglou, & Karavatos, 2006b. Fucetola, Seidman, Kremen, Faraone, Goldstein, & Tsuang, 2000. Kosmidis, Bozikas, Zafiri, & Karavatos, 2006), including the organization of information, the elaboration of different strategies for completing a goal and the coordination of behavior. Executive functions also include the use of abstract concepts (Ekerholm, Firus Waltersson, Fagerberg, Söderman, Terenius, & Agartz, 2012; Nieuwenstein, Aleman, & de Haan, 2001), effective inhibition of response (Bozikas, Kosmidis, Kiosseoglou, & Karavatos, 2006. Vöhringer et al., 2013) and decision making (Nieuwenstein, Aleman & de Haan, 2001). The cause of impaired executive function may associate with prefrontal cortex dysfunction in SZ patients (Andreasen, O'Leary, Flaum, Nopoulos, Watkins, et al., 1997. Carter, Perlstein, Ganguli, Brar, Mintun & Cohen, 1998). Executive dysfunction also causes the decline of verbal learning due to delayed retrieval of information (Albus et al., 1997; Riley et al., 2000).

2.1 Speech

Linguistic fluency is a category of executive functions distinguished into semantic and phonological. The tests used to assess linguistic fluency are the Design Fluency Test (Bozikas et al., 2006), the Verbal Fluency Test (Altshuler et al., 2004; Schretlen et al., 2007), the FAS Test (Sanchez-Morla et al., 2009), and the Controlled Oral Word Association Test (COWAT). More specifically, patients with schizophrenia have difficulty producing speech on demand. Tests assess patients' ability to create words from a specific

phonological or semantic category (Bowie & Harvey, 2006) and essentially reveal poor verbal information storage (Kerns, Berenbaum, Barch, Banich & Stolar, 1999) as well as ineffective retrieval of information from semantic networks (Goldberg, Aloia, Gourovitch, Missar, Pickar & Weinberger, 1998).

2.2 Memory

Memory is another cognitive field that is affected by the manifestation of SZ. When we talk about memory, we refer to the mental processes of coding, organizing, and retaining information on the one hand, and on the other hand, searching and retrieving stored data. More specifically, schizophrenia patients show reduced performance in visual and verbal memory (Young, Powell, Risbrough, Marston, & Geyer, 2009), which is related to learning difficulties and retrieving of new information (Albus, Hubmann, Mohr, Scherer, Sobizack, et al., 1997, Riley, McGovern, Mockler, Doku, Ceallaigh, et al., 2000, Young et al., 2009). Regarding reducing semantic memory, the researchers propose two types of models. In the first model, the patient has problems storing knowledge, and in the second one, the patient cannot access and retrieve knowledge (Warrington & Shallice, 1979).

Also, working memory is a field of memory that is affected in patients with schizophrenia. It is a mechanism with sub-specialized systems responsible for the temporary storage and processing of information and executing more complex mental tasks, such as comprehension, learning, and reasoning (Baddeley & Hitch, 1974). The same is true of verbal and nonverbal memory, where patients performed less well in their tests. There are, however, other cognitive impairments that have been identified in schizophrenia, such as the visual-spatial perception associated with the presence of parietal lobe dysfunction in patients with schizophrenia (Pantelis & Maruff, 2002; Bozikas et al., 2006).

2.3 Attention

Patients with schizophrenia experience a decline in attention, another area of knowledge. A healthy individual can process the most critical stimuli while ignoring the less important ones. According to William James (1890), attention is the mind's choice for conscious attention to one of many simultaneous stimuli or thoughts (Principles of Psychology, 1890). People in the high-risk group for schizophrenia are more likely to develop attention deficit disorder before the first psychotic episode (Cornblatt & Erlenmeyer-Kimling, 1985). When they experience the first episode, attention deficits are typically present and moderate (Caspi et al., 2003). The performance of patients with schizophrenia is significantly reduced in attention tests. The weakness was identified in visual, auditory, and selective attention (Bozikas et al., 2006b. Censits, Ragland, Gur & Gur, 1997). However, some studies indicated that patients with schizophrenia show little or no deficiency in some attention tests, specifically the Digit Span Forward (Meesters et al., 2013) compared to healthy participants. In another long-term study, patients with schizophrenia showed improvement in the CPT during their second evaluation

(Ekerholm et al., 2012), while Nopoulos et al. (1994) found stability in the same test (as reported in Rund, 1998).

2.4 Intelligence

A study focusing on neuropsychological performance in individuals with different IQs, found that patients with schizophrenia had lower IQ performance and higher verbal IQ while showing lower intelligence (Kremen et al., 2001). In addition, patients with high IQ performed better on information processing speed tests; consistently with a subsequent study that indicated that intelligence was linked to executive function performance (Badcock et al., 2005). Based on the above, a simple IQ test, can detect a possible manifestation of schizophrenia later in a person's life up to three years earlier. Examined 163 people aged 16-24, with a family history of schizophrenia using imaging brain tests. The findings were compared with a group of individuals who had no family history of the disorder. The results showed that 45% had symptoms of schizophrenia in the high-risk group, but only 12% developed the disorder (Rune Raudeberg et al., 2019).

2.5 Cognitive deficit's stability

An essential assessment of cognitive deficits is that they tend to stabilize (Heaton et al., 2001; Kurtz, 2005; Rund, 1998) and may even improve in part during the initial stabilization phase immediately after the first episode (Albus et al., 2002; S. Kristian Hill et al., 2004; Klingberg et al., 2008). A long-term study by the Heaton et al. (2001) research team showed stability in the neurocognitive function associated with schizophrenia. This study reviewed 142 patients with schizophrenia and 209 healthy subjects with an extended Halstead-Reitan test for 3 years, up to 10 years. No evidence of cognitive decline was found in any of the seven areas of neurocognitive capacity examined.

Job reviews also show steady neurocognitive deficits in patients with schizophrenia, at least in those living in the community. In fact, in a recent meta-analysis, patients with schizophrenia showed significant improvement in the majority of neuropsychological tests. Repeated evaluation of patients with the first schizophrenic episode is considered essential and is evaluated as a critical strategic move in studying the course of cognitive deficits. Long-term research on these patients provides an adequate and realistic assessment of cognitive performance. Such studies show that, in general, the neuropsychological deficits seen during the first schizophrenic episode remain constant over time. A possible exception to this may be verbal memory, as there is some further deprivation evidence. Interestingly, this particular mental function depends on the prefrontal and middle temporal cortex brain areas that have been found to decrease the volume during the disease progressively. In addition, the improvement of psychopathology seems to positively affect the course of cognitive deficits, making critical the need for adequate and comprehensive treatment of schizophrenia symptoms.

Some meta-analyses and systematic reviews underscore cognitive deficits' stability after a first psychotic episode, although there are several significant study limitations that should be taken into consideration. In the 13-year follow-up study,

adolescents with early-onset schizophrenia showed a significant cognitive decline as measured by the Wechsler IQ (Weiss et al., 2010). On the other hand, a 19-year follow-up study by Russell and his colleagues found no difference between patients' IQ with childhood schizophrenia (Rune Raudeberg et al., 2019). A recent meta-analysis reports improved cognitive function in patients, especially in the early years after a first psychotic episode (Rune Raudeberg et al., 2019).

Other studies, such as Hoff et al., observed stabilization of neurocognitive deficits during follow-up. After five years, cognitive test scores were 1-2 standard deviations below average scores, which did not change between the tests. However, verbal learning scores decreased, and executive function tests, spatial memory, concentration/speed, and general intelligence were associated with the improvement of positive symptoms.

3. Factors affecting cognitive performance stability

Some researchers suggest that cognitive performance stability in patients with schizophrenia persists after controlling for gender, age, age of onset, duration, initial cognitive impairment, symptom changes, and the presence of late dyskinesia.

3.1 Residence place

A recent study included patients living in the community who, as noted, may differ significantly from patients with chronic care (Rune Raudeberg et al., 2019). Indeed, Nemoto et al. (2014) showed that cognitive deficits vary between community-based patients and patients with chronic care through their research. This 5-year follow-up study included patients after hospitalization and indicated that patients' memory and attention improved significantly. Information processing speed and general intelligence decreased after an initial improvement while remaining better than in the beginning.

3.2 Birthplace

In another study, Rechenberg et al. (2009) examined a cohort of 1,037 children born in Dunedin, New Zealand, 35 of whom subsequently developed schizophrenia. The revised Wechsler Intelligence Scale for Children assessed cognitive functions at the age of 7, 9, 11, and 13. According to their findings, cognitive test performance in these 35 children improved with maturation. However, in several trials (information, similarities, vocabulary, and image completion), the authors identified a significant developmental delay compared to the control group at all measured points. This developmental delay even increased in several trials.

Further analysis of the same data concerning the group of people born in Dunedin, New Zealand, was carried out by Meier et al. Their study showed a significant reduction in cognitive performance in a sample of patients with schizophrenia in whom the onset of the disease occurred during their maturation period (13 to 38 years). On the one hand, they observed discrepancies between the lack of significant changes in IQ verbal controls and delayed memory performance. On the other hand, they found the most significant

impairment in information processing speed, learning, executive functions, and motor function. Thus, the Digit Symbol Coding Subtest test results at follow-up showed that patients who subsequently developed schizophrenia at the age of 7 to 9 years had no differences compared with healthy individuals at the age of 9 years. Up to 11 years of age, a slight decrease in yield was detected, and children from the age of 11 to 13 years, experienced a cognitive period with a tendency to improve, followed by a significant decrease later on.

3.3 Age

For some other researchers, age seems to be an essential factor in developing cognitive function in patients with schizophrenia, in contrast to the view of other researchers mentioned above. Harvey et al. Reported increased cognitive impairment in institutionalized elderly patients with schizophrenia in comparison to younger patients. A systematic review by Rajji and Mulsant suggests that cognitive function in elderly patients with schizophrenia remains stable until the age of 65 but later deteriorates sharply. Patients with schizophrenia before the age of 40 are also not homogeneous in their cognitive performance. Some studies show no cognitive decline on follow-up, while others have a relatively apparent cognitive deterioration.

3.4 Pharmacotherapy

Another factor to consider is the impact of medication on patients' cognitive function. A 5-year follow-up study included 54 patients with the first episode of schizophrenia who had received antipsychotic therapy. The neurocognitive assessment included full-scale IQ and executive function measurements, attention, verbal and non-verbal memory, verbal fluency, and motor skills. The results showed improvement in most areas: full-scale performance and IQ, constant visual attention, immediate pedestrian recall, and card sorting. The motor function test was the only test in which the scores deteriorated. The authors found a significant correlation between negative symptoms and verbal and full-scale IQ changes. The course of psychotic symptoms was associated with rapid displacement, whereas changes in disorganization measurements were related to motor function.

Meta-analyses of studies focused on patients with first-episode schizophrenia showed extensive neurocognitive deficits compared to the control group, with moderate to large effect sizes. People with early-onset schizophrenia also showed significant mental retardation, which was comparable to that of the more advanced stages of the disease, suggesting that cognitive deficits in schizophrenia are mainly neurodevelopmental. A follow-up meta-analysis of studies comparing the neurocognitive profile of drug naïve schizophrenia patients and healthy individuals confirms these results by showing a similar attenuation of the effect's magnitude on verbal and visual memory executive functions, and attention. It is worth noting that the effect's magnitude was comparable in these two meta-analyses despite the use of different neuropsychological tools.

4. Discussion

Based on the findings of the studies presented above, there is controversy about the course of cognitive deficits in patients with SZ. On the one hand, there is strong evidence of a gradual deterioration in patients' cognitive function, whereas, on the other hand, there is also evidence for cognitive deficits' stability or improvement. One important factor might be the relatively short period of the assessment of cognitive function, i.e., less than three years, which might not be adequate to determine the course of continuous cognitive changes. Therefore, it is considered reasonable to have difficulty describing a single direction for the development of cognitive deficits in all patients with schizophrenia. Hence, cognitive deficits in a subset of patients may remain constant throughout the disease, while in other cases, they may improve. Still, other patients may experience progressive deterioration. It is worth noting that wavy dynamics may be observed in the same patient's cognitive deficits depending on whether they experience recurrence or remission of the disorder.

5. Conclusions

As already mentioned, neuropsychology aims to understand a person's cognitive and other functions and the way they regulate healthy and pathological behavior. Schizophrenia as a mental illness is part of the pathological behavior that neuropsychology investigates.

People with schizophrenia have cognitive impairments and neurocognitive deficits in essential cognitive functions of the human brain. Patients' inability to respond and executive essential functions such as memory, attention, speech, and intelligence are revealed through studies. The findings follow tests that patients undergo, specifically designed to measure performance in each category of knowledge. Some studies assess performance tests in chronic patients, while others include cases and controls, which undergo the same tests, and the odds are compared between the two groups.

Many of the studies that have been conducted show a decline in patients with schizophrenia cognitive functions. There are areas where this reduction occurs to a greater extent, such as executive functions, and the consequences are more important for patients' daily lives. There are, however, areas such as deficits in psychomotor speed, of less importance. An important finding is that many studies have shown that there are cases of patients who showed stabilization of cognitive deficits after the disease's onset and not their continuous reduction.

Although studies on schizophrenia's neurocognitive deficits are extensive, and one would expect the results to lead to safe and unequivocal conclusions, this is not the case. As mentioned before, it is not uncommon for researchers to question the validity of tests used to measure individuals' performance. The fact remains that there are cases where patients show an improvement in their performance. An example is patients who

underwent the WAIS test related to intelligence, as observed by Klonoff et al. (1970) after a long study.

Evidence that a patient with schizophrenia has cognitive deficits is undoubtedly valuable. However, the different research findings can be considered equally important. Deficiency stability, improved patient performance during the disease, whether the deficiency is severe, mild, or moderate compared to other patients, can allow and lead to more accurate and better-targeted treatments for patients with schizophrenia.

Conflict of interest statement

The authors declare no conflicts of interest.

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