

Cognitive Function in Schizophrenia: A Review

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Abstract

Schizophrenia is a mental disorder characterized by delusion, hallucination, formal thought disorder, disorganized or catatonic behavior, negative symptoms (e.g. emotional blunting, decreased initiative, impoverished speech etc.) and cognitive dysfunction. Though not described as diagnostic criteria, cognitive dysfunction is the strongest determinant of functional recovery as it has a gradual deteriorating effect on social and occupational functioning. It precedes coincides and outlasts positive symptoms. Among different cognitive abilities it affects attention, memory, processing speed, social cognition and executive function most. Recent studies are showing schizophrenia affects those who have compromised cognitive function or low IQ. Moreover different brain imaging techniques have shown structural and functional abnormality in certain areas. This article has tried to answer few questions like, are cognitive dysfunctions inevitable in schizophrenic patients and if it is then what are the areas what is the nature of affection. It is also important to know how and why they affect the long term outcome of this disorder.

Keywords: Schizophrenia; Cognitive function

Introduction

Schizophrenia is well known disorder characterized by delusion, hallucination, formal thought disorder, disorganized or catatonic behavior and negative symptoms (e.g. emotional blunting, decreased initiative, impoverished speech etc.). Though cognitive dysfunction is well known feature of schizophrenia and long back it was commented by Kraepelin that “mental efficiency is always diminished to a considerable degree. The patients are distracted, inattentive. They cannot keep the thought in mind.” [1]. to give emphasis on its gradual deteriorating effect on cognition, cognitive functions had failed to be described either as a diagnostic criterion or as a course specifier in different diagnostic systems. In new DSM5 in section III (Emerging Measures and Models) it has been included in “clinician-rated dimensions of psychosis symptom severity” [2]. The low IQ or delayed reaction time in chronic schizophrenic patients has been looked upon as a result of lack of motivation or cooperation, grossly disordered thought process or lack of reality testing. Gradually with the advent of different brain imaging techniques it became evident that schizophrenic patients have larger lateral ventricles [3], they also have less blood flow or metabolism in the prefrontal cortex [4]. If we think of the functional outcome of schizophrenia, it is a remarkably disabling illness. Among young adults in developed countries, it ranks near the top of causes of disability in both men and women [5]. There is now increasing support for the idea that key aspects of disability, such as reductions in social ability and the capacity for independent living and vocational success, are the result of neurocognitive compromise.

Keeping this background in mind I shall try to answer the following questions:

Can Schizophrenic be neuropsychologically normal?

Whether it is a generalized effect or it affects certain area?

General and Specific cognitive abilities

Long term outcome of cognitive dysfunction

Prognostic significance

Conclusion

Can Schizophrenic be Neuropsychologically Normal?

Numerous studies document that schizophrenia is associated with cognitive deficits [6-8], but the overall degree of neuropsychological (NP) impairment varies greatly across patients [9]. In fact, a few previous studies suggest that in some schizophrenia patients, NP abilities are unimpaired or normal [10,11]. To explore the prevalence and characteristics of schizophrenia patients with normal NP abilities Palmer et al conducted a study which included 171 clinically stable schizophrenia outpatients and 63 normal comparison (NC) participants. Different cognitive areas tested were verbal ability, psychomotor skill, abstraction and cognitive flexibility, attention, learning, retention, motor skill and sensory ability. According to results patients were divided into 2 groups NP normal (deficit in >2 area) and NP impaired. They found that 25.5% of schizophrenic patients and 85.7% NC were NP normal where as 11.1% of schizophrenic patients had no deficit in any area. They also noted that in contrast to the NC participants, among NP-normal schizophrenia patients the most common area of impairment was in learning (i.e., encoding and immediate recall) [12]. Nevertheless, a normal NP ability of a schizophrenic patient at any point of time does not exclude the possibility that he has deteriorated because prior to the disease onset he may have an above normal intelligence. An interesting study was done by Kremen et al. in which they tested 76 schizophrenia patients and 92 controls and blindly rated their neuropsychological profiles and compared patients rated as within normal limits (WNL) to normal control participants and to patients rated as abnormal. Consistent with the idea of compromised neurocognitive function as a core feature of the illness, they tested whether, in comparison to controls, there was evidence of poorer cognitive function even in WNL

schizophrenia patients. They considered function as abnormal or compromised if result was 2 SDs. below the control mean. They used WRAT-R Reading scores as an estimate of premorbid intellectual ability. The discrepancies between standardized scores on the WRAT-R Reading and current IQ based on age-scaled Vocabulary and Block Design subtests served as one index of decline from premorbid level of function. Like the previous study 23% of the schizophrenia patients and 92% of the controls were classified as having neuropsychological profiles that were WNL. But pairwise comparisons showed that neuropsychologically abnormal schizophrenia patients were substantially impaired on all neuropsychological functions compared with controls specially in abstraction-executive function and perceptual-motor speed, whereas in general verbal ability was nearly WNL patients scored somewhat higher than controls. So they concluded that even apparently unimpaired patients have compromised neuropsychological function relative to their expected or premorbid level of intellectual ability [13]. In another similar study Wilk.C.M et al compared 64 schizophrenic patients with a sample of closely matched on full scale IQ (FSIQ) healthy comparison participants. Verbal knowledge was taken as a measure of premorbid ability. Used measures were Verbal Comprehension Index (VCI), the Perceptual Organization Index (POI), the Working Memory Index (WMI), and the Processing Speed Index (PSI) Immediate Memory Index (IMI) and the General Memory Index. Schizophrenic patients scored higher than healthy comparison participants on verbal comprehension and perceptual organization but lower on processing speed, working memory, immediate memory, a secondary analysis among those in the high functioning patients (FSIQ>110) showed deficit in immediate memory and high POI [14] So cognitive abnormalities are core features of schizophrenia, because they affect even the highest functioning patients with the illness.

Whether it is a Generalized Effect or it Affects Certain Area?

One could easily assume that studies providing data for a meta-analysis use different test for a single cognitive ability. The most cited met-analysis was done by Heinrichs and Zakzanis who cautiously stated that all areas of neurocognitive function are compromised in a large proportion of schizophrenia patients but long-standing arguments concerning "core" or selective deficits against a background of general impairment are unlikely to be resolved. The main problem they found while doing the analysis were organizing the myriad of neurocognitive test variables reported in the literature into a coherent classification and many neurocognitive tests are probably influenced by several component processes. Thus, scores on the Vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) [15] may reflect both basic language abilities and general intelligence; scores on the Trail Making Test [16] may reflect not only visual scanning and perception but also motor speed, hand-eye coordination, and attention [17]. Hence it may be misleading to categorize tests on the basis of a faulty assumption that test performance is determined by only one process. They organized 22 neurocognitive test variables into meta-analyses to summarize the magnitude of schizophrenia-control discrimination in the published literature which were memory, motor, attention, intelligence, spatial function, executive ability, language, and inter-hemispheric transfer processes [18]. Seidman LJ et al. also noted that chronic patients with schizophrenia were significantly more impaired than controls on seven of eight neuropsychological functions (all but verbal ability) [19]. However most of the analyses suggest that the most affected areas are verbal learning, psychomotor speed,

working memory, vigilance. Other areas affected are visual memory, problem solving, verbal fluency & executive function. Least affected areas are perceptual discrimination and basic linguistic ability (naming, receptive vocabulary) [20].

General and Specific Cognitive Abilities

General intellectual ability:

From long back a distinction has been made between general and specific cognitive abilities. Two widely used indices of generalized cognitive ability have been applied in schizophrenia research: intelligence quotient or IQ, and composite scores or profiles derived from test batteries comprising multiple neuropsychological tests. While both provide a measure of an individual's overall cognitive functioning, the results of these assessments often do not overlap to a substantial degree. Neuropsychological test batteries typically focus on assessment of multiple cognitive abilities, such as memory, executive functions, attention, visuospatial ability etc. and these include a strong component of novelty of testing requirements. IQ tests, on the other hand, have a lesser emphasis on specific abilities and novelty and greater emphasis on the assessment of crystallized abilities [21].

A recent meta-analysis of research on IQ in schizophrenia suggests that early-onset and adult-onset schizophrenia are associated with intellectual deficits across the lifespan. Preschizophrenic children, adolescents, and young adults perform below matched controls on a variety of standardized measures of intelligence. Significant IQ deficits are also apparent after the onset of the disorder. Moreover, IQ is positively related to several indices of prognosis, and, among hospitalized patients, there is negative within-subject covariance between intellectual performance and symptom severity. Although there is fairly consistent evidence that Verbal IQ is higher than Performance IQ among schizophrenic patients, a more specific pattern of subtest performance is not apparent. A central question raised by the results is whether IQ is an independently determined factor that can serve to mitigate the vulnerability of individuals who are constitutionally predisposed to schizophrenia, or whether intellectual deficit is one manifestation of the constitutional predisposition to the disorder [22].

Attention

Early descriptions of schizophrenia recognized attentional impairments as fundamental aspects of schizophrenia long before the advent of formal neuropsychological testing or modern experimental psychology [1,23]. It is clear that attention is not a unitary construct. Posner and Petersen [24] proposed that attention should be broken down into three main functions: alerting, orienting, and selecting or executive control. Alerting is defined as achieving and maintaining a state of high sensitivity to incoming stimuli, Orienting is the process of selecting information from sensory input and selecting or executive control is the mechanism for monitoring and resolving conflict among thoughts, feelings, and responses [25].

The selecting or executive control part of attention is affected in schizophrenia [26] which is a higher-level metacognitive attentional system related to the subjective impression of mental effort. This form of supervisory or executive attention comprises the mechanisms for monitoring and resolving conflict among thoughts, feelings, and responses. Therefore, this attentional system is concerned with such tasks as working memory, planning, switching, and inhibitory control.

Since frontal patients are less able to implement a set of instructed goals, the orbital frontal area is probably important for this executive faculty [27,28]. It is important to remember that attentional impairments may disrupt many other cognitive functions. One could assume that poor attention would prevent many types of information from being processed appropriately. However, correlational studies have generally demonstrated that attentional dysfunction explains only a small proportion of the variance in other cognitive functions in schizophrenia [29].

The classic test of selective attention is Stroop color-word task, in which a word (e.g., red) can be printed in incongruent colors (e.g., green). Depending on instructions, the task is either to name the actual word or name the ink color in which the word is written. The attentional task requires the subject to focus selectively on one dimension of the stimulus and ignore or inhibit contextually inappropriate response tendencies. Normal subjects are slowed when they have to name a color of ink that is incongruent with the word because they have to inhibit their overlearned tendency of reading the word. Schizophrenic patients may have differential problems on this task in reaction time or accuracy, a finding that has been taken to suggest that they have disproportionate difficulty in inhibiting overlearned tendencies (of reading the word), and may be susceptible to failure in conditions of cognitive conflict more generally, because they are unable to use the contextual information appropriately [30]. Other two areas of attention affected in schizophrenia are sustained attention and shift attention. A test of sustained attention CPT (continuous performance test) involves monitoring a random series of numbers or letters that are represented continuously, often at a rate of approximately one per second. Participants are asked to detect a target event by pressing a response button and to avoid responding to foils or distracting stimuli. Schizophrenia patients consistently miss targets. The difficulty may be in rapidly encoding and acting on the imperative stimulus [31].

In one study using different visual search tasks Fuller et al tried to find the precise attentional control of schizophrenic patients by focusing on two separable components of attention namely the control of attention and the implementation of selection. The control of attention refers to the processes that determine what information should be attended and that are responsible for directing attention toward relevant sources of information. The implementation of selection refers to the processes that operate once attention has been directed to an object, allowing the attended object to receive preferential processing. They found that the control of attention that is the source of patient impairment, whereas the implementation of selection may be surprisingly intact. This impairment can lead to impairment in tasks as mundane as scanning the TV listings for a preferred program or finding the right variety of soup on a shelf may require significantly more time and effort for patients than for people without schizophrenia. Attentional control will be impaired if the executive control system cannot accurately form and maintain an accurate representation of the task. This could be a result of impairments in working memory, because Logan (2004) has shown that working memory is used by executive systems to maintain and use information about task definitions. Thus, the present results can be explained by postulating that patients with schizophrenia have difficulty maintaining or using an accurate representation of a visual search task in working memory [32].

Memory

According to Kraepelin, in schizophrenic patients memory “is comparatively little disordered.”¹ Bleuler also supported this view by stating “memory as such does not suffer in this disease.” 19 Modern views of memory disorder in schizophrenia are based on more precise, standardized neuropsychological measurement techniques, and contrast with the early clinical observations of memory functioning.

Influential and well-researched classification schemes have distinguished two types of long-term memory, declarative memory and nondeclarative memory, characterized by several key differences. Declarative memory encompasses both episodic memory (memory for events) and semantic memory (memory for facts), whereas nondeclarative memory encompasses simple classical conditioning, nonassociative learning, priming, and procedural memory. Unlike declarative memory, nondeclarative memory can take place without conscious awareness that anything has been learned [33].

Deficits in declarative memory are consistently reported in schizophrenia. Of 110 studies reviewed by Cirello and Seidman, [34] found evidence of impairment among schizophrenia patients on measures of declarative memory. Meta-analyses consistently report severe impairments in immediate and delayed verbal and nonverbal memory in schizophrenia, commonly assessed using verbal or nonverbal list-learning tests [18, 35]. Nondeclarative memory has been considerably less studied in schizophrenia, and has not been the focus of meta-analytic investigations. Nevertheless, research suggests that this aspect of memory is relatively preserved in schizophrenia patients. For example, procedural learning (“learning by doing”) may be defined as the development of skills in which the strategy of execution cannot be explicitly described. Schizophrenia patients show near perfect performance or only mild impairment on tasks of procedural learning [36,37]. Thus the memory problem is global thus the patients show failures in both encoding and retrieval. Strategy driven semantic encoding or mnemonic processing and recognition (they are susceptible to false recognition) are impaired in them [38].

Working Memory

Patients of schizophrenia often show loss of volitional control over the maintenance and manipulation of even basic information. They appear to have difficulty in formulating plans, initiating them, and flexibly changing a strategy once it is no longer effective; they also have difficulty in using feedback efficiently. Moreover, patients sometimes have problems when interrupted; they appear to forget what they were doing after only short periods of interference. One construct that attempts to capture these types of processing failures is working memory, which can be defined as a system or mechanism where information is represented, maintained, and updated for a short period of time. Different parts of the prefrontal cortex are involved with each modality of representation in working memory [39]. This definition emphasizes the process of maintaining representation active above threshold, so that the activation of information relevant to the current task can be maintained under the focus of attention, particularly when individuals experience interference from internal or external events. Maintaining the mental representation under the focus of attention in the presence of distraction, internal or external, also requires updating of the representation. This definition separates working memory from ‘traditional’ short-term memory by emphasizing the maintenance of representation the focus of attention. Short-term memory, which is closely related to working memory, is a

more passive system where items (either encoded or transferred from long-term memory and activated) decay quickly, especially when interference is present [40]. Different tests of working memory are Tests are n back test, backward digit span tests, AX CPT with a delay, letter number span test etc. It can be tested both in verbal and visuospatial modality. Working memory deficit is present in schizophrenia independent of the specific modality of the task. To perform a working memory task successfully, one has to 'encode' the target, internally represent the target, maintain the mental representation of the target while inhibiting irrelevant information, and retrieve the mental representation at the right moment. Dysfunction in one of these sub-processes may result in impaired performance. Recently several studies reported that poor encoding may contribute to the working memory deficits of schizophrenia patients. Working memory deficits in schizophrenia are reliably found across very diverse methods and approaches. It is Independent of specific modality though visuospatial working memory seems to be more consistent [41]. According to Baddeley four major components of working memory (i) the visuo-spatial sketch pad, a short-term storage buffer for visual information; (ii) the phonological loop, a short-term storage buffer for verbal information; (iii) a central executive that supports the manipulation and transformation of information held within the storage buffers; and (iv) an episodic buffer, in which complex, multi-modal events are integrated and stored on-line [42]. The central executive has been associated with the function of DLPFC in numerous studies, while the storage buffers have been associated with both inferior frontal and posterior parietal function [43]. Patients with schizophrenia have difficulty on the Brown-Peterson test, in which words have to be remembered over short delays during which covert rehearsal is prevented, presumably because of a compromised executive component [44].

Executive Function

The term "executive functions" was used to denote a group of higher cognitive functions of the prefrontal cortex, and has been used synonymously with the term "frontal-lobe functions." More recent conceptualizations of executive functions include several subprocesses, [45] and the view that not all executive processes are uniquely sustained by the frontal cortex. Specifically, some executive processes may be sustained by a distributed cortical network, rather than by a unique frontal region which may or may not be associated with the frontal lobes [46]. Executive functioning refers to volition, planning, purposive action, and self-monitoring of behavior. It describes a wide variety of higher order cognitive processes that allow the flexible modification of thought and behavior in response to changing cognitive or environmental contexts. Schizophrenic patients exhibit executive functioning deficits and these deficits are associated with treatment-refractory symptoms like negative symptoms, poor functional outcome [47,48]. Executive dysfunction might contribute to impairment in working memory and attention [49].

There is clear evidence that executive functioning involves multiple components. One view of executive functions suggests that there are at least five key components 1) attention and inhibition, 2) task-management, 3) planning, 4) monitoring, and 5) temporal coding [50]. Therefore, poor performance on this one task could be accounted for by impairment in a number of possible cognitive mechanisms. This can make it difficult to understand the nature of executive functioning deficits in people with schizophrenia when inferences are drawn on the basis of tasks that might be multicomponential. For example, it is

not uncommon for different schizophrenia studies to involve the same set of tasks (e.g., Wisconsin Card Sorting task, verbal fluency, Stroop) and yet to group these tasks in different ways and to report results for presumably different aspects of executive functioning. Numerous behavioral and imaging studies have shown that individuals with schizophrenia display impairments on a wide variety of tasks that presumably require rule generation and selection. For example, numerous studies have found that individuals with schizophrenia exhibit deficits on the Wisconsin Card Sorting task [51] along similar lines, people with schizophrenia also exhibit deficits on the Intradimensional Extradimensional shift task [52]. Moreover, people with schizophrenia have also been found to be impaired on the Switching Stroop task, with poor performance associated with increased disorganization symptoms, and with evidence that this is a specific deficit and not due to generalized poor performance [53]. Overall, rule generation and selection seems to be a cognitive neuroscience construct that can be readily measured in humans and animals, plays an important role in executive functioning ability, and is impaired in schizophrenia. A number of studies have provided evidence of impaired performance monitoring in schizophrenia. In particular, many studies have reported reduced ACC activity in people with schizophrenia (involving conventionally large effect size differences), which has been found when making errors or during high-conflict trials, including functional magnetic resonance imaging and electroencephalography studies. Moreover, there is evidence that impaired performance monitoring is associated with negative and disorganization symptoms [54] and predicts poor executive functioning in schizophrenia [55,56].

Social Cognition

In the mid nineties, social cognition began to be a focal point of research because it was thought to be a factor that could partly explain the deterioration of social functioning in persons suffering from schizophrenia because poor social functioning was a major cause of disability of schizophrenia. Currently, results of various studies suggest that social cognition is a mediator variable between basic cognition or neurocognition and social functioning [57,58]. Social cognition refers to the set of processes and functions that allow a person to understand and benefit from the interpersonal environment [59]. The most important areas of social cognition are: emotion processing, theory of mind, social perception, social knowledge (social schema), and attributional bias. Emotional processing is a construct involving a broad range of aspects related with perception and using emotions. The findings in the area of emotional processing indicate that schizophrenics have a marked deficit in facial and vocal affect recognition [60]. These deficits are not related to age, gender and level of medication or dosage of neuroleptics and these deficits in facial affect recognition occur in recognition and discrimination [61-63].

Happiness is the most easily recognized facial expression followed by surprise, and the judgment of fear is less accurate than other emotions. However the review of Edwards et al emphasizes on the methodological limitations of the studies due to the ambiguous characteristics of the participants and the wide variety of instruments used, which makes the validation and generalization of the results difficult [64]. The ability to infer the mental states (beliefs, thoughts, and intentions) of others in order to predict and explain their behavior has been conceptualized as the possession of a "mentalizing" ability or "theory of mind" [65, 66]. Persecutory delusions reflect false beliefs about the intentions and behavior of others that could arise from

theory of mind deficits. Frith proposed that theory of mind deficits underpin the origin of delusions of persecution, delusions of reference, delusions of misidentification, third-person auditory hallucinations, some aspects of thought disorder (disordered pragmatics), and negative symptoms (asocial behavior, blunted affect). He hypothesized that theory of mind skills in people with persecutory delusions develop normally (in contrast to individuals with autism) but are “lost” during an acute psychotic episode [67]. A set of studies used so-called first- and second order theory of mind stories. In a first-order story, a character has a false belief about the state of the world; in a second-order story, a character has a false belief about the belief of another character. Correct inference of the mental states of characters is required to understand the actions within the stories that are a result of false beliefs or intentional deceptions. Patients with persecutory delusions had impaired performance on questions concerning the mental states of the characters within the stories and, to a lesser degree, on reality questions (assessing their memory of the factual content of the stories). Patients with negative symptoms and those with thought disorder also showed impairment on questions regarding mental state, but this difficulty was significantly associated with more pronounced memory impairments. Patients with passivity features and those in symptomatic remission performed the tasks as well as normal subjects, indicating that any theory of mind deficit is a state rather than a trait variable [68].

Attribution theory provides a framework for understanding the causal explanations that individuals give for their own behavior and the behavior of others [69]. It has been estimated that normal people make a causal attribution (a statement that includes or implies the word “because”) every few hundred words [70]. Normal subjects consistently demonstrate a self-serving attributional bias in explaining the causes of events; that is, they tend to take credit for success (internal attribution of positive events: the “self-enhancing” bias) and to deny responsibility for failure (external attribution of negative events: the “self-protective” bias to enhance their self esteem. Studies with clinical groups have typically used questionnaires that ask participants to infer the likely causes of hypothetical positive and negative events. Patients with persecutory delusions (with diagnoses of paranoid schizophrenia or delusional disorder) show an exaggeration of this self-serving attributional bias. Moreover paranoid patients are additionally abnormal in that negative self-referent events are attributed to active malevolence on the part of the other person (external personal attribution) rather than to the play of circumstances or chance (external situational attribution) [71].

Long term Outcome of Cognitive Dysfunction

Several views exist regarding long term outcome of cognitive dysfunction of schizophrenia. Previously it was suggested that cognitive deficits become progressively worse throughout the long duration of the illness. After an insidious onset, patients’ intellectual functions become weaker and social skills become coarser [72]. A second view suggests that cognitive deficits, once they arise, remain relatively stable; this view is thus consistent with the notion of a static encephalopathy [73]. In the study of Weickert et al about 50% of a large series of treatment-refractory patients exhibited a large decline in IQ from estimated premorbid levels, although a minority of patients had marked cognitive limitations from early on [74]. This is to say that subtle premorbid deficits exist in the majority of patients. Recent population- based studies have demonstrated attenuations in intelligence measures in future schizophrenic patients [75,76], in

addition to delays in the attainment of some early developmental milestones [77]. A number of cross-sectional studies searched for evidence of decline during the chronic phases of the illness. Davidson et al. [78] reported a decline of two to three points per decade in a global measure of cognitive functioning, the Mini-Mental State Examination, across the range of 25 to 95 years whereas the decline in patients with Alzheimer disease is 1.5 points per year. Consistent with these results, Harvey et al. [79] recently found that elderly patients in this cohort display a marked decline on a clinical global rating of functioning. However, long term effect of high dose neuroleptics, long term institutionalization and effect of aging could be responsible for this decline. In a cross-sectional approach Hyde et al compared cohorts of schizophrenic patients. Each cohort was matched on a measure of premorbid intellectual ability. No significant differences between age cohorts were noted on tests like the Mini-Mental State Examination, Dementia Rating Scale, verbal list learning, and semantic fluency. Thus, over five decades of illness, no progression was noted [80]. All the above finding suggests that in the a sharp decline in cognitive ability, including general intellectual efficiency, occurs around the time of the onset of clinical symptoms, which is followed by an arrest in deterioration and a long period of impaired but stable cognitive function. This view of the natural history of schizophrenia is consistent with a neurodevelopmental rather than neurodegenerative nature of the disease.

Can cognitive functions improve over long run? Spaulding et al. assessed cognitive changes in disabled and stabilized chronic patients over 6 months in an enriched psychosocial treatment environment. The study showed improvements in 9 of 12 measures of cognitive functioning in chronic schizophrenia patients with especially severe residual impairments. Measures of memory and executive functioning showed improvement, while measures of reaction time and continuous attention did not. Thus, there is evidence that at least under certain conditions; some aspects of impaired schizophrenic cognition are subject to improvement in the chronic course [81].

Prognostic Significance

In chronic stage schizophrenic patients become functionally disabled due to reduction in social skill, occupational failure and needs support. Studies suggest that neurocognitive deficits may be critical for functional outcome [82]. Cognitive impairment may also contribute in a unique manner to outcome. Patients’ deficits in learning new information, rapidly completing tasks, purposefully recalling old information, and generating novel plans or hypotheses may have an impact on their vocational success, ability to take part in social transactions, and make decisions. Though it is not clear which neurocognitive measures are the most useful predictors and correlates of functional outcome, however meta-analyses demonstrate that four neurocognitive constructs are significantly related which are Secondary/Episodic memory, Immediate memory, Attention/vigilance, Executive functioning/ card sorting [83]. If we think of other clinical symptoms, psychotic symptoms (hallucinations and delusions) are poor predictors and correlates of functional outcome [83]. Negative symptoms are more highly correlated with functional outcome, but across studies, the relationships are neither stronger nor more consistent than those for neurocognitive deficits [84]. Little is known about disorganized symptoms, which often constitute a separate syndromal dimension that includes formal thought disorder. It is likely that some cognitive domains have direct, causal relationships, although others may be related to functional outcome through

mediators, such as social cognition or the application of knowledge and reasoning to problem solving.

Conclusion

Though schizophrenia has been regarded as a psychotic disorder, cognitive under performance precedes the clinical onset, remains throughout life, has a genetic basis and influences functional outcome. A recent meta-analysis by Khandaker et al. [85] has shown that low IQ increases the risk for developing schizophrenia in a dose-response fashion (effect size 0.43): every point decrease in IQ increases the risk by 3.7%. Another meta-analysis, also found low IQ to increase the risk for schizophrenia, with an effect size of about 0.5. Interestingly, this risk was already evident by age 13 years, many years prior to psychosis onset [86]. Another important aspect is whether impairment starts before clinical illness. One study compared the population average on childhood scholastic test performance as measured by the Iowa State tests of basic skills and educational development to 70 subjects who later went on to develop schizophrenia. These tests were administered to all children across the state of Iowa in grades 4, 8, and 11 (corresponding to the ages of 9, 13, and 16 years) assessing 5 cognitive domains. Although the (prospective) patients did not differ from the state average at ages 9 and 13 years, they underperformed significantly at age 16 years (with an effect size of around 0.35), with the most pronounced deficits in language skills. Thus, cognitive functioning related to scholastic test performance appears to decline between the ages of 13 and 16 years in the subjects who go on to develop schizophrenia [87]. Though at present we are not in a position to explain the clinical feature as a manifestation of mere cognitive impairment, it is obvious that identifying this impairment at a prepsychotic period may help to start an early intervention.

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