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Cognition in Schizophrenia: Natural History, Assessment, and Clinical Importance

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Retrospective studies have demonstrated that schizophrenic patients often have poor premorbid cognitive function and social adjustment. Cross-sectional studies of the cognitive performance of schizophrenic patients aged 20 to 90 years indicate that there is a gradual decline in cognitive function throughout the adult life span. Comparison studies of Alzheimer's disease patients, geriatric schizophrenic patients, and normal subjects indicate that Alzheimer's disease patients have marked impairments in memory and executive function, with impairments in language and constructional ability developing later in the disease. In contrast, schizophrenic patients manifest more general cognitive impairment with less impairment in memory and more impairment in visuospatial and language ability early in the course of dementia. Neuropathological findings indicate that the dementia associated with schizophrenia is pathophysiologically distinct from that of Alzheimer's disease. Functional impairment in patients with schizophrenia is closely related to cognitive deficit but not to positive and negative psychotic symptoms. Based on these findings, assessment strategies for evaluation of antipsychotic drug therapies are proposed to incorporate measures of psychosis, cognition, and function.
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KEY WORDS: *Schizophrenia; Cognitive impairment; Alzheimer's disease; Brain pathology; Assessment tools*

Neurocognitive impairments are recognized important features of schizophrenia (Bilder 1997). These deficits appear to affect all patients to some degree and may contribute to poor long-term outcome. Early studies of dementia progression over the life span of patients with schizophrenia have shown inconsistent results; however, these studies were limited by lack of standardized diagnostic criteria and lack of specificity of evaluation techniques (Bleuler 1978; Goldstein and Zubin 1990; Hyde et al. 1994; Keefe et al. 1987; Schwartzman and Douglas 1962). More recent studies have indicated that progressive cognitive impairment with a distinct pattern of deficits is an important aspect of the syndrome of schizophrenia (Harvey et al. 1999; Davidson et al. 1996). This cognitive decline has a trajectory over the course of the illness that is different from that of psychotic symptoms and may be the major contributor to poor functional outcome in elderly patients (Davidson et al. 1995; Harvey et al. 1998).

Novel approaches to therapy for schizophrenia must include outcome measures that take into account cognitive and functional deficits in addition to psychotic symptoms. This paper will review some recent studies investigating cognitive impairment in schizophrenic patients as well as studies that compare the cognitive deficits observed in schizophrenic patients to those of patients with Alzheimer's disease. These results are used to propose a strategy for evaluation of the effects of schizophrenia treatment on measures of cognition.

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COGNITIVE DEFICITS IN SCHIZOPHRENIA

Temporal Issues

Schizophrenia is a lifelong illness. Given the importance of the biological effects of aging on the brain, it is important to consider the cognitive manifestations of schizophrenia in the context of aging. Significant issues include the natural history of cognitive dysfunction over the life span and the temporal relationship between the onset of psychosis and cognitive deficits. Difficulties with this approach are the result of the complex interactions between aging, schizophrenic symptoms, cognitive impairment, and factors associated with the illness, including poor education, poor cooperation, and presence of concomitant medical and neurological illnesses (Davidson et al. 1995). Characterization of specific cognitive deficits and understanding of the clinical significance of these deficits also may have significant implications for therapeutic development.

Impaired attention and poor eye tracking have been observed in patients with schizophrenia as well as at-risk individuals (Cornblatt and Keilp 1994; Levy et al. 1994). A review of 40 studies that used various versions of the Continuous Performance Test (CPT) concluded that impaired attention is consistently present in schizophrenic patients in a pattern specific to the disease (Cornblatt and Keilp 1994). Deficits in attention are detectable in unaffected children of parents with schizophrenia and may predict later behavioral abnormalities. Eye-tracking dysfunction also has been consistently demonstrated in these patients and their first-degree relatives (Levy et al. 1994). The presence of these abnormalities in those at risk for development of schizophrenia suggests that the biological abnormalities responsible for psychotic symptoms are genetically linked with specific cognitive impairments.

The course of cognitive dysfunction over the life of a patient with schizophrenia has been a matter of debate. Although several studies have supported the model of schizophrenia as a progressive dementing illness (Bilder et al. 1992), other studies have supported the view that cognitive impairment in schizophrenia fits the model of a static encephalopathy (Goldberg et al. 1993; Goldstein and Zubin 1990; Hyde et al. 1994). Hyde et al. (1994) performed a cross-sectional study to assess cognitive performance in schizophrenia across a wide age range. Seventy-four hospitalized patients with chronic schizophrenia aged 18 to 69 years were included. All patients were receiving neuroleptic drugs and most also were receiving anticholinergic agents. A comparison of cognitive measures among five age-derived cohorts was performed. No evidence of accelerated intellectual decline was found. Scores on the Mini-Mental State Examination (MMSE), Dementia Rating Scale, List Learning, Semantic Fluency, or perseverative errors on the Wisconsin Card Sort Test were not significantly different between cohorts. Performance on the Boston Naming Test significantly declined with increasing age; however, the observed decline was more related to age than to length of illness. Mean performances on the majority of tests were abnormal across all cohorts, although a progressive decline in cognitive function was not observed.

Davidson et al. (1995) studied schizophrenic symptoms and cognitive performance in 393 chronically institutionalized schizophrenic patients stratified into seven age groups of 10-year intervals, from 25 to 85 or more years. MMSE scores in these patients declined from a mean of 27.6 in the youngest age group (25–34 years) to 9.6 in the cohort aged 85 years and older (Table 1); scores consistent with dementia occurred in most patients over the age of 65 years. The raw scores on the Positive and Negative Syndrome Scale (PANSS) and the percentile rank according to norms for each age group are also shown in Table 1. Significant effects of age group on MMSE score ($p < .001$) were found. Positive symptom scores decreased significantly with age ($p < .01$), and an increase in negative symptom scores with age approached statistical significance ($p < .06$). There was a statistically significant correlation between negative symptom scores and MMSE scores, but not between positive symptom scores and MMSE.

If it can be assumed that age cohort differences in this cross-sectional study reflect decline in individual cognitive performance, the decline is very slow, averaging approximately 2 points per decade on the MMSE. This is in contrast to the cognitive decline of Alzheimer's disease, which proceeds at a rate of 3 to 4 points per year (Morris et al. 1993). The findings of this cross-sectional study suggest that age-associated changes in structural and functional parameters superimposed on static abnormalities related to schizophrenia may produce the slowly progressive decline in cognitive function observed in these patients.

Harvey and colleagues (1999) performed a longitudinal study of institutionalized geriatric patients with schizophrenia. Patients aged 65 years or older were assessed using the Clinical Dementia Rating Scale (CDR) (Berg 1988), which evaluates six cognitive and functional domains, and were followed for 30 months. At baseline, CDR scores of 0, 0.5, or 1, corresponding to no or mild dementia, were reported. Worsening of dementia was defined as achieving a CDR score of $\geqslant 2$ on follow-up. The percentage of patients who had worsened was 12.6% and 15% at 12 months and 30 months, respectively. Although a substantial number of patients were lost to follow-up during this period, findings are consistent with a pattern of worsening cognitive and functional impairment. This decline was not associated with neuroleptic treatment or with negative symptom severity, but rather with more severe baseline positive symptoms.

Table 1. Mini-Mental State Examination (MMSE) Scores and Subscale Scores on the Positive and Negative Syndrome Scale of Seven Age Groups of Institutionalized Schizophrenic Patients (Davidson et al. 1995)

			Positive and Negative Syndrome Scale					
			Negative Symptom Score			Positive Symptom Score		
Age Group (years)	MMSE Score Mean	MMSE Score SD	Mean	SD	Percentile Rank[a]	Mean	SD	Percentile Rank[a]
25–34	27.6	3.1	22.2	5.6	50	21.3	7.6	60
35–44	23.3	5.6	24.3	8.5	65	21.6	6.6	60
45–54	22.1	7.7	22.7	7.1	55	22.1	4.9	65
55–64	20.4	5.9	25.0	8.9	70	23.3	6.1	70
65–74	16.3	6.7	25.9	8.4	75	18.7	5.8	45
75–84	14.2	7.9	28.8	3.7	85	18.0	6.6	40
85 and older	9.6	7.3	28.7	7.7	85	16.7	6.7	30

[a] According to norms for the scale.

Characterizing the Abnormalities

The development of sensitive and specific standardized assessment tools that can be used to characterize and follow deficits related to dementia has only recently occurred. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) developed a neuropsychological battery that characterizes the primary cognitive manifestations of Alzheimer's disease (Morris et al. 1988). Test measures include category fluency and Boston naming, which test language impairment; list learning, delayed recall, and recognition, which are related to memory; and drawing or praxis, which is psychometrically separate. The MMSE is also part of the CERAD battery. These measures have been shown to have substantial test-retest and cross-center interrater reliability and to be valid in discriminating patients with mild-to-moderate dementia from normal controls (Morris et al. 1989).

These measures are useful in the detection and staging of Alzheimer's disease and have determined that the deficits develop at different stages of the disease (Welsh et al. 1992). In early, mild disease, delayed recall is the most prominent feature of the disease. Decreased performance on confrontation naming is also a feature of mild disease but is less severe than delayed recall deficits at this stage and is less reliable in detecting early disease. Decreased performance on praxis and fluency testing are features of more advanced disease and are useful in differentiating moderate from severe disease. These findings are consistent with the known pathophysiological progression of Alzheimer's disease, which begins in the medial temporal lobe, progresses to the association cortex, and involves the sensory cortex only in the late stages of the disease (Geula and Mesulam 1996).

Subsequently, the CERAD battery was used to assess the cognitive impairments of chronically hospitalized schizophrenic patients (Harvey et al. 1996). In contrast to Alzheimer's disease, all aspects of cognitive impairment worsened uniformly with the increasing global severity of dementia as measured by the MMSE. Deficits did not show distinct patterns based on disease severity.

Davidson et al. (1996) compared cognitive performance using the CERAD battery among patients with Alzheimer's disease with a group of geriatric patients with schizophrenia who were matched for age, gender, education, and global cognitive impairment. A matched group of normal subjects was also included for comparison. The CERAD measures demonstrated that the pattern of cognitive deficits in schizophrenia was distinct from that of Alzheimer's disease. Across all levels of cognitive impairment, patients with schizophrenia performed more poorly than Alzheimer's disease patients on naming and constructional praxis tests and controls but were less impaired on delayed recall measures (Table 2). Deficits tended to be less sharply differentiated across cognitive domains at all levels of global impairment for schizophrenic patients than for patients with Alzheimer's disease, consistent with a more diffuse neuropathologic pattern than that observed in Alzheimer's disease. Considering this and other studies of cognition in schizophrenic patients, it appears that cognitive deficits of schizophrenia in descending order of severity are attention, executive function/decision making, memory/new learning, psychomotor skills, expressive language, receptive language, and praxis.

NEUROPATHOLOGY OF DEMENTIA IN SCHIZOPHRENIA

Improvement in understanding of the cognitive impairment of schizophrenia syndrome in the past decade has

Table 2. Performance on Neuropsychological Tests for Patients With Schizophrenia, Patients With Alzheimer's Disease, and Normal Comparison Subjects (Davidson et al. 1996)

	Comparison Subjects[a] (n = 66)		Patients with Alzheimer's Disease (n = 66)		Schizophrenic Patients (n = 66)	
Test	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Naming	14.4	0.8	11.5	2.8	10.2[b]	3.3
Praxis	10.0	1.3	7.6	2.6	6.2[c]	2.8
Word list memory						
Trial 1	5.0	1.7	1.8	1.5	2.2	1.6
Trial 2	7.4	1.5	2.8	1.7	2.9	1.9
Trial 3	8.3	1.3	3.4	1.7	3.7	2.3
Delayed recall	6.9	1.8	0.8	1.3	1.4[d]	1.7

[a] Comparison subjects performed better than both groups of patients on all measures ($p < .05$).
[b] The schizophrenic patients performed significantly worse than the patients with Alzheimer's disease ($F = 8.24$, df = 1, 65, $p < .01$, matched sample ANOVA).
[c] The schizophrenic patients performed significantly worse than the patients with Alzheimer's disease ($F = 10.89$, df = 1, 65, $p < .001$, matched ANOVA).
[d] The schizophrenic patients performed significantly better than the patients with Alzheimer's disease ($F = 7.02$, df = 1, 65, $p < .01$, matched sample ANOVA).

been accompanied by renewed interest in the basic biology and neuropathology of the disease. Powchik et al. (1998) examined brain tissue from 100 consecutive autopsied patients with schizophrenia who had a mean CDR of 2.3 (SD = 1.2, range = 0–5) and 135 patients with Alzheimer's disease. A series of psychiatric elderly subjects who did not meet *DSM-III-R* criteria for schizophrenia or a developmental disorder were also examined.

Of the 100 geriatric schizophrenic patients, 48 had no significant neuropathological findings. Findings consistent with Alzheimer's disease were present in nine patients. Three patients had other recognizable dementias, including two with Parkinson's disease and one with multi-infarct dementia. These findings can be examined in light of epidemiologic data, which indicate that clinically diagnosed Alzheimer's Disease is present in approximately 20% of the population older than 70 years of age (Evans et al. 1989). The fact that neurofibrillary tangles and senile plaques of Alzheimer's disease are not present in schizophrenic patients with significant cognitive impairment indicates that the dementia of schizophrenia syndrome is pathophysiologically distinct from that of Alzheimer's disease even though a few patients may have both diseases. Thus, it is essential that efforts continue and be coordinated nationally, if not internationally, to further study the neurobiology of these diseases.

COGNITIVE IMPAIRMENT AND CLINICAL OUTCOME

The cognitive impairment of schizophrenia has a significant impact on overall outcome in patients with chronic schizophrenia. Harvey et al. (1998) compared the cognitive, symptomatic, and adaptive functioning of 97 chronically hospitalized geriatric schizophrenic patients, 37 patients with chronic schizophrenia who resided in nursing homes, and 31 community-dwelling patients admitted for acute exacerbation of schizophrenia (see Table 3). Cognitive functioning was assessed using the MMSE and the CERAD battery. Additional assessments were made using the PANSS and the Social Adaptive Functioning Evaluation (SAFE) scale, a 17-item measure of social-interpersonal, instrumental, and impulse control skills.

Each of the three populations were discriminable from the other two. Community-dwelling patients with acute illness were the least cognitively impaired, and nursing home patients displayed the most severe adaptive deficits. The greatest discriminator between nursing home patients and community-dwelling patients was the profound deficit in adaptive functioning seen in the nursing home patients. The severity of cognitive deficits was a strong predictor of adaptive functioning for all three groups and was a strong predictor of overall outcome. The severity of psychotic symptoms did not discriminate as strongly between these groups, although positive symptoms were greater among chronically hospitalized patients than those in nursing homes, and negative symptoms were least among community dwellers than among those in chronic care settings.

In the longitudinal study conducted by Harvey and colleagues (1999), patients were assessed using the MMSE, the PANSS, and the SAFE scale at baseline and at an average follow-up period of 2.5 years after referral for nursing home care. Both MMSE scores and SAFE scale total scores worsened significantly over the fol-

Table 3. Clinical, Cognitive, and Adaptive Functional Scores of Geriatric Schizophrenic Patients in Three Settings (Harvey et al. 1998)

	Chronic Psychiatric Hospitalization (n = 97)		Nursing Home (n = 37)		Acute Hospitalization (n = 31)	
Measure	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Positive and negative syndrome scale						
Positive symptoms	21.28	6.03	15.51	5.84	22.40	4.77
Negative symptoms	30.19	8.59	32.19	7.71	25.47	8.45
Social adaptive functioning evaluation scale	40.09	12.46	46.08	10.78	18.60	7.73
Mini-mental state examination	9.95	9.80	7.60	8.37	22.40	4.78
Composite neuropsychological battery[a]	−0.16	0.65	−0.19	0.64	1.25	0.78
Individual cognitive measures						
Modified Boston naming test	5.34	5.55	4.57	4.89	12.93	1.70
Praxic drawing examination	2.60	3.26	2.54	3.30	7.83	2.30
Animal category fluency	4.92	4.80	4.18	3.51	8.13	4.51
Word list delayed recall savings[b]	0.10	0.02	0.11	0.19	0.56	0.77

[a] Developed by the consortium to establish a registry for Alzheimer's disease (Morris et al. 1988).
[b] The proportion of information learned at the final learning trial that was reproduced at delayed recall.

low-up period, while PANSS positive and negative subscale scores remained stable. The only measures that predicted decline in SAFE scores were baseline levels of adaptive functioning and decline in cognitive function. This correlation occurred regardless of baseline levels of cognitive functioning. These two studies indicate that while levels of psychotic symptoms are considered to define the schizophrenia syndrome, it is actually the degree of declining cognitive impairment that best predicts the functional status and degree of care ultimately required by the patient with schizophrenia (Harvey et al. 1998, 1999).

Cognitive Assessment Scales

Increased understanding of the pathophysiology of Alzheimer's disease in recent years has led to ongoing development of novel drug therapy. To assess the efficacy of potential therapeutic agents, the United States Food and Drug Administration (FDA) developed guidelines stating that a drug treatment for dementia must be shown to improve two independent outcome measures compared with placebo: 1) a performance-based assessment of cognitive function; and 2) a clinician's global assessment of the patient's clinical condition (Ad Hoc Dementia Assessment Task Force 1991). The first of these ensures that core deficits that may not be apparent on casual observation alone are evaluated, and the second ensures that the treatment effects measured are clinically significant. Other countries also have drafted guidelines similar to those of the FDA (Mohs and Ferris 1998). In addition, the European Union's Commission on Pharmaceutical and Medical Products stressed the importance of functional measures, such as Activities of Daily Living (ADL) (Committee for Proprietary Medicinal Products 1997).

Performance-based cognitive assessment scales for Alzheimer's disease should satisfy several criteria, including the ability to measure all major Alzheimer's disease symptoms that are considered clinically significant. Moreover, they should be reliable, brief, and applicable over a broad range of symptom severity. Validity should be indicated by the fact that they reflect the progressive decline associated with the disease.

The Alzheimer's Disease Assessment Scale (ADAS), which was developed in the early 1980s and is now widely used, was designed specifically to be used as an outcome measure in clinical drug trials (Mohs et al. 1983). Development of this scale was initially based on a comparison of the cognitive effects of normal aging with those observed in dementia (Table 4). Those functions normally not affected or minimally affected by Alzheimer's disease, such as reading, vocabulary, long-

Table 4. Cognitive Functions Affected by Normal Aging and Dementia

	Normal Aging	Dementia
Reading	No	No
Vocabulary	No	No
Long-term factual memory	–	–
Immediate memory span	–	–
Sustained attention	–	– –
Language (naming)	–	– – –
Serial learning	– –	– – –
Motor speed	– –	– – –
Delayed recall	– –	– – – –
Visuomotor skills	– –	– – – –

Table 5. Distribution of Items on the Alzheimer's Disease Assessment Scale (updated from Mohs et al. 1983)

Symptom Assessed	Number of Items	Number of Points
Cognitive behaviors	12	75
Memory	3	27
Orientation	1	8
Language	5	25
Praxis	2	10
Concentration	1	5
Noncognitive behaviors	7	35
Depressed affect	2	10
Psychosis	2	10
Agitation/motor activity	3	15
Total	19	110

term memory, and immediate memory span, were not included in the scale. Those cognitive functions that differentiate dementia from normal aging make up the cognitive portion of the ADAS (ADAS-Cog). The content of the ADAS is listed in Table 5. In addition to cognitive measures, this assessment instrument includes measures of the behavioral and affective disturbances that often occur in patients with Alzheimer's disease.

Performance-based measures of cognition have been used in the context of clinical trials with meaningful results. In a double-blind placebo-controlled trial of donepezil, for example, cognitive improvement was demonstrated in the treatment group in both ADAS-Cog scores and MMSE scores, while these scores declined in patients who received placebo (Rogers et al. 1998). These cognitive measures were validated by the clinical global impression of change (CGIC) which also showed improvement with drug treatment. Functional measures were more variable but generally favored the drug-treated groups.

Cognitive Assessment Scales in Schizophrenia

Although measures developed for Alzheimer's disease patients have been used to assess cognitive deficits in patients with schizophrenia (Harvey et al. 1992), there are several issues that should be addressed before any one tool is considered optimal. The core cognitive domains that adequately identify patients with cognitive impairment and reflect changes in that impairment must be defined. This may be difficult due to the global nature of deficits that occur in schizophrenia; measures used in clinical trials must be broad enough to detect all clinically important effects. Assessment scales that are too extensive, however, may also create problems. In trials that have used extensive batteries of multiple domains, such as the donepezil trial (Rogers et al. 1998), portions of data were missing for individual patients, making data more difficult to interpret. The optimal number of domains necessary for adequate cognitive assessment of patients with schizophrenia has not yet been defined.

An ideal assessment tool for cognitive function in schizophrenia must be useful for a wide range of patients, including those with cognitive deficits as well as varying degrees of both positive and negative symptoms. In addition, patients may be of widely different ages and educational levels. While some global measures have been designed to be more useful at different stages of the disease, such as the ADAS-Late Version (ADAS-L) (Kincaid et al. 1995), an instrument that is highly discriminant at all stages of disease would be ideal.

Measures of efficacy used in clinical trials of novel therapies for schizophrenia must have significance for the clinician for trial results to be translated into clinical practice. While multiple measures of individual domains are often useful and of interest to neuropsychologists, they are of limited interest to less-specialized clinicians. Although several cognitive domains should be evaluated, the overall impact of treatment on cognition will need to be assessed in any treatment trial, therefore, summary measures are desirable. In addition, these assessments should also correlate with functional measures that reflect the patient's ability to live in the world and ultimately indicate the level of care that the patient will require. Criteria for a battery useful for to assessing treatment effects on cognition in schizophrenia are presented in Table 6.

Treatment of Cognitive Deficits

A large number of studies using conventional antipsychotics in schizophrenic patients have demonstrated that their therapeutic efficacy is limited to the positive symptoms of the disease. However, with the development of atypical antipsychotics and the recognition that the severity of negative symptoms and cognitive deficits are associated with increased functional disability (Green 1996), there has been a movement toward investigating the effects of antipsychotic treatment on cognitive deficits. Keefe et al. (1999) recently performed a

Table 6. Criteria for an Ideal Assessment Tool to Evaluate Treatment Effects on Cognition in Patients with Schizophrenia

Criteria
• Good test-retest reliability
• Assesses all major cognitive domains impaired in schizophrenic patients
• Suitable for a broad range of schizophrenic patients
• Performance correlates with functional measures
• Provides a single measure of cognitive status plus assessments of individual cognitive domains

meta-analysis of 15 studies that examined the effects of a variety of atypical antipsychotic agents (e.g., clozapine, risperidone, ziprasidone) on cognitive deficits in schizophrenic patients (Keefe et al. 1999). The results of this meta-analysis showed that atypical antipsychotics, when compared with conventional antipsychotics, improved cognitive functions in patients with schizophrenia. Cognitive functions that responded best to treatment with atypical antipsychotics included verbal fluency, digit-symbol substitution, fine motor functions, and executive functions. Attentional processes were also responsive; whereas, learning and memory functions were the least responsive. Because the tests showing the greatest improvement following treatment with atypical neuroleptics all involve psychomotor speed as well as cognition, it is possible that some of the observed improvement is due to the reduced extrapyramidal side effects of atypical antipsychotics (Keefe et al. 1999).

Although all currently available antipsychotic agents have some antagonistic activity at D_2-receptor sites, they vary substantially with regard to their activity at other receptor sites. Atypical antipsychotics affect multiple neurotransmitter systems, including cholinergic, adrenergic, serotonergic, and dopaminergic types. It is the activity of these agents at non-D_2 receptor sites that may have important clinical consequences, including selective effects on the cognitive deficits of schizophrenia. Unfortunately, at present, the relationship between receptor subtype and cognitive function is poorly understood (Meltzer and McGurk 1999). Despite the fact that the results of the meta-analysis by Keefe et al. (1999) appear promising, the results of large-scale clinical trials are required to elucidate the extent to which specific cognitive deficits in schizophrenia can be improved by currently available treatments and what neurotransmitter receptors are involved.

CONCLUSIONS

Neurocognitive impairment appears to affect all schizophrenic patients to some degree and contributes to deficits in adaptive functioning. Although the cognitive deficits associated with schizophrenia worsen with increasing age, the rate of decline is not as great as that of Alzheimer's disease on other late-onset progressive dementias. Age-associated changes in structural and functional parameters superimposed on the static abnormalities of the disease may produce the slowly progressive decline in cognitive function observed in schizophrenic patients. Importantly, the cognitive deficits of schizophrenia are distinct from those of Alzheimer's disease, with deficits in attention, executive function and decision making, and new learning most severely impaired in patients with schizophrenia. With the recognition of these symptoms, studies have examined the correlation between psychotic symptoms, cognitive impairment, and adaptive functioning. The degree of cognitive impairment appears to correlate with and predict functional status and degree of care required by the patient with schizophrenia. Based on these findings, the development, validation, and routine use of assessment tools for cognitive function in schizophrenic patients are important in the evaluation of novel therapies for schizophrenia.

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