Schizophrenia from a Neuropsychiatric Perspective

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Abstract

Our understanding of schizophrenia has increased substantially in recent years. This is due to technological advances that have improved our ability to assess neuropsychiatric function and the genetic underpinnings of the disease. While diagnostic classification still relies on the presentation of the more overt symptoms of the disease, the neuropsychiatric perspective provides a more accurate and comprehensive understanding of the illness. This perspective provides insight into the etiology and treatment of schizophrenia. This article provides an overview of schizophrenia from the broad viewpoint of neuropsychiatry.

Key Words: Schizophrenia, neuropsychiatry, cognition.

SCHIZOPHRENIA IS A DISEASE defined by a number of symptoms that differ across individuals in their presence, frequency, severity, and topography. This heterogeneity in symptoms has complicated the search for the etiology of the disease and the mechanisms for its treatment. This article paper will review schizophrenia as a neuropsychiatric disease. Signs and symptoms of schizophrenia will be considered within the conceptual framework of neuropsychiatry, including aspects of consciousness and awareness, orientation, perception, cognitive impairments, affect, thought and language, and neurological soft signs. The classical symptoms of schizophrenia (e.g., positive symptoms such as delusions and hallucinations and negative symptoms such as blunted affect and social withdrawals) will not be reviewed specifically here, but will be discussed within the context of the neuropsychiatric domains, where appropriate.

Consciousness and Awareness

The study of consciousness and awareness has been complicated in general by the difficulty in utilizing these constructs. Consciousness has been defined in degrees to encompass a number of processes from the most basic (e.g., a simple response to sensory stimulation) to the awareness of one's own complex thought processes. These constructs rely heavily on a phenomenological approach, and difficulties in the assessment of internal experiences are well understood. It is difficult to assess and quantify these constructs because patients with schizophrenia rarely accurately describe such overt behaviors as symptoms (1) and their own functional abilities (2). Therefore, assessments of internal experiences that rely on self-reporting are likely to have questionable validity.

The process of self-monitoring allows individuals to distinguish self-generated thoughts and behaviors from those generated by others. This cognitive process has been used to attempt to explain some schizophrenic symptomatology. For example, patients with schizophrenia, particularly those with positive symptoms such as hallucinations and delusions, tend to have deficits in self-monitoring (3). These monitoring deficits may have a causal relationship with clinical symptoms, since schizophrenia patients with hallucinations or formal thought disorder (compared to schizophrenia patients without these symptoms and healthy individuals) have deficits in the ability to match their own behavior with its consequences (4). Delusions, especially those that heavily influence behavior, are also associated with deficits in monitoring the origin of one's ideas and the reasons for one's actions (5). Patients with auditory hallucinations tend to misperceive internal stimuli as originating from the external environment, and these misperceptions can be tactile (6), verbal (7, 8), or visual in nature (9). Taken together, these findings suggest that deficits in self-monitoring may underlie some symptoms of schizophrenia, particularly delusions

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and hallucinations. This is particularly relevant because the cognitive causes of these experiences have proven difficult to identify in previous research.

Cognitive abilities such as attention, memory and problem solving are important predictors of everyday functional outcomes, such as independent living, interpersonal relationships, and occupational success. While cognitive impairments may be the single best predictor of everyday functioning outcomes, they are not particularly strong predictors. For example, a considerable amount of the variance in these everyday outcomes is not accounted for by impaired performance on cognitive tests. Some of this lack of overlap may be accounted for by social cognition, which has emerged recently as an important concept in understanding the impact of the disease. Abilities in this domain include the identification or recognition of another person's emotions (and by inference their internal experiences) based on his or her facial expression or tone of voice (10, 11). An important theoretical model of social cognition is the Theory of Mind, which posits that people make sense of the world by conceptualizing their own and others' behaviors in terms of their own beliefs and desires (12). Deficits in social cognition secondary to the Theory of Mind have been used as a partial explanation for the social withdrawal into autism that has been described in schizophrenia since the 19th century (14). Schizophrenia patients with negative symptoms may show some signs of exaggerated social withdrawal, and many of these patients have difficulty explaining their own or making sense of others' internal experiences; these deficits in social cognition are not a consequence of cognitive impairment (13).

Assessment of "metacognitive" processes is another mechanism associated with consciousness and awareness. As distinguished from self-monitoring, described above, which is the ability to identify the origin of stimuli, metacognitive processes involve the ability to monitor the nature and quality of one's cognitive operations and to regulate behavior and thought in response to changing external stimuli. The consideration of these monitoring processes may also assist in making the results of cognitive testing more generalizable to the patient's behavior in the real world. For example, schizophrenia patients' performance on formal neuropsychological tests measuring cognitive abilities such as verbal memory, problem solving, working memory, and processing speed accounts for only a modest amount of variance in explaining everyday functioning (14, 15). Moreover, the relationship between cognition and real world functioning may be mediated by other symptoms of the illness (16) and external environmental barriers, such as social conditions and decreased incentive to seek employment due to disability payments (17).

Since it is more "ecologically" valid (i.e., generalizable to the real world), deficits in social cognition should explain some part of the functional deficits in schizophrenia. While it is not yet largely represented in the literature base, there is some evidence that impairments in social cognition are not fully determined by the severity of other cognitive deficits (18) and that social cognitive factors may mediate the relationship between neurocognition and functioning in the real world (19). This influence might occur because the ability to realistically evaluate one's competence, likelihood of success in performing skilled acts, and reactions of others to one's behavior is an integral part of real-world functioning. If one is highly competent but unaware of this competence, the likelihood of attempting skilled acts would be reduced. If one overestimates one's ability or misperceives others reactions to them, then one's behavior may be poorly matched in the environmental situation, increasing the likelihood of failure, regardless of level of skill.

Koren and colleagues (20) have proposed experimental paradigms for assessing metacognitive skills that measure confidence and control over responses to traditional cognitive tasks. For example, many typical problem-solving tasks require a careful step-by step process in which each successive step is informed by the results of the immediately previous strategic effort. If, however, the ability to estimate the reasons for failure is reduced or, particularly, if the ability to detect failure is reduced, then the likelihood of developing a successful trial and error strategy is grossly limited. Thus, people with schizophrenia may fail in problem-solving tests not because of a global deficit, but rather because of highly specific deficits in applying information that they have just learned (e.g., the accuracy of their last response) to their next problem-solving step (i.e., their next response). These paradigms offer a methodology that provides some additional information that goes beyond correctness of responses on test items in terms of understanding the complex task of interacting with the external environment.

Orientation

Cognitive deficits and poor self-awareness are cardinal features of schizophrenia; gross disorientation to time and place is not as commonly found.

An exception is found in patients with a very adverse course of illness and severe progressive cognitive impairments; in such cases, disorientation to time and place may be present (21). Most schizophrenia patients do not appear to be disoriented to person, and they are typically oriented to time and place. However, a substantial minority (approximately 25%) of younger patients tend to be disoriented with regard to their age (22, 23). In later life, schizophrenia is associated with a worsening of cognitive performance that often resembles dementia in its severity and scope, with multiple, generalized, severe-to-profound cognitive deficits (24, 25). Age-disorientation is a stable and more common feature of the illness in later life and is most common in patients with severe global cognitive impairment (26). Its stability, along with a lack of correlation with treatment history, premorbid adjustment, education, or amount of social interactions (27, 28), suggests that this feature may be a trait of some patients and predictive of poorer everyday outcomes and poor response to antipsychotic treatments as well.

Perceptual Organization

The ability to organize sensory input is a fundamental basis for cognition. Obviously, any dysfunction in sensory systems will have consequences for higher-order cognitive processes. While perceptual dysfunction is found in a number of patients across sensory modalities, there is evidence that these deficits are specific to a limited subset of patients with the illness. As mentioned above, schizophrenia is a disorder characterized by heterogeneity across individuals with the same diagnosis and within-patient variability in symptom severity over time. We noted earlier that certain deficits in self-monitoring appear to be associated with positive symptoms. On the other end of the schizophrenia spectrum are patients who might not have frank psychosis through much of their illness, but have many negative symptoms. These patients, with negative and disorganized symptoms as opposed to predominantly positive symptoms, display poorer perceptual organization (29, 30). Similar findings of poorer perceptual organization have been found in those with deficit syndrome (31), those with poorer premorbid social functioning (32), and in patients in the chronic phase of the illness (33).

A series of studies by Javitt and colleagues have identified early (i.e., basic) visual and auditory processing abnormalities in schizophrenia. These impairments probably contribute to the more obvious and frequently studied higher-order cognitive processes and may provide some explanatory potential for deficits in object recognition (34) and auditory recognition (35), and underlie impairments in social cognition (36). It will be interesting to determine whether these cognitive impairments are as closely associated with functional outcomes, or not. If these deficits, which might be easier to target with specific pharmacological agents or behavioral strategies, correspond to improvements in higher-order cognitive processes, one might be more likely to see real world treatment effects.

Cognitive Impairments

Cognitive deficits were described as primary features of schizophrenia in the seminal descriptions of the disease (37, 38). Much of the research and treatment focus since these early descriptions, however, has been on the more obvious features such as positive symptoms and thought disorder. A return to the study and, later, treatment of cognitive deficits in schizophrenia has followed two trends. Evidence of lack of treatment progress throughout the 20th century (39) raised concerns that treatment of positive symptoms of the illness, though necessary, was not sufficient for recovery or even promoting independent living in many cases. Additionally, a growing body of work suggested that cognitive deficits were the best predictors of dysfunction across many domains, such as interpersonal relations, occupational skill acquisition and work success, and treatment success (14, 15). In this article, we provide a brief review of cognitive impairments in schizophrenia. See Bowie and Harvey (40) for a comprehensive review of this important topic area.

Cognitive impairments are found across most domains (e.g., attention, working memory, verbal fluency, processing speed, executive functions, verbal memory) in the vast majority of schizophrenia patients. These impairments tend to be moderate in magnitude (i.e., one to two standard deviations below the performance mean of healthy individuals), with superimposed severe deficits in domains such as verbal learning and executive functioning (41). Even patients who perform within the normal range of functioning on neuropsychological tests are impaired relative to their estimated intellectual functioning (42). Thus, it has been proposed that cognitive impairment is universal in schizophrenia (43). Deficits in cognition are considered a primary feature of schizophrenia because they are detectable even before the onset of frank psychosis (44). Cognitive deficits are also detectable in healthy first-degree relatives of schizo-

phrenia patients (45), and in individuals on the schizophrenia spectrum who do not meet criteria for schizophrenia (46) and are independent of other symptoms (47). By the time of the first episode of psychosis, deficits are present and moderate-to-severe across many domains (48) and mild intellectual decline appears to occur during this first episode (49). Cognitive dysfunction appears to remain stable in its severity and topography through middle age (50). However, in late life, global declines may occur in chronically ill patients (24, 25), but declines in patients with a less chronic course have been reported to be much more specific, possibly restricted to complex information-processing tasks that measure processes that are difficult to observe clinically and detectable only with specific neuropsychological instruments (51, 52).

Affect

Disturbances in affective expression (e.g., blunted affect) and experience are hallmark negative symptoms in schizophrenia. It is generally accepted that negative symptoms represent a distinct feature of the illness (53). The expression of affect is distinct from other negative symptoms such as social dysfunction and disorganization (54), and shares less variance with cognition, outcome domains and positive symptoms. Blunted affect has been incorporated into a categorical model of schizophrenia known as the deficit syndrome (55). These patients, with severe emotional blunting and little interest in purposeful activities, are characterized by a particularly poor course of treatment for refractory schizophrenia.

Depressive symptoms, also present in many schizophrenia patients (56), are difficult to distinguish from blunted affect. Recent work suggests that self-reported depressive symptoms are an important barrier to occupational and interpersonal performance, independent of cognitive dysfunction and other symptoms. They may serve as rate-limiting factors in patients with schizophrenia, in that they may be a hindrance to real world *performance* even in patients who have the *ability* to perform tasks (16). The presence of mood symptoms, such as depression and mania, contributes to the diagnostic distinction between schizophrenia and schizoaffective disorder. Mood symptoms are a necessary consideration for clinicians, because they can further interfere with the patients' functioning (16) and quality of life (57).

Thought and Language

Along with negative and positive symptoms, organized thought disorder has constituted a fundamental feature of schizophrenia throughout its diagnostic history. Thought disorder, measured by language output, has three common manifestations. It can be characterized by a paucity of speech with limited expression of thoughts; by poor connectedness, referred to as loosening of associations; or by unusual and/or illogical thinking.

Schizophrenia patients often (up to 40% of consecutive samples) display poverty of speech, defined as a reduction in the amount of speech. These patients typically offer little information voluntarily, and their responses to questions are often perfunctory and brief. Alternately, approximately 25% of patients with schizophrenia may have pressured speech, similar to those with mania, where it is more commonly observed. This may manifest as an increase in the amount of words offered (which is often accompanied by abnormalities in the connectedness of speech, described below), the rate of speech, or increased volume and pitch.

Disconnected speech is distinct from poverty of speech in schizophrenia, in that it typically involves an excess of speech. Examples of disconnected speech include circumstantiality (long-winded and wandering speech that circles the topic area without really describing it), derailment (speech that shifts away from the topic area), tangentiality (off-topic responses to questions), and loss of goal (speech that is completely removed from the topic). This manifestation of thought disorder occurs at a higher rate in schizophrenia, with approximately 56% of patients displaying derailment.

Other evidence of communications abnormalities includes unusual symptoms such as neologisms (personally created words that hold a unique meaning to the speaker), word approximations (real words that are assigned a new meaning), clanging (speech that is connected by rhymes or other phonological mechanisms), and echolalia (repetition of another speaker's words). These aspects are less common (e.g., 2% display neologisms) than disconnected speech and poverty of speech. Thus, although they are highly distinctive, they are not useful diagnostic indicators.

The causes of thought disorder in schizophrenia are still being explored. Some models suggest that they are attributable to failures to monitor the source of information (58), i.e., the patient manifests difficulty in discriminating the source of information in short-term memory, confusing internal thoughts with externally presented speech. Schizophrenia patients demonstrate errors in context processing, or the ability to use information from the surrounding environment to facilitate the efficient processing of information (59). Barch and

Berenbaum (60) found that different aspects of formal thought disorder could be reliably observed by manipulating the context in which the speech was produced. Another potential causal mechanism of formal thought disorder is related to deficiencies in the structure of semantic networks. Patients with schizophrenia have difficulty accessing semantic information (61), and their language output tends to be poorly organized in terms of semantic relationships (62). Disconnected speech is relatively stable over short-term follow-up periods, with a general increase in underproductivity in later life (63).

Conclusions

Schizophrenia is a complex disease that manifests with a heterogeneous profile across patients. Conceptualizing the illness from the perspective of neuropsychiatry enables the practitioner to better understand the most clinically relevant aspects of the disease. It is now well understood that cognitive impairments are present and substantial in nearly all schizophrenia patients, even those experiencing their first episode of psychosis. These deficits may become more marked in later life and are an important treatment target, because they are the best predictor of a patient's level of interpersonal skills, occupational functioning, and self-care. Although patients' cognitive impairments are severe and they may be disoriented as to their own age, they do not typically evidence disorientation to person, time or place. An important clinical distinction involves negative versus affective symptoms. Depressive symptoms have at least a semantic overlap with the negative symptoms of schizophrenia, yet they appear to be distinct features of the illness. There are therapeutic implications for distinguishing affective from negative symptoms, making careful examination of these symptoms necessary in clinical practice.

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