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Neuropsychological impairment and psychopathology in first-episode schizophrenic patients related to the early course of illness

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Abstract The objective of the present study was to explore whether the early course of illness including first onset of psychotic symptoms influences neuropsychological functioning and psychopathology in first-episode schizophrenics. Patients with a short prodromal period (n = 20) and patients with a long prodromal period (n = 20) and controls matched with regard to age, gender and education (n = 40) were administered a battery of standardized neuropsychological tests and psychopathological rating scales. The results indicate an overall difference in neuropsychological performance with the schizophrenic patients scoring lower than controls. Schizophrenic patients scored significantly lower in all subtests except in visual memory and abstraction/flexibility than controls. No significant difference between neuropsychological performance between patient samples was found. Psychopathology was more pronounced in the long prodromal period group rating higher on negative and affective symptoms compared with the short prodromal period group. The data suggests that neuropsychological deficits in first-episode schizophrenia are independent of the early course of schizophrenia, and although negative symptoms are associated with the length of the prodromal period, they do not imply greater neuropsychological impairment.

Key words First-episode schizophrenia · Early course · Prodromal period · Neuropsychological functioning · Negative symptoms

Introduction

Length of illness and age of onset are two clinical demographic variables that are commonly used to characterize the course of schizophrenia, and which may be sources of diverse cognitive impairment. Most authors divide the early course of schizophrenia into three phases: the premorbid period the prodromal period, and the acute psychosis (Haas and Sweeney 1992; Keshavan and Schooler 1992; Loebel et al. 1992; Beiser et al. 1993). The premorbid phase characterizes the period before the illness onset, and the following prodromal period is defined as the beginning disease process, but without any prominent psychotic symptoms (Malla and Normann 1994). The prodromal symptoms are not specific for schizophrenia and can be found in the early phase of other psychiatric illnesses. Häfner et al. (1993) defines illness onset as being the first nonspecific sign of mental disturbance, and episode onset as the first specific sign, namely first-rank symptom, or the point in time when the operational criteria of a diagnostic system are fulfilled.

The deterioration in schizophrenia was an important part of Kraepelin's description and diagnosis of dementia praecox. He emphasises that "the unmistakable symptoms of dementia appear already within the first year", and that "weak-mindedness" which developes at an early stage of illness "usually only changes slowly and insignificantly" (Kraepelin 1919, 1971). While some studies have found cognitive deterioration to continue long after onset of illness, further neuropsychological measures of deficit processes suggest that cognitive decline stabilizes shortly thereafter. Several studies comparing first-episode, subchronic and chronic schizophrenia patients find equivalent neuropsychological dysfunction across samples (Hoff et al. 1992a; Andreason 1994). Similarly, no deterioration in cognitive function is found in studies comparing chronic schizophrenia patients in age-related cohorts (Goldberg et al. 1993; Mockler et al. 1995). Diverging results show worse deficits for chronic samples and dysfunction correlated to age postulating progressive cognitive impairment in the course of the illness (Bilder et al. 1992; Sweeny et al. 1992; Davidson et al. 1995). Investigations administering a battery of standardized neuropsychological tests to patients with first-episode schizophrenia, chronic schizophrenia and healthy controls matched for age, gender, ed-

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ucation and parental socioeconomic status showed a differential cognitive deficit in both patient groups relative to controls (Albus et al.1996). For both schizophrenia samples most pronounced deficits were found in visual-motor processing and attention (VSM). Comparing the neuropsychological profiles chronic schizophrenics performed relatively worse in VSM and abstraction/flexibility than first-episode patients (Albus et al. 1996). These findings suggest that neuropsychological dysfunction is already present in first-episode schizophrenics, and that in chronic patients mainly frontally based dysfunctions are more pronounced.

Neuropsychological testing of schizophrenia patients has demonstrated impaired performance in virtually all cognitive dimensions, especially attention, abstraction, flexibility, learning and memory. While some authors hypothesise a generalized deficit in schizophrenic patients (Malec 1978; Braff et al. 1991; Blanchard and Neale 1994), others, finding generalized neuropsychological impairment, have shown pronounced deficits on tasks related to language, verbal learning, semantic and visual memory, information processing and attention (Saykin et al. 1991; Nuechterlein 1991). Findings of impairment in abstraction/flexibility using the Wisconsin Card-Sorting Test (WCST) proposing disturbances in prefrontal functions (Weinberger et al. 1986; Goldberg et al. 1987; Fuster 1989; Morice 1990) and investigations suggesting a preeminent role of frontotemporal or temporo-hippocampal dysfunction in schizophrenia (Saykin et al. 1991, 1994; Taylor and Abrams 1984; Liddle and Morris 1991) contribute to the hypotheses of localizable deficits.

Psychopathological research in schizophrenics has led to a classification of symptoms as either positive or negative in nature. Patients presenting mainly negative symptoms have been referred to as type II (Crow 1985), negative (Andreasen and Olsen 1982) or deficite syndrome (Carpenter et al. 1988) patients. The prevalence of the negative syndrome in first-episode schizophrenia has been estimated at 4–10% (Mayerhoff et al. 1994).

The present study was designed to evaluate neuropsychological functioning and psychopathology in first-onset schizophrenia comparing two samples: patients with a long prodromal period, defined as occurrence of non-specific or prodromal symptoms over a long period of time before index admission, and patients with short prodromal period defined as a comparably short illness duration before the manifestation of psychotic symptoms leading to first hospitalization. Comparing samples allows conclusions about potential differences between patients differing in the duration of prodromal periods and untreated psychosis before first hospitalization.

While most studies concentrate on the comparison between first-episode and chronic schizophrenia, nothing is known about differences in cognitive functioning related to the course of untreated illness before onset of first psychotic symptoms. Also there is little information on the relation of the deficit syndrome, i.e. negative symptoms to the length of the prodromal period and to neuropsychological impairment in first-episode schizophrenia.

The bulk of findings suggest that the cognitive decline process is active around illness onset leading to the assumption that neuropsychological deficits are fundamental manifestations of schizophrenia, independent of the early course of illness. Therefore, there should be no difference in neuropsychological functioning between the short and long prodromal period groups. The alternative hypothesis assumes that neuropsychological deficits increase with duration of the illness, i.e. patients with a long prodromal period show greater neuropsychological impairment than patients with short illness duration prior to acute psychosis.

Equally for psychopathology we addressed the following questions: Are negative symptoms more distinct in patients with a longer premorbid and prodromal period, and does an existing negative syndrome in first-episiode schizophrenia imply greater neuropsychological impairment?

Subjects and methods

Two samples, 20 patients with a short prodromal period (non-specific symptoms for 0–2 years; median: 0.3 years), and 20 patients with a long prodromal period (non-specific symptoms for 5–19 years; median: 9.8 years), were drawn from a total of 68 consecutively recruited inpatients with first episode schizophrenia admitted to the State Mental Hospital Haar. Neither the duration of psychotic symptoms before, nor the age at index admission differed significantly between patient groups. To establish a deficit profile, normal control subjects were individually matched to schizophrenics with regard to gender and education. The patient groups were balanced for age. Table 1 summarizes the demographic and clinical characteristics of the three groups investigated.

First-episode schizophrenics meeting DSM-III-R criteria for schizophrenia, or schizophreniform disorder with cumulative lifetime treatment with neuroleptics for no longer than 12 weeks prior to admission, were included (Liebermann 1993). The diagnosis of schizophrenia and schizophreniform disorder was assigned using a structured interview based on DSM-III-R criteria (SCID; Spitzer et al. 1987). In the group of patients with a short prodromal period 11 were diagnosed as having schizophrenia, and 9 as having schizophreniform disorder. All subjects were screened for a history of moderate or severe head trauma or other neurological disorders, current alcohol or other substance abuse, and systematic medical diseases that are likely to affect central nervous system functions. At the time of testing all patients received butyrophenones.

The onset of illness was determined with the IRAOS (Häfner et al. 1992), a semistructured interview to assess early signs and symptoms of schizophrenia, including prodromi, specific (e.g. thought disorders, delusions, auditory hallucinations) and non-specific symptoms (e.g. worrying, restlessness, irritability, impairment of appetite, sleep and sexual interest, of thinking and concentration, lack of energy and self-confidence), changes in social and work performance, previous treatment, the long-term development of the illness, and the social course of the disease. The items rating psychopathology and social variables contained in the IRAOS are based on the Present State Examination (PSE; Wing et al. 1973), Disability Assessment Schedule (DAS-M; WHO 1988, revised version by Jung et al. 1989) and the Past History and Sociodemographic Description Schedule (PHSD; Jablensky et al. 1980), whereas some items were comprised of general variables, and some new items were added. With this instrument data were collected from interviews with the patient as well as with at least one key informant (e.g. a relative) independently. Additional objective data were provided by contacting previously involved psychiatrists or general practitioners.

Table 1 Demographic characteristics of patients and controls, and psychopathological results of the two patient samples (short and long prodromal period). BPRS Brief Psychiatric Rating Scale; SANS Scale for the Assessment of Negative Symptoms; PANSS Positive and Negative Syndrome Scale; ANOVA analysis of variance

	Short prodromal period (n = 20) Mean + SD	Long prodromal period (n = 20) Mean + SD	Controls (n = 40) Mean + SD	ANOVA		
				d*f*	*F*	*P*
Age (years)	30.9 + 7.6	32.2 + 8.8	31.7 + 8.8	2.79	0.11	n.s.
Length of prodromal episode (years)	0.7 + 0.8	11.0 + 4.5		1.39	102.69	< 0.001
Daily dosage of neuroleptics (CPE)	438 ± 213	457 ± 198				
	Number	Number	Number	*df*	χ^3	*P*
Gender male/female	10 of 10	10 of 10	20 of 20	2	0.00	n.s.
Education						
No graduation	2	2	1	6	2.35	n.s.
Elementary	5	6	12			
Secondary	6	6	11			
High school	7	6	16			
BPRS			*t*	*P*		
Total score	30.5 + 5.9	37.5 + 8.7	–2.88	< 0.01		
Anxiety/depression	5.1 + 1.8	7.6 + 2.9	–3.19	< 0.01		
Anergia	5.9 + 2.2	8.4 + 3.9	–2.35	< 0.05		
SANS						
Composite score	24.5 + 14.3	40.6 + 19.8	–2.84	< 0.01		
Affective flattening	8.4 + 6.8	14.3 + 100.0	–2.12	< 0.05		
Abulia/apathy	2.5 + 2.8	5.2 + 4.6	–2.11	< 0.05		
Anhedonia	8.4 + 6.3	12.7 + 5.4	–2.22	0.05		
PANSS						
Negative score	9.6 + 2.9	15.2 + 70.0	–3.24	< 0.01		
HAMD	4.6 + 3.6	7.7 + 6.0	–1.86	> 0.01		

Psychopathological status was evaluated by rating a semi-structured interview by means of the Brief Psychiatric Rating Scale (BPRS; 24 items; Overall and Gorham 1976; Lukoff et al. 1986), Scale for the Assessment of Negative Symptoms (SANS; Andreasen 1982, 1989), Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987, 1988) and Hamilton Depression Scale (HAMD, original version; Bech 1993). The trained and experienced raters were blind with regard to diagnosis, IRAOS-data, medication and neuropsychological performance. The interviews were videotaped. To control for interrarer reliability taped interviews were rated individually by all raters and results compared.

All subjects were administered a neuropsychological test battery designed to evaluate a broad range of functions, by two trained and experienced psychometrists. Neuropsychological tests yield a large number of dependent measures, so internally consistent summary scales were constructed as described by Bilder et al.(1988), Saykin et al. (1991) and Hoff et al. (1992b). Because of their high intercorrelation, verbal cognitive measures were combined with the language tests to the verbal intelligence and language skills, and strongly correlated tests of verbal memory and learning were combined, as suggested by Saykin et al. (1994). Own results show sufficient internal consistencies for both verbal intelligence and language (Cronbach's Alpha 0.68) and for verbal memory and learning (0.86). The measures of information processing and attention dysfunctions (CPT and SAT) were not combined because of missing intercorrelations (r = –0.06).Thus, the tests covered the following neuropsychological areas: verbal intelligence and language, spatial organization, verbal memory and learning, visual memory, short-term memory, visual-motor processing and attention, information processing and attention and abtraction/flexibility. The measures of verbal intelligence and language (VBL) were the two subtests, "Information" and "Similarities" of the HAWIE-R (Wechsler 1981), a lexographic subtest of the LPS (Horn 1983) and the semantic Supermarket Test (Genzel 1991), which is adopted from the Dementia Rating Scale (Mattis 1976), were administered to measure verbal fluency. Spatial organization (SPT), used in measuring non-verbal intelligence, was assessed with the Block Design and Picture Completion tests, both subtests of the HAWIE-R. The tests thought to reflect verbal memory and learning (VBM) were evaluated by the "Logical memory" subtest (immediate and delayed recall) of the revised Wechsler Memory Scale (WMS-R; Wechsler 1987), the California Verbal Learning Test (CVL; Delis et al. 1987), and the "Paired Associate Learning Test", an additional subtest of WMS-R. The measures to evaluate visual memory were the "Visual reproduction" subtest (immediate and delayed recall) of the revised Wechsler Memory Scale (WMS-R). Short-term memory (STM) was assessed by the "Digit-span" subtest of the HAWIE-R and a reading span test. The Color–Word interference test (Stroop 1989), the Trailmaking Test (TMT; Reitan 1958), as well as the Digit Symbol Test, a subtest of the HAWIE-R were used to measure speeded visual-motor processing and attention (VSM). The measures of information processing and attention dysfunctions in schizophrenia patients were the Continuous Performance task (CPT; Rosvold et al. 1956), and the Span of Apprehension Test (SAT; Neale 1971). Abstraction- and conceptual flexibility (ABS) were assessed using the modified WCST (Heaton 1981a), a test version of 48 response cards, the WCST being regarded as the best single measure reflecting prefrontal cortical function (Heaton 1981b).

Table 2 Z-scores (mean and SD) of the two patient samples (short and long prodromal period) investigated in nine areas of neuropsychological functioning and profile mean based on the test performance of the total control group (n = 40)

	Short prodromal period (n = 20) Mean + SD	Long prodromal period (n = 20) Mean + SD	Controls (n = 40) Mean + SD
Verbal intelligence and language (VBL)	–0.61 + 0.63	–0.37+ 0.78	0.0 + 0.58
Spatial organization (SPT)	–0.89 + 0.94	–0.85+ 1.02	0.0 + 0.78
Verbal memory and learning (VBM)	–1.47 + 0.91	–1.41+ 1.18	0.0 + 0.73
Visual memory (VIM)	–0.84 + 1.42	–0.84+ 1.95	0.0 + 0.94
Short-term memory (STM)	–0.51 + 0.68	–0.44+ 0.67	0.0 + 0.82
Visual-motor processing/attention (VSM)	–1.98 + 0.70	–1.51+ 1.14	0.0 + 0.74
Information processing/attention (CPT)	–0.83 + 1.02	–0.97+ 0.77	0.0 + 0.89
Span of apprehension (SAT)	–1.34 + 1.41	–0.77+ 1.65	0.0 + 0.86
Abstraction/flexibility (ABS)	–0.86 + 1.36	–0.24+ 0.98	0.0 + 0.94
Profile mean	–1.04 + 0.52	–0.82+ 0.74	0.0 + 0.49

Table 3 Intercorrelations between neuropsychological tests of first-episode schizophrenic patients (short and long prodromal period, n = 40)

	VBL	SPT	VBM	VIM	STM	VSM
Verbal intelligence and language (VBL)						
Spatial organisation (SPT)	0.61**					
Verbal memory and learning (VBM)	0.56**	0.26				
Visual memory (VIM)	0.59**	0.41*	0.49**			
Short-term memory (STM)	0.28	0.19	0.12	0.23		
Visual motor-processing/attention (VSM)	0.53**	0.45*	0.34	0.54**	0.31	
Information processing/attention (CPT)	–0.02	0.10	–0.07	0.15	0.32	0.33
Span of apprehension (SAT)	0.14	0.39	0.11	0.03	0.04	0.26
Abstraction/flexibility (ABS)	0.34	0.26	0.41*	0.32	0.21	0.30
Profile mean	0.73**	0.68**	0.61**	0.74**	0.43*	0.75**

Pearson correlation, two-tailed: * p = 0.01, ** p = 0.001

To prevent potentially confounding effects of an acute psychotic disorganization, neuropsychological and psychopathological testing was administered at the time of remission under neuroleptic treatment during first admission (2–9 weeks after admission to the hospital).

The tests and interview were administerd 2.2 weeks (M = 2.2; min. 0.9, max. 16.8 weeks) after admission, and there was no significant difference between patient samples (long prodromal episode: M = 2.2; short prodromal episode: M = 2.3 weeks). The total battery of neuropsychological tests was usually completed within 3–4 h, the psychopathological rating in approximately 1 h. The tests and interview were given to an individual patient on three occasions over a period of 3–4 days. All patients of both samples completed the investigation.

Statistical analysis

With respect to sociodemographic and psychopathological variables, groups were compared by performing the Student's t-test and analysis of variance (ANOVA). Based on means and standard deviation of the control group, which was matched to the patient samples, regarding age, gender and education, all raw neuropsychological test scores were converted to Z-scores (standard equivalents). The Z-scores were grouped by function (mean scores).

For the overall neuropsychological function score multivariate analysis of variance (MANOVA) was carried out for both samples and the control group, with illness-onset as the between-group factor. In a second step, univariate analyses of variance were carried out for each neuropsychological function. These univariate analyses of variance should be considered as exploratory, not as a confirmatory analysis. To test for significance the Bonferroni procedure was performed. Intercorrelations between neuropsychological tests, and between psychopathological and neuropsychological results were computed using Pearson correlation.

Results

Psychopathology

Comparing total scores the SANS composite score and the PANSS negative score were significantly higher for the group with a long prodromal period than the short prodromal period group. No significant difference for the PANSS positive score between patient groups was found. The BPRS total score (24 items) was significantly higher for the long prodromal period sample than for the group with a short prodromal period. The same tendency was found for the HAMD total score (p = 0.07). Regarding subscales significantly higher scores for affective flattening (SANS), abulia/apathy (SANS), anhedonia (SANS), anxiety/depression (BPRS) and anergia (BPRS) were found for the long prodromal period group compared with the short prodromal period sample (see Table 1 for significant results of psychopathological evaluation.) Comparing psychopathological results with neuropsychological results, no significant (p > 0.01) correlations were found for either of the samples.

Neuropsychology

The Z-scores of the neuropsychological tests for both patient groups and controls are shown in Table 2. For in-

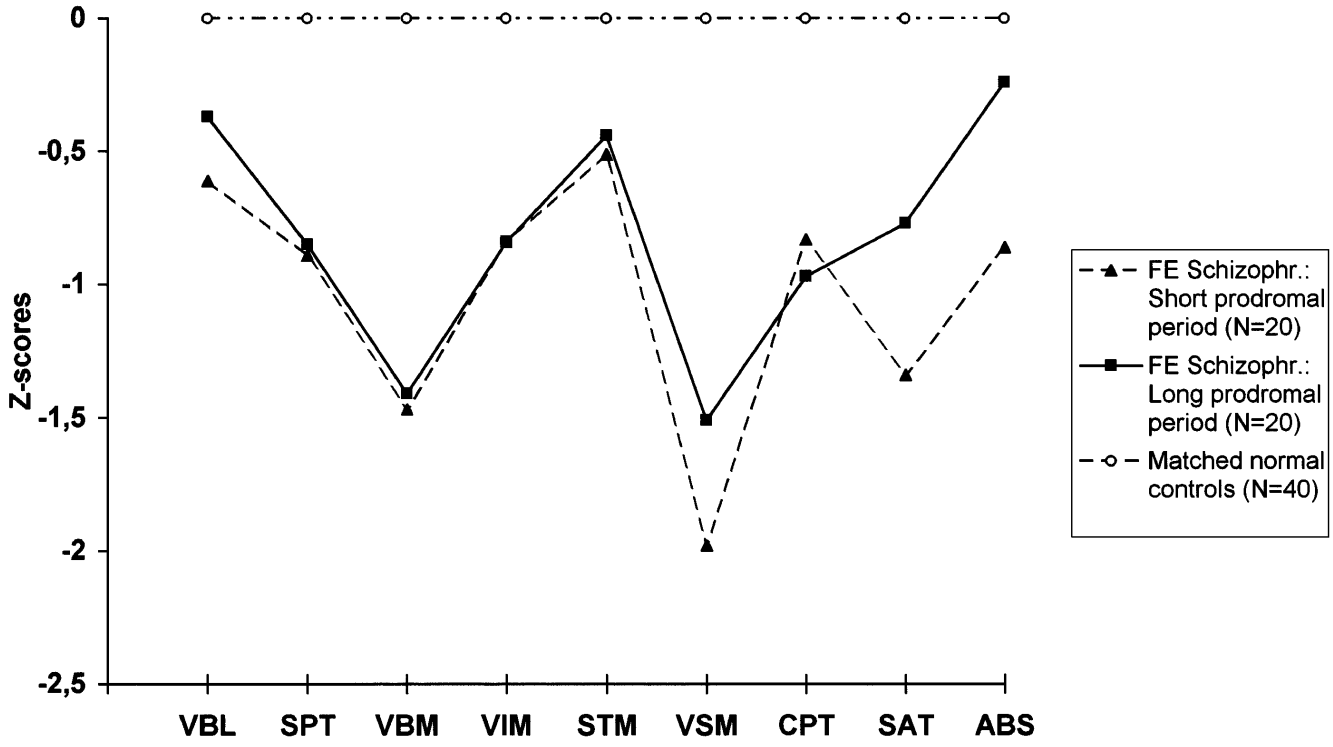

Fig. 1 Neuropsychological profile of schizophrenic patients with a long prodromal period (n = 20) and a short prodromal period (n = 20) relative to healthy controls (n = 40), whose performance is set to zero. Functions are verbal intelligence and language (VBL), spatial organization (SPT), verbal memory and learning (VBM), visual memory (VIM), short-term memory (STM), visual-motor processing and attention (VSM), information processing and attention (CPT), span of apprehension (SAT) and abstraction/flexibility (ABS)

tercorrelations between neuropsychological tests see Table 3.

The MANOVA shows that the profiles of both patient groups lies well below the zero line (see Fig. 1), representing the control group, indicating an overall difference in performance with the schizophrenic patients scoring lower than controls (df = 10; F = 11.2; $P < 0.01$). Univariate analysis of variance shows that both patient groups scored significantly lower in VBL (df = 1,78; F = 11.6; $P < 0.01$) SPT (df = 1,78; F = 19.7; $P < 0.01$), VBM (df = 1,78; F = 51.5; $P < 0.001$), VSM (df = 1,78; F = 82.1; $P < 0.001$), CPT (df = 1,78; F = 20.3; $P < 0.01$) and SAT (df = 1, 78; F = 14.3; $P < 0.01$). No differences between performances of patient groups and the control group was found for VIM (df = 1,78; F = 7.5; n.s.), STM (df = 1,78; F = 8.1; n.s.) and ABS (df = 1,78; F = 5.2; n.s.). No significant difference was found in overall neuropsychological performance between the patient sample with a short prodromal period and the long prodromal group (MANOVA: df = 10; F = 0.85; n.s.).

Discussion

Psychopathology was more pronounced in the group with a long prodromal period than in the group with a short prodromal period, with significantly higher overall scores in the BPRS, SANS and PANSS negative score. Regarding sub-scales, the long prodromal episode group rated higher only in items concerning negative and affective symptoms (affective flattening, abulia/apathy, anhedonia, anxiety/depression and anergia), not on prominent psychotic, namely first-rank symptoms. Patients were tested at the time of remission; therefore, the results do not inform on differences in psychopathology between groups during acute psychosis.

Although our patients were rated during the first episode of schizophrenia, the specific psychopathological symptoms found correspond to the large-scale epidemiological study by Häfner et al. (1992) on schizophrenia, where early signs of mental disorders reported by the patients were anxiety, restlessness, depression, impairment of appetite and sleep, of thinking and concentration, withdrawal, suspicion and lack of energy. Koreen et al. (1993), finding a prevalence of depressive symptoms in 75% of first-episode schizophrenics [patients who met extracted Hamilton and/or syndromal (Research Diagnostic Criteria) criteria], suggest that depressive symptoms may represent a core part of the acute illness or may occur as a subjective reaction to the experience of psychotic decompensation.

With regard to the course of the illness, the results are in agreement with the findings of Fenton et al. (1991), that schizophrenia with many negative symptoms is associated

with an insidious illness onset, whereas schizophrenia with few negative symptoms is associated with an acute onset. Authors examining the relationship between negative symptoms and premorbid variables have repeatedly found that patients with negative symptoms had significantly lower levels of premorbid functioning (Fenton and McGlashan 1991; Kelley et al. 1992). Although the data suggest that deterioration in premorbid functioning is assosiated with the development of a negative symptom syndrome, conclusions about worse intellectual premorbid functioning in this patient group should be considered carefully. The results show that the length of the prodromal period relates to the prevalence of negative symptoms but seems to have no significant influence on the degree of neuropsychological impairment. Non-significant intercorrelations between psychopathological and neuropsychological results show that in our sample the presence of negative symptoms does not reflect in neuropsychological functioning. Compared with our results, Berman et al. (1997) find negative symptoms associated with poor performance on cognitive tests reflecting particularly frontal functions. These diverging results can be explained by the different patient samples drawn. In Berman's study veteran chronic schizophrenic inpatients with a more pronounced deficit syndrome were recruited in contrast with our firt-episode patients.

Schizophrenic patients show overall neuropsychological impairment compared with controls. Yet in both patient groups the composite indexes for visual memory, short-term memory and abstraction/flexibility did not differ significantly to controls. Therefore, the differential deficit found only partly supports the assumption of an underlying generalized neuropsychological impairment in schizophrenics (Malec 1978; Braff et al. 1991; Blanchard and Neale 1994).

Comparing patient samples, i.e. patients with a long and patients with a short prodromal period, the neuropsychological subtests show no significant differences in cognitive functioning, indicating that the extent and the pattern of neuropsychological deficit in first-onset schizophrenia is independent of the early course of illness. Investigating neuropsychological impairment in first-episode and chronic schizophrenics, no differences in the shape of neuropsychological profiles were found (Albus et al. 1996). Our findings suggest a steady pattern of deficits at least in the early course of illness, rather than a change in the deficit profile related to the duration of illness, as suggested by the majority of authors comparing first-episode to chronic schizophrenic patients (Hoff et al. 1992a; Bilder et al. 1992; Sweeney et al. 1992; Saykin et al. 1994; Andreason 1994).

Possible factors that could have affected the neuropsychological test scores were lack of motivation, medication and the effect of acute psychotic state. In general, medication partially improves cognitive performance, particularly on measures of attention and information processing (Spohn et al. 1977). Comparing patient groups with and without medication, Hoff et al. (1992) found no differences in neuropsychological measures, except for tests of motor speed. The type and dosage of neuroleptics in both patient groups at time of testing is comparable. The patients were tested at a time of remission. In general, there is little evidence that the severity of illness affects neuropsychological test scores (Faustmann et al. 1988; Heaton et al. 1981b).

The individual subtests show pronounced deficits on tasks related to verbal memory and learning (VBM), indicative of dysfunctions in the temporal-hippocampal system (Saykin et al. 1994), as well as in visual motor processing and selective attention (VSM), indicative of frontal lobe dysfunctions (Buchanan et al. 1984; Hoff et al. 1992). Especially the Stroop test and TMT, two tests assessed to evaluate VSM, are considered to tap frontal lobe functions (Buchanan et al. 1984; Fuster 1989; Morice 1990; Hoff et al. 1992a). Our results therefore support the assumption that frontal dysfunction is an important underlying deficit in first-episode schizophrenia. Less evidence for impaired performance was found in abstraction/flexibility measured by the WCST-R. The WCST has been reported to be the best single measure of prefrontal functioning (Goldberg et al. 1987; Morice 1990); consequently, disturbances in prefrontal functioning in first-episode schizophrenics are not substantiated by our data.

In conclusion, the data presented suggest that neuropsychological deficits are manifestations of schizophrenia, independent of the early course of schizophrenia, and although negative symptoms are associated with the length of the prodromal period, they do not imply greater neuropsychological impairment in first-episode schizophrenia.

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