1 The course of cognitive impairment in patients with schizophrenia

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Introduction

Although a vast literature pertaining to neuropsychological deficits in schizophrenia has amassed over the past 45 years, the exact timing and course of the neuropsychological deficits remains obscure. Some authors have provided evidence for a decline of intellect from premorbid levels subsequent to the onset of schizophrenia, while others have failed to obtain evidence for such a decline of intellect. Finally, some studies have suggested that patients with schizophrenia suffer severe cognitive and intellectual damage early in their development, while other studies would, by inference, imply that there is no basis for such severe cognitive deficits early in the development of patients with schizophrenia. The focus of this chapter will be to review the literature pertaining to the nature and extent of cognitive deficits in schizophrenia including studies pertaining to the presence or absence of intellectual decline in an effort to synthesize these disparate findings into a unified description of the course of cognitive impairment in schizophrenia.

General intellectual decline

Numerous investigators have described a decline in the intellectual abilities of patients with schizophrenia subsequent to the onset of disease. In a small sample of 10 hospitalized patients with schizophrenia, Rappaport and Webb (1950) obtained an average deficit of 33 points between pre- and postmorbid measures of Intelligence Quotient (IQ). In a group of US Armed Forces inductees who went on to develop schizophrenia, Lubin *et al.* (1962) observed declines from premorbid cognitive levels ranging between 0.17 and 0.3 standard deviation units. In a group of Canadian armed forces servicemen who went on to develop schizophrenia subsequent to their initial testing, Schwartzman and Douglas (1962) demonstrated a 15.2 point decline between pre- and postmorbid intellectual levels.

In a group of 63 hospitalized patients with schizophrenia, Nelson *et al.* (1990) observed significant differences between present and premorbid estimates of IQ. Premorbid estimates of IQ have been used routinely as a means of comparing current cognitive deficits with prior intellectual ability or potential before the onset of illness. These premorbid estimates are

based upon the traditional belief that certain neuropsychological tests are sensitive to brain damage (the so-called 'no hold' tests) while others remain insensitive (the so-called 'hold' tests, for example the ability to read and pronounce words which is usually acquired at an early age). Several studies have demonstrated the validity of using reading and pronunciation tests as estimates of premorbid intellectual ability in patients with schizophrenia. Dalby and Williams (1986) demonstrated that although there were high correlations between reading and intelligence in normal controls, average reading ability was contrasted with lower intellectual levels in patients with schizophrenia. Nelson *et al.* (1990) also obtained premorbid intellect estimates in patients with schizophrenia that were significantly below the average for normal. Additionally, the findings of Kremen *et al.* (1996) further supported the construct of 'hold' versus 'no hold' tests in patients with schizophrenia by showing similarities between spelling and reading scores while current IQ and arithmetic scores represented relative deficits from spelling and reading.

In a group of 57 hospitalized patients with schizophrenia, Goldberg *et al.* (1993a) obtained differences between a premorbid measure of IQ (reading words) and current 'postmorbid' IQ levels. In monozygotic twin pairs discordant for schizophrenia, Goldberg *et al.* (1995) have demonstrated an IQ discrepancy in which the unaffected twin scored on average 10 points higher than the affected twin. This finding suggests that the genetic potential of the twin with schizophrenia would be 10 points above their current IQ score. Additionally, in a group of first-episode psychotic adolescent inpatients, Goldberg *et al.* (1988a) also observed a significant difference between performance IQ scores and reading relative to a control group of non-psychotic adolescents.

Although the finding of intellectual decline after the onset of disease is common in studies of schizophrenia, it is by no means exclusive. In a group of patients with schizophrenia, Albee *et al.* (1963) were unable to obtain evidence of a deficit between pre- and postmorbid measures of IQ. More recently, based on a sample of 34 patients with schizophrenia displaying low pre- and postmorbid IQ scores, Russell *et al.* (1997) suggested that any deficit in the intellectual function of patients with schizophrenia is due to an early decline which predates the onset of disease.

The results of Albee *et al.* (1963) and Russell *et al.* (1997) may be interpreted alternatively as reflecting a sampling bias since only low functioning individuals were studied, which may have influenced the outcome. The Albee *et al.* sample was drawn from inner city students, while patients in the Russell *et al.* study were drawn from a population of children who had received treatment at a child psychiatry clinic due to behavior and learning problems, of which a substantial minority were already psychotic. These limitations, however, do not obviate the fact that some patients with schizophrenia manifest obvious cognitive limitations from early in development (Torrey *et al.*, 1994).

Evidence for severe early developmental cognitive impairment

Numerous reports document low premorbid IQ scores in children who later developed schizophrenia (Lane and Albee, 1964, 1965; Offord and Cross, 1971; Offord, 1974; Jones and Offord, 1975; Nelson *et al.*, 1990). This would suggest that early developmental anomalies

might be responsible for the cognitive impairment observed in schizophrenia. In a meta-analysis of the research pertaining to the premorbid intelligence of patients with schizophrenia, Aylward *et al.* (1984) determined that the premorbid intelligence of children with schizophrenia is below that observed in normal children that do not go on to develop schizophrenia. In a birth cohort study in which 4746 people born in Great Britain during one week of 1946 were followed up to 16 years of age, Jones *et al.* (1994) have shown that those participants that went on to develop schizophrenia displayed low premorbid levels of educational achievement, retardation in the attainment of neuromotor developmental milestones and premorbid speech abnormalities. Effect sizes ranged between 0.37 and 0.51 for mathematics, 0.26 and 0.60 for non-verbal abilities and between 0.33 and 0.60 for verbal abilities. In another birth cohort study, a small but significant diminution in the intellect of patients with schizophrenia was observed prior to onset of psychotic symptoms (Crow *et al.*, 1995). In a large population-based cohort of Swedish army conscripts, David *et al.* (1997) reported that a higher frequency of patients that went on to develop schizophrenia displayed low premorbid IQ scores (<96) relative to non-psychotic individuals.

Additionally, other studies (Taylor and Abrams, 1984; Braff *et al.*, 1991; Goldstein and Shemansky, 1995) make a strong case that there are groups or clusters of patients with schizophrenia who display rather severe and diffuse cognitive impairments in adulthood which, at least in some patients, may have existed before the emergence of diagnostic symptoms. On the basis of a cluster analysis, Goldstein and Shemansky (1995) identified a group of severely cognitively impaired patients with schizophrenia whose cognitive performance was indistinguishable from the performance of dementia patients. Braff *et al.* (1991) provided evidence that patients with schizophrenia displayed diffuse neuropsychological deficits encompassing multiple cognitive domains. Finally, Taylor and Abrams (1984) obtained marked to severe cognitive impairment that encompassed all cortical regions with the exception of the non-dominant temporal cortex in a group of patients with schizophrenia.

Evidence for minimal cognitive impairment

In stark contrast to studies that report severe and extensive cognitive deficits in patients with schizophrenia, several studies have characterized groups of relatively high functioning patients with schizophrenia. On a circumscribed battery of neuropsychological tests, Schwartz (1967) obtained similar performances in college-educated patients with schizophrenia and normal controls. Thirty one percent of the 54 patients with schizophrenia who were administered the Wechsler Adult Intelligence Scale (WAIS) in the Dudek (1969) study had a Full-Scale IQ (FSIQ) in the range of 120–140. More recently, on the basis of a cluster analysis of the neuropsychological data obtained from 186 patients with schizophrenia, Goldstein and Shemansky (1995) were able to identify a high functioning group of patients. Finally, Palmer *et al.* (1997) reported a subgroup of 27% from a study of 171 patients with schizophrenia whose neuropsychological performance, inclusive of IQ, was indistinguishable from the performance of a normal control group. Results from these studies clearly suggest that there is also a subgroup of patients with schizophrenia who do not experience intellectual decline or severe cognitive impairment before or after the onset of illness.

Variation of cognitive abilities in schizophrenia

The inconsistencies present in the literature may be due to the inclusion of non-representative samples and a focus on specific neuropsychological variables pertinent to the specific hypotheses being tested. In a recent study (Weickert *et al.*, in press), we assessed a sample of 117 chronic, hospitalized patients with schizophrenia who were admitted consecutively to a tertiary care research facility. Furthermore, these patients were characterized on the basis of preserved or compromised intellectual abilities in an attempt to clarify the nature and extent of cognitive deficits manifest in schizophrenia. Thus, we assessed premorbid intellect in addition to measuring neuropsychological function in a variety of cognitive domains, such as memory, attention, working memory and perception. All participants were administered a four-subtest version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), consisting of the Arithmetic, Digit Symbol Substitution Test (DSST), Picture Completion and Similarities subtests, in order to obtain an estimate of their current FSIQ as described by Missar *et al.* (1994) and Kaufman (1990). Additionally, all participants received the Reading subtest of the Wide Range Achievement Test-Revised (WRAT-R) in order to obtain an estimate of premorbid intellectual levels. As noted above, the Reading subtest of the WRAT-R is thought to reflect preserved abilities since it is a test of decoding skills which are acquired routinely prior to the onset of disease and appear to remain unaffected by the disease process in analogous fashion to the 'hold' subtests of the WAIS-R (Dalby and Williams, 1986; Nelson *et al.*, 1990; Kremen *et al.*, 1996). We specifically sought to answer the following questions: (i) is there a pattern of intellectual change from before to after illness onset that is characteristic of schizophrenia; and (ii) what are the nature and extent of cognitive deficits in patients with schizophrenia?

Based on previous findings, an attempt was made to divide the sample of patients with schizophrenia into two groups as follows.

(i) To define a group of patients that undergo *intellectual deterioration* from premorbid levels as defined by a drop of at least 10 points from the premorbid IQ estimate. We used 10 points as a cut-off because it was about one standard deviation from the mean difference score in our control sample.

(ii) Identify a group of patients that do not undergo *intellectual deterioration* from premorbid levels as defined by a drop of <10 points, no change or a slight increase from premorbid IQ estimate. The non-declining group was subdivided further based on previous findings and our own clinical observation as follows:

   (a) Specify a group of *premorbidly compromised* patients defined as exhibiting premorbid IQs below 90 and no decline in current IQ from the premorbid level.

   (b) Describe a *cognitively preserved* group defined as exhibiting premorbid IQs above 90 and no decline in current IQ from the premorbid level.

At first glance, this scheme may appear arbitrary, as it would necessarily be inclusive. However, there was no *a priori* reason to suggest that the proportions of patients that met criteria for these three subgroups would differ by chance.

The results of our study demonstrate a decline of intellectual abilities occurring with psychotic symptoms in half of the chronic inpatients sampled. Therefore, this intellectually

declining group was the modal group. The remaining 50% of the chronic in-patients tested in this sample did not appear to experience a significant decline of intellectual abilities. The lack of a significant decline in the intellectual abilities of 50% of the chronic patients with schizophrenia in the current study partially supports previous findings of a lack of intellectual decline with the onset of disease (Albee *et al.*, 1963; Russell *et al.*, 1997). Of these non-declining patients, approximately half (i.e. 25% of the total sample) appear to have experienced an early compromise of intellectual abilities, as evidenced by premorbid intellectual estimates in the mildly impaired range and impairment in a wide variety of other cognitive domains. The remaining patients that do not appear to experience a decline of general intellect present a neuropsychological profile that resembles normal, with the exception of specific deficits in the cognitive domains of executive function/working memory and attention.

In general, the intellectually deteriorated patients displayed deficits in the cognitive domains of attention, memory, executive function and occulomotor speed. The premorbidly compromised group of patients exhibited deficits in nearly all cognitive domains tested, specifically, attention, memory, executive function, language, occulomotor speed and visuospatial perception. Finally, the cognitively preserved group of patients displayed deficits in the cognitive domains of executive function, as measured by the number of categories attained on the Wisconsin Card Sorting Test (WCST), and attention, as measured by a vigilance and distractibility composite score on a version of a Continuous Performance Test (CPT).

Premorbidly compromised patient group

In this group of patients, intellectual compromise accompanied by a wide range of cognitive impairments appears to date back to the early developmental period in that reading ability was in the impaired range. In this respect, our results were similar to the finding of Russell *et al.* (1997) who obtained low premorbid IQ (mean IQ = 84.1) in a sample of children who had early contact with child guidance clinics, i.e. had developmental difficulties. The cognitive domains affected in the premorbidly compromised group of our study include memory, visuospatial perception, attention, executive function/working memory, language and psychomotor speed.

Only the premorbidly compromised patient group performed significantly worse than normal controls on the Boston Naming Test, a putative measure of semantic memory, which is believed to access information from the lexicon, and on a visuospatial test of the ability to make judgements about the relationships between lines in two-dimensional space. These findings implicate temporal and parietal cortical dysfunction in the premorbidly compromised group in a stronger way than do the neurocognitive profiles of the other groups in which impairment in episodic and working memory implicate frontal and medial temporal lobe structures.

The premorbidly compromised group was similar to those previously described by Watson (1965), DeWolfe *et al.* (1971), Donnelly (1984), Taylor and Abrams (1984), Braff *et al.* (1991) and Goldstein and Shemansky (1995). For example, similarly to previous studies

(Goldberg *et al.*, 1993b; Paulsen *et al.*, 1995), the premorbidly compromised group of patients with schizophrenia displayed significant differences from normal on tests of declarative memory such as the immediate and delayed logical memory of the Wechsler Memory Scale-Revised (WMS-R) and for all measures of the California Verbal Learning Test (CVLT). Also similarly to previous studies that have demonstrated deficits of attention in patients with schizophrenia relative to normal controls on various versions of the CPT (Mirsky *et al.*, 1992; Servan-Schreiber *et al.*, 1996), our premorbidly compromised group displayed significant differences on measures of attention. The premorbidly compromised schizophrenic group differed from normal controls with respect to the mean number correct on the distractibility version of the CPT, and the normal control group differed from each of the schizophrenic groups on the basis of the combined vigilance and distractibility scores. The premorbidly compromised patients with schizophrenia also displayed significant differences from normal controls on the mean percentage of perseverative errors exhibited on the WCST, which supports previous findings with respect to differential performances between patients with schizophrenia and normal controls on this measure of executive/frontal lobe function (Fey, 1951; Goldberg *et al.*, 1988b; Sullivan *et al.*, 1994). On a test of psychomotor speed and scanning ability, forms A and B of the Trail Making Test, the premorbidly compromised schizophrenic patients displayed significant differences from normal controls and cognitively preserved schizophrenic patients, supporting previous studies demonstrating slowed reaction times for groups of schizophrenic patients (Vrtunski *et al.*, 1986) and differential performances between schizophrenic patients and normal controls on form B of the Trail Making Test (Braff *et al.*, 1991).

It is also important to note that the premorbidly compromised group from our study is strikingly similar to patients displaying so-called 'deficit' syndromes in neurocognitive measures (Buchanan *et al.*, 1994, 1997). Especially notable in the patients of Buchanan *et al.* were poor performances in general intellect, visuospatial analysis, judgement of line orientation and vigilance on a CPT. As in the studies of Buchanan *et al.*, the premorbidly compromised group in our recent study also performed more poorly, although not always significantly so, on tests of working memory and declarative memory. Finally, with respect to the premorbidly compromised group, the pattern of neuropsychological deficits described above would suggest that parieto-occipital, temporal and frontal function are compromised, implicating a pan-cortical impairment.

Intellectually deteriorated patient group

This finding of intellectual decline in 50% of our sample is consistent with the longitudinal findings of Lubin *et al.* (1962) and Schwartzman and Douglas (1962), and with more recent studies finding discrepancies between putative premorbid ability and current IQ (Dalby and Williams, 1986; Goldberg *et al.*, 1993b, 1995; Gold *et al.*, 1994; Frith, 1996; Kremen *et al.*, 1996). As mentioned previously, this decline in intellect was accompanied by a distinct neurocognitive profile. Specifically, impairment was evident in the cognitive domains of memory, working memory, attention, psychomotor speed and occulomotor scanning. Unlike the premorbidly compromised group, the cognitive domains of visuospatial perception and

lexical access were unaffected. We recognize that the intellectual decline is not necessarily monolithic in the sense that all areas (or WAIS-R subtests) are not affected equally. Rather, the decline of intellectual abilities appears to reflect impairment in those abilities specifically associated with working memory or those subtests that load highly on the so-called freedom from distractibility factor, such as the DSST.

Although the premorbid intellectual estimate appears relatively intact in the intellectually deteriorated group of patients, this does not preclude a neurodevelopmental mechanism in the etiology of cognitive deficits in this patient group, since subtle neurodevelopmental changes may precede and ultimately set the stage for later cognitive impairment and psychiatric disturbance (Weinberger, 1987). We and others do not believe that this decline is progressive, but rather that it is restricted to the first 3–5 years of the illness (Hyde *et al.*, 1994; Mockler *et al.*, 1997). Parenthetically, this profile of cognitive impairment implicates fronto-temporal dysfunction.

The finding of a group of intellectually deteriorated schizophrenic patients in this study is similar to that observed in the previous work of Rappaport and Webb (1950), Lubin *et al.* (1962), Schwartzmann and Douglas (1962) and Nelson *et al.* (1990). Similarly to previous studies (Goldberg *et al.*, 1993b; Paulsen *et al.*, 1995), the intellectually deteriorated groups of schizophrenic patients displayed significant differences from normal on tests of declarative memory such as the immediate and delayed portions of the WMS-R and for all measures of the CVLT. The current study also displayed significant differences on measures of attention, which is similar to previous studies that have demonstrated deficits of attention in schizophrenic patients relative to normal controls on various versions of the CPT (Mirsky *et al.*, 1992; Servan-Schreiber *et al.*, 1996). The intellectually deteriorated schizophrenic groups differed from normal controls with respect to the mean number correct on the distractibility version of the CPT, and the normal control group differed from each of the schizophrenic groups on the basis of the combined vigilance and distractibility scores. The intellectually deteriorated schizophrenic patients also displayed significant differences from normal controls on the mean percentage of perseverative errors exhibited on the WCST, a measure of executive/frontal lobe function. This result supports previous findings of differential performances between schizophrenic patients and normal controls with respect to the percentage of perseverative errors on the WCST (Fey, 1951; Goldberg *et al.*, 1988b; Sullivan *et al.*, 1994). On a test of psychomotor speed and scanning ability, forms A and B of the Trail Making Test, the intellectually deteriorated schizophrenic patients displayed significant differences from normal controls and intellectually preserved schizophrenic patients. These findings support the results of previous studies, which have demonstrated slowed reaction times for groups of schizophrenic patients (Vrtunski *et al.*, 1986) and differential performances between schizophrenic patients and normal controls on form B of the Trail Making Test (Braff *et al.*, 1991).

Cognitively preserved patient group

As mentioned previously, an unexpectedly large portion (25% of the total sample) of the intellectually intact patients displayed only mild impairment in the cognitive domains of

executive function/working memory and attention/vigilance. Unlike the intellectually deteriorated group, the cognitively preserved patients displayed no deficits in the cognitive domains of episodic memory or psychomotor speed. In contrast to the premorbidly compromised group, the cognitively preserved group did not display deficits in the fundamental cognitive domains of language and visuospatial perception.

The cognitively preserved group was similar to previously described preserved groups (Schwartz, 1967; Dudeck, 1969; Elliott *et al.*, 1995; Goldstein and Shemanśky, 1995; Evans *et al.*, 1997; Palmer *et al.*, 1997). In fact, in the study of Palmer *et al.*, the finding that 27.5% of patients with schizophrenia exhibited overall neuropsychological ratings within the normal range closely resembles the 24.8% of patients in our study that displayed a current IQ >90 and no intellectual decline from premorbid levels. Unlike our results, the study of Palmer *et al.* did not observe significant differences between neuropsychologically 'normal' patients with schizophrenia and normal controls on the basis of the WCST. However, based on the means and variances in our group, we might also expect to find certain patients who appeared 'intact' with respect to their WCST scores.

Elliott *et al.* (1995) also obtained impaired performances on a WCST analog in a group of patients with schizophrenia who displayed intact intellectual abilities. They employed a test of attentional set shifting designed to provide a more detailed analysis of the nature of WCST errors. Their study demonstrated that patients with schizophrenia were capable of shifting their attention to an old, previously learned concept or 'set'; however, these same patients had difficulty when they were required to shift their attention to an extradimensionally new or novel set. To the extent that a decrease in the number of categories attained reflects an inability to shift attention to a novel stimulus, our finding of a decrease in the number of categories attained on the WCST in a cognitively preserved group of patients with schizophreina would support the findings of Elliott *et al.*

Although the study of Palmer *et al.* (1997) demonstrated a so-called 'normal' neuropsychological performance in 27.5% of their schizophrenic patients, only 11.1% of the schizophrenic patients examined in their study failed to display declarative memory deficits, which corresponds to the performance of the cognitively preserved group in our study with respect to WMS-R and CVLT measures. Additionally, the lack of differences between the cognitively preserved schizophrenic group and normal controls on form B of the Trail Making Test in our study also supports the previous findings of Palmer *et al.* of a lack of deficits in 11.1% of the schizophrenic patients on this measure of psychomotor speed. Also in our study, the lack of differences between the cognitively preserved schizophrenic group and normal controls on the percentage of perseverative errors exhibited on the WCST supports the previous findings of Palmer *et al.* of a lack of WCST deficits in 11.1% of the schizophrenic patients on this measure of executive function. It bears repeating, however, that the current finding of a significant difference between the cognitively preserved schizophrenic patients and normal controls with respect to the mean number of categories attained on the WCST is in contrast to the conclusion from the study of Palmer *et al.*, which demonstrated that a group of 'neuropsychologically normal' patients could not be separated from normal controls on the basis of WCST performance.

Diagnostic subtype, symptoms and age of onset

With respect to relationships between clinical symptoms and intellectual stability, those individuals classified as disorganized on the basis of clinical interview were somewhat more likely to experience a decline in intellect from premorbid levels. While we did not find differences between our groups with respect to negative symptoms displayed during the entire course of the disease, we recognize that our measure was related to the presence or absence of symptoms and not to severity of symptoms. A select positive symptom, auditory hallucinations, was found to occur at the highest frequency in the premorbidly compromised group. Additionally, patients experiencing later manifestation of cognitive deficits, the intellectually deteriorated group, displayed an increased frequency of delusional thinking.

Furthermore, we found a lack of a differential age of onset between the groups, especially with respect to the premorbidly compromised group. This would suggest that even though the disease may manifest itself non-specifically as cognitive deficits relatively early in development, the psychotic features are not triggered until later, usually in early adulthood. Thus, the organization and activational changes that initiate the cognitive deficits may not always be related directly to the initiation of the psychotic features of the disease. Alternatively, because all of our patients were chronic and to some degree treatment refractory, we may have been unable to detect differences in age of onset because of cohort effects.

IQ and schizophrenia

Although the decline in IQ of the intellectually deteriorated group involved to some degree the four subtests of the WAIS-R, the measures that are thought to demand more working memory, DSST and Arithmetic, appear to be more severely affected. Interestingly, with respect to WAIS-R measures, in our study even the cognitively preserved patient group differed from the normal control group only on the basis of their Age Scaled Scores on the WAIS-R DSST (though FSIQ did not differ). The DSST is thought to be an indicator of working memory integrity in so far as it involves self-monitoring, the brief maintenance of information including that of locations, and oculo-motor scanning (Wilson *et al.*, 1993). Thus, IQ does not reflect simply a unitary function, but, as has been demonstrated repeatedly, is comprised of multiple factors. In particular, IQ does not decline *en masse*, but rather the freedom from distractibility or working memory factor appears to be most susceptible to the core neurobiological disturbance underlying schizophrenia.

Overall, we believe that these results may be interpreted from at least two broad perspectives. First, they could be viewed as reflecting a severity dimension in which the premorbidly compromised group is most impaired with widespread cortical involvement (as evidenced by deficits in most cognitive domains), and the intellectually preserved group is least impaired with specific and circumscribed alteration in frontal system function (evidenced by working memory and attention deficits). On the other hand, it is possible that the groups are genetically and/or environmentally distinct, involving different neural trajectories that manifest themselves via different cognitive courses. They thus would represent valid subtypes of illness. These alternatives cannot be resolved with the available data.

Synthesis of the findings

Results from the current study suggest that the cognitive deficits associated with schizophrenia may emerge along three developmental trajectories based on the degree and timing of impairment of general intellect. One course suggests that the disease process manifests itself as cognitive impairment that may be relatively profound and widespread at an early stage of development and is present subsequent to the onset of psychotic symptoms. These premorbidly compromised patients may have experienced early developmental stressors and/or a genetic predisposition leading to the observed cognitive deficits. A second course suggests that the cognitive deficits may become manifest concurrently with the onset of psychotic symptoms, resulting in a more circumscribed pattern of deficits that encompasses the cognitive domains of executive function, attention and long-term memory. This process is, however, self-limiting, as patients do not go on to a full-blown dementia (for discussions, see Goldstein and Zubin, 1990; Heaton *et al.*, 1994; Hyde *et al.*, 1994; Mockler *et al.*, 1997). This occurs in the presence of intellectual decline. Finally, the third course suggests that while cognitive impairment may be concurrent with symptom onset, the debilitating cognitive deficits associated with the disease process may be relatively subtle, being restricted to the domains of executive function/working memory and attention. It is unclear whether the deficits in this group precede symptoms or emerge concurrently.

Furthermore, based on these findings, it would appear that deficits associated with the function of the prefrontal cortex, i.e. deficits of executive function/working memory and attention, constitute a necessary and perhaps sufficient type of cognitive impairment in schizophrenia. With the exception of the DSST of the WAIS-R, the number of categories attained on the WCST and correct responding on the CPT were the only cognitive measures that provided significant differences between the cognitively preserved group of patients and the normal control group. As such, these deficits can be considered to be 'core' cognitive deficits in schizophrenia.

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