

Neurocognitive Dimensions of Schizophrenia: An Update

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ABSTRACT

Individuals suffering from schizophrenia sometimes hold the promise of a bleak future. There are added concerns of suicides and severe disruption in all spheres of life ranging from education to personal relationships. Schizophrenia covers a vast array of symptoms and dysfunctions namely attentional dysfunctions, dysfunction of the processing speed and executive control, emotional processing dysfunctions, hallucinations and reduced insight. The purpose of this paper is to understand the neurocognitive components behind the symptoms of schizophrenia. The elucidation of clear paradigms on the cause of their maladjustments can help in the formulation of an effective cognitive remediation programme which cognitive neuropsychology tries to answer.

Keywords: *Cognitive Neuropsychology, Schizophrenia, Cognitive Dysfunctions, Neurological Assessments, Executive Functions, Neuroscience*

Mueser & McGurk (2004), describe schizophrenia as a severe psychiatric disorder which features hallucinations, delusions, cognitive impairment, and social withdrawal (As cited in Aleman, 2014). It is also characterised by fuzzy thoughts, inability to differentiate from real and fantastical contexts, and an inability to react in an emotionally responsive way with others. Tragically, the disorder has an early onset usually between 20 to 35 years of age which causes severe disruption in all spheres of life ranging from education to personal relationships. Such individuals sometimes hold a promise of a bleak future. Jablensky et al (1995), state statistics which say that nearly 15% of individuals suffering from schizophrenia commit suicide and the annual incidence rate is between 0.16 and 0.42/1000 persons at risk. General textbooks say that men and women have an equal chance of being diagnosed with schizophrenia, but there is sufficient evidence which states that men have a higher risk factor (Aleman, Kahn, & Selten, 2003).

DSM-V states the criteria for which an individual is diagnosed with schizophrenia, out of which the most commonly reported symptoms are bizarre delusions and prominent hallucinations of voice. These symptoms have a more permanent effect. Such individuals typically have abnormal functioning such as lacking volition; poverty of speech, poverty of movement and poverty of ideas. Hallucination and delusions aren't always present as symptoms, but the patients would have experienced them at least once in the course of its onset.

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Symptoms of schizophrenia are broadly boxed as “Waxing and waning”, the acute and chronic phases respectively. Because of the complexity and severity of the symptoms, a neuropsychologist is posed with several obstacles while trying to understand the rudimentary causes for the manifestation of these symptoms in the brain.

LITERATURE REVIEW

The nature of neurocognitive deficits in schizophrenia

Schizophrenia covers a vast range of symptoms. When neuropsychological tests are administered on patients with schizophrenia, the group average result falls below the normal mean performance on most of the tests. The research on these domains has been exhaustive and elucidate clear paradigms on the cause of their maladjustments.

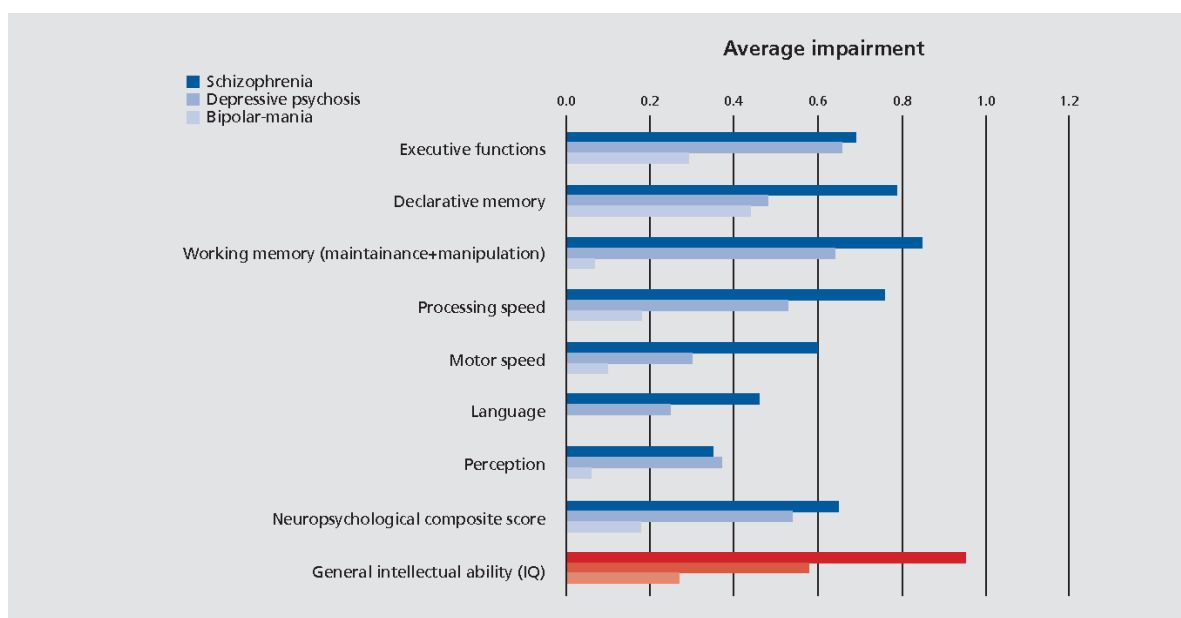


Figure 1: Neuropsychological performance profile of schizophrenia, psychotic major depressive disorder, and psychotic bipolar disorder. Performance was compared with healthy controls and is presented in standard deviation units (effect sizes). Data are from the AESOP first-episode study. 53 (Reichenberg, 2010)

Cognitive dysfunction

It is astounding to know that cognitive dysfunction, although a characteristic of schizophrenia, isn't listed among the symptoms in DSM-V. Reichenberg & Harvey (2007) say that substantial neurological research shows that there are considerable deficits in attention, memory, executive functioning, and general intellectual abilities, especially the impairments are more prominent in episodic memory and executive control processes. Schaefer et al (2017) confirmed yet another meta-analysis which concluded that cognitive deficits are largely stable and universal showing the similar patterns worldwide and over a span of decades. The neurological impairments are predisposed to a genetic susceptibility and some features are common amongst patients are their nonpsychotic relatives even before the onset of schizophrenia, wherein the strongest maladjustment is seen in memory and executive functioning (Sitskoorn et al, 2004; Snitz et al, 2006). A study done by Wilk et al. (2005) showed that there were deficits in memory and speed visual processing even after IQs were kept the same with schizophrenia patients and the control group. It was later seen that the brain regions that played an important role in cognition were the temporal and

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frontal cortices (Minzenberg et al, 2005) and increased prefrontal activation during working memory tasks.

The importance of the temporal and frontal cortex has now been increasingly understood in the treatment of schizophrenia. Achim and M. Lepage (2015) argues that the genetic and environmental risk factors in schizophrenia can be well understood by using the technology of neuroimaging, keeping the etiology in mind (as cited in Aleman, 2014).

Table 1 Specific neuropsychological impairments in schizophrenia (Caletti et al., 2013)

Kolb & Wishaw (1983)	'Fronted and temporal lobe' tasks
Saykin et al. (1995)	Memory and learning
McKenna et al. (1990)	Semantic memory
Shallice et al. (1991)	Executive tasks
Shqeirat & Mayes (1988)	Effortless tasks

Attention. Attentional deficits were categorized as a symptom of schizophrenia long before experimental testing or neurological tests were available. Posner and Petersen (1990) have presented three subsets of attention: alerting, orienting, and executive control (As cited in Reichenberg, 2010). Alert being the state of maintenance of wakefulness, orienting is the ability to separate the useful information amongst the sensory haul, and executive control as the ability to allocate an appropriate response among the various choices available. Alerting has received a considerable amount of attention in terms of research, Continuous Performance Tests are used to study the process as opposed to orienting which hasn't received that much attention. Heinrichs et al. (1998); Dickinson & Ramsey (2007); Fioravanti et al. (2005) have suggested that patients with schizophrenia experience moderate to severe deficits in the attentional domain of cognition.

Executive functions. The term executive functions have a long history. It was aimed at bringing more emphasis and possibly give a more precise word to the functions of the prefrontal cortex. It has gained a unique viewpoint over the years. All executive functions aren't located in the prefrontal cortex, fractionation into subprocesses (Miyake et al., 2000). The executive functions are also sustained in the cortical networks and may be related to the frontal lobes (Andres & Linden, 2001, as cited in Reichenberg, 2010). Executive dysfunction is of importance as schizophrenia has many similar symptoms to those of frontal lesions such as reduced spontaneity, avolition, mental rigidity, and lack of social judgment (Benson, Miller & B.L. 1997, as cited in Reichenberg, 2010). Secondly the "neurodevelopmental hypothesis" suggests that schizophrenia has an early onset, namely during the fetal stage or gains its roots from the environment but is generally dormant until the maturational process of the frontal lobes of the brain begins (Murray & Lewis, 1987; Weinberg 1998, as cited in Reichenberg, 2010).

Processing speed. Processing speed refers to the capacity with which the brain carries out cognitive functions. Psychometrically it refers to the number of simple tasks an individual can complete during a short interval. Processing speed is important as many higher cognitive functions are dependent on it such as retrieval of memory, perception and decision making. Coding tasks, such as the Wechsler Digit Symbol Coding can measure the processing speed

(Lezak et al., 2004), and show that it is significantly impaired in patients with schizophrenia and other neuropsychiatric disorders (Dickinson et al., 2007). According to Lezak et al. (2004) and Heinrichs (1998) and many other meta-analyses, such patients have severe to moderate difficulty in processing speed.

Cognitive and neural basis of hallucinations

Visual, auditory, somatosensory, olfactory and gustatory, all types of hallucinations are possible in schizophrenia. But it has been found that auditory hallucinations are the most common. McCarthy-Jones et al. (2013) noted that patients complain of hearing abusive language or opinions on their behaviour. Around half of the patients complain of these voices coming from outside their minds, and the opposite true for the other half, though the voice they hear is not their own. Antipsychotics are useful in reducing hallucinations of around 70% of patients. For the remaining 30% fMRIs are used, patients are asked to locate the areas of hallucination occurrence on the scan images. These images are contrasted and investigated with normal brain functioning scans or times when the hallucination period is not there. According to Jardri et al. (2011) and Kuhn et al. (2012) superior temporal gyrus to the left, other cortical areas such as inferior frontal gyrus (Such as the Broca's area), thalamus and basal ganglia are reported to be activated during hallucinatory episodes (As cited in Aleman, 2014).

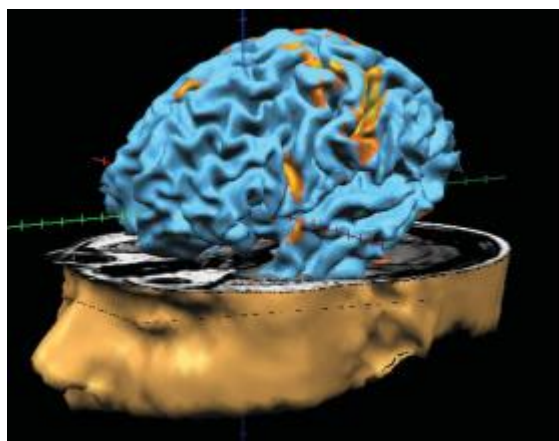


Figure 2: Activation of brain areas during language processing as measured with an fMRI scan (Philips 3T, Neuroimaging Center Groningen). Such language-related regions in the inferior frontal gyrus (Broca's area), temporoparietal cortex (Wernicke's area), and anterior cingulate are also seen to be active during auditory-verbal hallucinations.

Emotional Processing Abnormalities: Perception and Regulation

Although most researchers consider schizophrenia as a “non affective” disorder, which is purely cognitive, there is sufficient research to say that it is also an emotional disorder. A meta-study by Kohler et al. (2010) showed that patients with schizophrenia showed a large lack of emotional perception (As cited in Aleman, 2014). The patient is unable to recognize the tone of voice along with an inability to recognize facial expressions. Many studies mentioned in Aleman (2014) have reported that these patients lack community skills, social skills and problem solving. Yu et al (2010) have mentioned a lower activation in processing in schizophrenia and found reduced activation in bilateral amygdala, parahippocampal gyrus, and fusiform gyrus, right superior frontal gyrus and lentiform nucleus of patients with schizophrenia. In another study Baas et al. (2008) found that when compared with healthy

individuals a lower amygdala activation was found in patients with schizophrenia when they were asked to rate faces on the level of trust in fMRI scans.

Reduced Insight/Awareness of Illness

Reduced insight is a characteristic feature of psychosis. It is not only detrimental to the patient but also to the immediate family, caretakers and doctors as it impedes their attempt to help. The neural bases of insight are however a scientific mystery. Aleman et al. did find associations between reduced insight and poor cognition in terms of cognitive-shifts which in turn were controlled by the frontal cortex. Nair et al. reported that there are very small associations between insight and neurocognition. A number of studies have tried to find a cause for lack of cognitive insight in terms of abnormalities in the brain. These studies are mainly done through self-evaluation. Though the neurological basis in such studies is still to be understood, trying to understand insight is highly important in psychosis. Insight is also important in emotional regulation. A patient without insight would have a hard time trying to understand the implications of his judgements or behaviours. It has been found that empathy is a key ingredient as a patient, it can lead to better insight and hence regions of the brain that are actively involved in empathy should be researched upon like anterior insula, cingulate cortex, and regions subserving action simulation and mentalizing (Engen & Singer, 2013).

Apathy

Apathy or lack of interest in daily activities or general lack of initiative is another characteristic feature of schizophrenia. It may even come off as indifference. Bottlender et al. (2010) say that understanding apathy is important for clinical diagnosis in terms of severity of illness, unemployment and trying to understand the worst case scenario (as cited in Krabbendam and Jolles, 2003). Apathy is a negative symptom, and more focus is on the research of positive symptoms may be due to their outlandish nature. Apathy deserves its own spotlight and there are many supporters for establishing apathy as a syndrome with its own neurobiology (Reekum et al, 2005). Different types of apathy have been differentiated based on the neural circuit it affects. For example an oculomotor circuit would affect a form of apathy related to neglect as compared with a motor circuit activation. Apathy, being a less understood symptom one can only imagine how cumbersome it would be in treating this particular symptom. Glutamatergic signalling (Noetzel et al, 2012) and noninvasive neurostimulation using rTMS are one of the few available treatment methods that have shown some signs of progress. Some studies have even gone so far as to giving the brain a 10Hz stimulation on the dorsolateral prefrontal cortex daily. It has also been suggested by Aleman (2014) that the use of fMRIs along with rTMS could be beneficial in future research.

Treatment of cognitive and functional deficits

There has been substantial research in treatment of schizophrenia over the past decade, which also includes interventions. But these interventions aimed at social, vocational and remediation, very little focus has been given to cognition. It is of tremendous importance that cognitive interventions be included in the treatment of schizophrenia largely because it could be because of these cognitive deficits that social and vocational deficits underlie. Wykes et al. (2011) have suggested that social and cognitive interventions in the treatment of schizophrenia go hand in hand for better results (As cited in Greena & Harvey, 2001).

Conventional antipsychotics

These drugs were mainly designed for the treatment of positive symptoms and not for the betterment of cognitive functions. Though many of these drugs target the neurotransmitter systems, they do affect cognition either directly or indirectly. Ethical concerns fall upon researchers while trying to investigate drug influences on cognition. For example, it is not advisable to a patient to stop their medication just to see the effect of the drug on the brain. Though there are many studies which have shown that the effect of antipsychotics on cognitive functioning are so far only trivial. Seidman et al. (1993) proved that significant drug dosage reduction did not show any marked cognitive changes (As cited in Green & Harvey, 2001). In another study conducted by Verdoux et al. (1995) showed that these drugs actually slightly improved cognition. The anticholinergic properties of antipsychotic drugs are an exception to this case. They are known to damage memory function in patients with schizophrenia (Goldberg et al., 1993a; King, 1990; Spohn and Strauss, 1989, as cited in Green & Harvey, 2001)

Atypical antipsychotics

Clozapine, risperidone and olanzapine are some of the atypical drugs used. It was due to these drugs that treatment of cognition in schizophrenia received actual importance. Green and Harvey (2001) conducted several studies trying to reach to a conclusion of whether these drugs improve cognitive functioning. Verbal fluency, digit–symbol substitution, fine motor function and executive functions were the most affected areas by the atypical drugs. Though cognitive functioning on these dimensions did not reach a normal level, they were still substantially behind. This study gave insight into cognition enhancing drugs in schizophrenia, and it's increasing implication. According to Friedman et al. (1999) atypical drugs that increase dopamine receptors or the use of cholinomimetic drugs could be used (As cited in Green & Harvey, 2001).

Cognitive remediation

Cognitive remediation over decades has taken many forms, from laboratory-based exercises to interactive softwares. For instance, Medalia et al. (2001) used a software 'Where in the USA is Carmen Sandiego?' to inculcate problem solving in patients. The software included an investigative game, where the players had to help in finding/guessing the suspect. Green et al. used the WCST to study more single tasks such as whether performance can be improved by increasing one specific modification, example, reinforcement. Bell and colleagues (2001) used cognitive enhancement therapy, wherein feedbacks were given about cognitive functioning to the patients once in two weeks, 26 weeks of cognitive exercises for 5 hours each, and once a week social group. In contrast, Medalia et al. (2000, 2001) used a computer training method which consisted of 10 sessions of 25 minutes, twice weekly for 5 weeks (As cited in Green & Harvey, 2001).

The contribution of cognitive neuropsychology

Schizophrenia has a wide range of deficit symptoms, however there is no distinguishing deficit characterised to only schizophrenia. Attention, memory and executive function deficits are present not only in schizophrenia but other disorders such as unipolar or bipolar depression. The severity of the symptoms nonetheless are more severe in schizophrenia (Martinez Aran et al., 2000; Heinrichs & Zakzanis, 1998). Furthermore, clinical neuropsychologists find it difficult to differentiate between neurological disorders and traumatic brain injuries based on neurological assessments. Hence neuropsychologists do not and cannot rely on neurological tests to distinguish schizophrenia from other neurological ailments. Adding to this the problem that no single test can diagnose

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schizophrenia completely. Palmer et al. (1997) states that even the neurological assessment test results of patients with schizophrenia come out to be normal on various neurological domains. In short, neurological test results of schizophrenia can only be interpreted in the context of their qualitative analysis of the test, premorbid functioning and the course of deficits. When two individuals score the same on a test one cannot automatically interpret it as both of them having the same underlying dysfunction (Davidson & Keefe, 1995). Moreover, the reasons behind the poor performance of patients with schizophrenia on neurological tests is because of cognitive deficits and problems with brain processes which is usually not the case with neurological ailments. Moreover, clinical neurological tests were aimed at seeing the causes of brain lesions on behaviour. These tests are able to help researchers/clinicians identify the various cognitive deficits associated with schizophrenia, but they are unable to identify the nature or the origins of schizophrenia. According to Green & Harvey (2014), such tests could be aided with tests that describe the psychopathology of the disorder so as to support the results with a theory, enhancing our knowledge about the disorder. Clinical neuropsychological assessments may not be useful for patient-to-patient care, but it has been useful in its treatment and prognosis such as devising a cognitive remediation program.

CONCLUSION

Schizophrenia has a wide range of deficits. Attention, memory and executive functions are the main areas which are affected by schizophrenia. Neuropsychological assessments have helped in the better understanding of this disorder. This review paper has mentioned several examples where the neurological assessments have been used and possible scope for future research. The beginnings of specific cognitive deficits in trying to understand this disorder have already started. These deficits are measured in their association with a functional outcome (Reichenberg et al. 2006). Impairments in cognitive functioning are becoming ways to find susceptibility to the disorder and increase chances for better prognosis and treatment interventions. There has been success in understanding auditory hallucinations in terms of impairments in the functional areas of the frontal cortex. Hence the importance of understanding cognitive deficits. We have learnt more about schizophrenia in the last 10 years than the previous 100 years. The future holds promise as well as challenges.

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Conflict of Interest

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