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Review article

Cognitive impairments in schizophrenia: a review

Niaz Mohammad Khan, Muhammad Zillur Rahman Khan, Md. Khairul Bashar, M M Jalal Uddin

Abstract

Background: Cognitive deficits in schizophrenia are profound and affect most of the patients.

Objectives: To find out the recent advancement and findings related to cognitive impairment in schizophrenia.

Methods: This narrative review was conducted with available literatures after meticulous search in PubMed, PubMed Central, Google, Google Scholar with the searching keywords.

Results: The most prominent of the cognitive deficits in schizophrenia are memory, attention, working memory, problem solving, processing speed, and social cognition. These impairments exist prior to the initiation of antipsychotic treatment and are not caused by psychotic symptoms in patients who are able to complete cognitive testing, which include most patients. The various cognitive deficits in schizophrenia have all been shown to be associated with functional outcomes such as difficulty with community functioning, difficulty with instrumental and problem-solving skills, reduced success in psychosocial rehabilitation programs and the inability to maintain successful employment.

Conclusions: Cognitive deficits are better able to explain important functional outcomes, such as work performance and independent living; than positive or negative symptoms.

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Keywords: Cognitive impairments; schizophrenia

Introduction

Schizophrenia is a severe psychiatric disorder characterized by a wide range of symptoms. These include positive symptoms, such as hallucinations and delusions, negative symptoms, such as apathy and amotivation, and impaired cognition. It affects approximately 1% of population worldwide. Cognitive features are an important but neglected component of schizophrenia. Cognitive deficits in schizophrenia are profound and affect most of the patients. Patients with schizophrenia perform 1.5 to 2.0 standard deviation below healthy controls on a variety of neurocognitive tasks. The most prominent of these deficits are memory, attention, working memory, problem solving, processing speed and social cognition.[1] These impairments exist prior to the initiation of antipsychotic treatment[2] and are not caused by psychotic symptoms in patients who are able to complete cognitive testing, which include the overwhelming majority of patients.[3] The various cognitive deficits in schizophrenia have all been shown to be associated with functional outcomes such as difficulty with community functioning, difficulty with instrumental and problem-solving skills, reduced success in psychosocial rehabilitation programs[4] and the inability to maintain successful employment.[5] In fact, cognitive deficits are better able to explain important functional outcomes, such as work performance and independent living, than positive or negative symptoms.[6] Schizophrenia is now almost universally recognized as a neurobiological disorder with a strong neurocognitive component.[6,7] In contrast to earlier cognitive studies of schizophrenia

that were frequently focused on distinguishing schizophrenia from "brain damage",[8] or on the description of schizophrenic thinking on a strictly psychological level[9] , an enormous and still growing body of neuropsychological research on schizophrenia over the last few decades has been based largely on either of two premises: (a) specification of the neurocognitive pattern(s) associated with schizophrenia may help clarify the neuroanatomical and/or neurophysiological systems that underlie expression of the disorder[10] and (b) recognition that identifying cognitive strengths and weaknesses within persons with schizophrenia and the relationship of such cognitive abilities/deficits to psychosocial or independent living functions, might prove clinically useful in developing effective placement and rehabilitative plans.[11]

Methods

With this background, the literature review was done to find out the facts and findings that would help to understand the cognitive impairment in schizophrenia better and how to address it in clinical practice. This narrative review was conducted with available literatures after meticulous search in PubMed, PubMed Central, Google, Google Scholar with the searching keywords. The keywords were cognitive impairment, schizophrenia and outcome. Several articles were found, and the authors selected the articles which were relevant, available and updated. Several peer reviewed literatures were cited which are mentioned in the reference section.

Results and discussion

Neuropathological basis of cognitive impairment in schizophrenia precise delineation of the neuropathology underlying schizophrenia in general, or its associated neurocognitive deficits, have both remained elusive despite efforts extending back over a century.

There are some general patterns reviewed below. Brain MRI studies of schizophrenia have found lower gray matter volumes (especially in the superior temporal gyrus and in medial temporal lobe and limbic structures including the amygdala, hippocampus, and parahippocampal gyrus), volume reductions in the frontal and parietal lobes, lack of normal asymmetries, enlargement of the caudate (perhaps related to medication), and developmental abnormalities such as presence of cavum septum pellucidum [thought to reflect aberrations in neurodevelopment; patients with larger cavum septum pellucidum may show worse performance on learning and other cognitive measures.[12] There are also frequent abnormalities in the size or shape of the corpus callosum,[13,14] supporting the view of schizophrenia as a disconnection syndrome and, as with earlier CT findings, there are enlarged ventricles.[15,16] Functional imaging studies have found lower activity in the prefrontal cortex and abnormal activation in the temporal lobes during performance of both verbal and visual tasks.[17,18] These findings are also true for PET and SPECT, where the literature suggests problems in the prefrontal and temporal regions of the brain.[19]

In resting state network studies using fMRI, results are mixed as to the effect that schizophrenia has on connectivity.[20] Overall, the main areas that are implicated in both resting state and activation-based fMRI studies on an assortment of cognitive-based tasks include parts of the cerebral cortex (i.e. prefrontal, cingulate and temporal areas), the limbic system (specifically the hippocampus, striatum and thalamus), and the cerebellum.[21] Additional information has come through studies employing Diffusion Tensor Imaging (DTI), which measures the fractional anisotropy of white matter tracts (i.e. how intact the tracts are). In schizophrenia, rather consistent findings are abnormalities in these tracts, leading to increased diffusivity in the prefrontal and temporal lobes, corpus callosum, uncinate fasciculus, cingulum bundle and arcuate fasciculus.[22,23] Other significant central nervous system findings in schizophrenia are in neurochemical dysfunction (e.g. reduced N-acetyl aspartate in the frontal and temporal lobes, hypercortisolemia and hypothalamo–pituitary–adrenal axis dysregulation and an increase in D_2 receptors in the striatum), neurophysiological dysfunction (including abnormal prepulse inhibition, decreased P300 amplitudes, and REM sleep abnormalities) and at autopsy, decreased dendritic density accompanied by normal or increased neuron density and absence of gliosis.[7]

Level and domains of cognitive impairment

Schizophrenia is best characterized as involving broad neurocognitive deficits across most cognitive domains. The average cognitive deficit associated with schizophrenia appears to be approximately one standard deviation (SD) below the mean of healthy

comparison subjects.[24] In regard to specific cognitive domains, the general trend in the literature seems to be that the strongest effect sizes are associated with tests of episodic memory (particularly free recall) and processing speed, with the least (but still medium to large effect size differences) associated with measures of crystallized verbal knowledge and visual-spatial skill. For instance, among studies reviewed by,[25] the lowest mean effect sizes were seen with the Wechsler Block Design (d=0.46) and Vocabulary (d=0.53) subtests; the strongest mean effect size was seen on tests of "Global Verbal Memory" (d=1.41). Similarly, the largest effect sizes were associated with tests of memory (d=1.18) and the lowest with tests of language function (d=1.01) and global cognitive function or IQ (d=1.01).[26] In a recent meta analysis of studies of persons in their first-episode of schizophrenia, also found the largest effect sizes, on average, to be associated with tests in the domain of auditory memory (d=1.20).[27] More recent studies indicate that approximately 15% to 30% (with most estimates between 20% to 25%) of schizophrenia patients have neuropsychological profiles in the normal range.[27,28] For instance, using a previously validated procedure for systematic clinical ratings of results from an expanded Halstead-Reitan battery found 47 of the 171 (27.5%) people with schizophrenia had "neuropsychologically normal" profiles.[29] So it can be said that approximately 75% of schizophrenic patients have cognitive function in an impaired level.

Course of cognitive impairment in schizophrenia

There is compelling evidence that schizophrenia is associated with early premorbid cognitive deficits.[30] Results of two meta-analytic reviews of studies documenting premorbid IQ among persons who subsequently developed schizophrenia suggest presence of at least a mild premorbid cognitive deficit, with an average premorbid Full Scale IQ of 90 to 95 compared to the population mean of 100, with SD of 15.[31] One longitudinal study shows that persons who developed schizophrenia had lower IQ scores when tested as children relative to the non-schizophrenic controls; moreover, the persons with schizophrenia, on average, showed a decline of approximately 10 IQ points (adjusted for changes seen in the control group) from age seven to the time when they were re-tested in their 30s.[32] There has been somewhat less consensus regarding the long-term course of cognitive deficits after onset of illness, but even in that regard, a general agreement appears to be emerging that, contrary to Kraepelin's initial suggestion that dementia praecox is characterized by a course of progressive decline, the cognitive deficits in schizophrenia tend to stabilize[33] and may even partially improve during the initial stabilization phase immediately after first onset.[34]

Treatment aspect of cognitive impairment in schizophrenia

The general wisdom about the lack of beneficial effects of conventional neuroleptic medications on cognitive deficits in schizophrenia may not be true. A meta-analyses of the available empirical literature found, contrary to conventional wisdom, that there might indeed be some beneficial neurocognitive effects of conventional neuroleptic medications, which while modest in size (mean effect size d=0.22), at least warrant further empirical inquiry.[35] The era of "atypical" or "second generation" antipsychotic medications is a long and circuitous one dating back to the late 1950s, but systematic study of the effects of second generation antipsychotic medications on the neuropsychological deficits in schizophrenia began in the early to mid-1990s. The subsequent decade brought some suggestions that second-generation antipsychotic medications might partially improve certain aspects of neurocognitive functioning.[36] The largest and most comprehensive investigation of the cognitive effects of antipsychotic medications was provided by the NIMH-sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study. The CATIE study involved a randomized double-blind comparison of schizophrenia treatment for up to 18 months with any of the five medications, including four second generation antipsychotics (olanzapine, quetiapine, risperidone, or ziprasidone) and one conventional neuroleptic (perphenazine). The cognitive effectiveness analyses were based on 817 patients who completed at least a baseline and 2-month follow-up assessments. There was a significant improvement in overall cognitive performance within each of the treatment groups, and there were no significant differences between the treatment groups in terms of changes in any of the five specific cognitive domains. Similar findings were seen in the subset of

participants for whom 6 or 18-month follow-up data were available. The difference in cognitive scores from 2 to 18-month was negligible, suggesting the bulk of improvement occurred in the first two months of treatment.[37] The findings from more recent report from the European First Episode Schizophrenia Trial also suggested no differential cognitive benefit of second generation antipsychotics versus conventional neuroleptics.[38] The question of differential cognitive benefits of second generation versus conventional neuroleptic medications is not fully settled.[39] Using the data from the Research on Asian Psychotropic Patterns for Antipsychotics (REAP-AP) study, it was found that a direct association between disorganized speech and the adjunctive use of mood stabilizers, cumulative dose of anxiolytics and hypnotics, and an inverse association with the adjunctive use of antiparkinson drugs.[40] In recent years, there has been an increasing recognition of the need for psychosocial rehabilitative interventions for schizophrenia. At the post-treatment assessment, those in the cognitive training group reported fewer cognitive problems and more use of compensatory strategies than those in the pharmacotherapy-alone group.[41,42] Cognitive remediation was associated with significant improvements across all three outcomes cognitive performance, symptoms, and psychosocial functioning in schizophrenia.[42]

Conclusions

The presence of cognitive impairment in schizophrenia patients is essential for diagnosis, management, and further studies about the etiological aspect of the disorder. Recent proposals have been made to include cognitive impairment as a diagnostic tool for schizophrenia in DSM V and ICD 11. Though there are several studies regarding cognitive function in schizophrenia in other countries, it has not been studied thoroughly in Bangladeshi schizophrenia patients. So, this issue should be given more emphasis in research matters.

Niaz Mohammad Khan, Associate Professor, Psychiatry, National Institute of Mental Health (NIMH), Dhaka, Bangladesh; **Muhammad Zillur Rahman Khan,** Associate Professor, Psychiatry, Patuakhali Medical College, Patuakhali, Bangladedsh; **Md. Khairul Bashar,** Assistant Professor, Psychiatry, Shaheed Syed Nazrul Islam Medical College, Kishoreganj, Dhaka, Bangladesh; **M M Jalal Uddin,** Associate Professor, Psychiatry, National Institute of Neuro Sciences (NINS), Dhaka, Bangladesh.

Correspondence: Niaz Mohammad Khan, Associate Professor, Psychiatry, National Institute of Mental Health (NIMH), Dhaka-1207, Bangladesh.
Email: nmadil27@gmail.com

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