Premorbid Functioning, Cognitive Functioning, Symptoms and Outcome in Schizophrenia

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Submitted: February 25, 1992
Accepted: November 17, 1992

In this study we examined the relationship between premorbid functioning, outcome, cognitive functioning and positive and negative symptoms of schizophrenia. Cognitive functioning and symptoms were examined longitudinally in a sample of 39 subjects with schizophrenia (according to the DSM-III criteria). Subjects were assessed at admission to hospital and six months later during a period of relative remission. Premorbid functioning was significantly associated with negative symptoms but not with positive symptoms at both the acute phase and the remitted phase of the illness. Outcome was also associated with negative symptoms at admission and with both positive and negative symptoms at follow-up. Deficits on cognitive tests of verbal reasoning and concept formation were significantly associated with poor premorbid functioning and outcome.

Key Words: schizophrenia, premorbid functioning, cognitive functioning, negative symptoms

INTRODUCTION

A consistent finding in the literature is a link between negative symptoms and poor premorbid functioning in patients with schizophrenia (Andreasen and Olsen 1982; Pogue-Geile and Harrow 1984; 1986; Kay et al 1987). Patients with schizophrenia and poor premorbid functioning have also been shown to differ from other schizophrenic patients on several measures — symptoms, brain functioning, course, social outcome and response to treatment (Walker and Lewine 1988).

The exact relationship between poor premorbid functioning and the outcome of schizophrenia is difficult to ascertain, since asociality, which occurs before the onset of schizophrenia, is not easily distinguished from the early onset of the illness which presents as social difficulties in the prodromal period (Keefe et al 1989). For example, Buchanan et al (1990) found that patients with schizophrenia and deficit symptoms had poorer premorbid adjustment and more neurological impairment than non-deficit patients. They did not find an association between poor premorbid functioning and neurological impairment. Based on the results of several studies (Dworkin 1990; Dworkin et al 1988; 1990), Dworkin suggested that negative symptoms, positive symptoms and early social competence reflect relatively independent processes in the development of schizophrenia.

In a longitudinal study, Pogue-Geile and Harrow (1984; 1986) reported that negative symptoms during the post-acute phase of schizophrenia were prognostic indicators of later overall functioning. However, negative symptoms tended to identify patients who were already functioning poorly, rather than preceding a later decline. Furthermore, these researchers also found that positive symptoms during the post-acute phase were also prognostic indicators of later poor functioning and that the prognostic effects of positive and negative symptoms were additive. This work suggests that negative symptoms may represent one of the many possible pathways to poor functioning and that a history of difficulties in social

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functioning alone is not sufficient to account for the presence of negative symptoms.

Keefe et al (1989) report that poorer premorbid socio-sexual functioning was associated with more severe left-to-right ventricular asymmetry, more severe negative symptoms, fewer positive symptoms and poorer current social functioning. It has been suggested that poor premorbid functioning is an early manifestation of schizophrenia or a possible vulnerability factor of the disorder (Nuechterlein and Dawson 1984).

It is therefore unclear whether early poor social functioning is part of the individual's predisposition to it or an early expression of the illness. Very few studies have examined associations between premorbid functioning and other variables at different points during the course of schizophrenia.

The purpose of this study was to determine whether the associations between premorbid functioning, schizophrenic symptoms, cognitive functioning and outcome in a sample of patients with schizophrenia would be consistent from a period of acute relapse to a period of relative remission. More specifically, the association between premorbid functioning and positive and negative symptoms and cognitive functioning and the association between outcome and positive and negative symptoms and cognitive functioning were to be assessed. These associations were to be examined at two points in the illness — at admission to hospital and six months later, during a period of relative remission.

METHODOLOGY

Subjects

The sample consisted of 39 inpatients with schizophrenia (25 males and 14 females) who were consecutively admitted on a voluntary basis to the psychiatric unit of a general hospital. All subjects gave their informed consent after the nature of the procedures had been fully explained. The subjects were required to have a diagnosis of schizophrenia according to the DSM-III criteria. The exclusion criteria were as follows: evidence of an organic central nervous system disorder; significant and habitual drug or alcohol abuse in the past year; and mental retardation. Whether or not the subject met the exclusion criteria was determined by a review of the subject's chart, a clinical interview and a medical assessment on admission. The average age of the sample was 30.9 years (range = 17 to 54 years, SD = 8.73); the average years of education was 11.5. The average number of admissions was 5.26 (range = 1 to 16, SD = 3.70), and the average age at the first admission to hospital was 22.4 years (range = 13 to 39 years, SD = 5.44).

All the subjects were taking antipsychotic medication at the first assessment. At the follow-up assessment, all but two patients were on maintenance doses of medication; chlorpromazine equivalents were calculated. The cognitive profile of the two patients who were not on medication did not differ significantly from the mean cognitive scores of the other subjects (Addington et al 1991).

The male and female subjects did not differ in their positive and negative symptoms at admission to hospital. The males subjects had significantly more flat affect ($t = 2.72$, $p < 0.05$) and more anhedonia ($t = 2.69$, $p < 0.05$) at follow-up than the female subjects (Addington and Addington 1991). A comparison of the cognitive functioning of the males and females revealed no significant differences (Addington et al 1991).

Test instruments

The following measures were used in this study.

1. DSM-III criteria for schizophrenia based on the expanded version of the Present State Examination (PSE) were used for diagnosis.
2. Abbreviated Phillips Rating Scale of Premorbid Adjustment in Schizophrenia (Harris 1975).
3. Outcome Scale, developed by Strauss and Carpenter (1972).
4. Scale for the Assessment of Negative Symptoms (SANS) (Andreasen 1981).
5. Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen 1984).
6. The Wechsler Adult Intelligence Scale (WAIS) (all subtests).
7. Wechsler Memory Scale (WMS): both immediate and delayed recall were measured for both the verbal and non-verbal material. The subjects were given a delayed recall test of the WMS logical stories, paired associates and visual reproduction approximately 30 minutes after the initial recall test (Milner 1975; Taylor 1979).
8. Rey-Osterrieth Complex Figure (Rey 1942; Osterrieth 1944). The subject is instructed to copy the figure as exactly as possible. The time to complete the task is recorded, and both the test figure and subject's drawings are removed. A delayed recall trial is given after 45 minutes, when the subject is asked to reproduce as much of the figure as he or she can remember. This test is considered to be a measure of the non-verbal memory function of the right temporal lobe.
9. Newcombe Word Fluency (Newcombe 1969). This test was designed to assess verbal fluency in subjects who have suffered brain damage. The subjects are asked to name as many different items as possible from given categories in a 60 second period. The categories are as follows: objects; animals; and alternately birds and colours. This test has been noted to be a good indicator of damage to the left hemisphere (Newcombe 1969).
10. Chicago Word Fluency (Thurstone and Thurstone 1943). The subjects are allowed five minutes in which to write down as many words as possible beginning with the letter "s". They are then allowed a further four minutes for the more difficult task of writing down four-letter words

beginning with the letter "c". Impaired verbal fluency has been found to be associated with frontal lobe damage (Milner 1975).

11. Jones-Gotman Design Fluency Test (Jones-Gotman and Milner 1977). This test is intended to be a non-verbal analogue of the word fluency test. The test has two parts: a free condition lasting five minutes, and a fixed condition lasting four minutes. The subjects are asked to draw as many different, unnameable figures as they can. Creations are restricted to those that neither represent actual objects nor were derived from such objects; scribbles are not permitted. The second part of the test is presented as being similar to the first, except that this time each drawing has to consist of exactly four lines. Definitions of a line are explained as follows: straight line, circle, and curve. This test has been found to be sensitive to anterior lesions of the non-dominant hemisphere in particular to frontal lobe function and often to temporal lobe functioning (Jones-Gotman and Milner 1977).
12. The Wisconsin Card Sorting Test (WCST). The subject is presented with four stimulus cards, bearing designs that differ in form, color or number. The subject's task is to sort a series of cards that vary along these dimensions. The correct sorting strategy is changed, without warning, every time the subject correctly sorts ten consecutive cards. Testing is completed when the subject successfully completes six categories or sorts 128 cards, whichever comes first. The scores are calculated for the number of categories achieved, the number of errors and the number of perseverative responses. The WCST is considered to be sensitive to lesions in the frontal lobe (Milner 1975).

Procedures

The assessments began as soon as patients were sufficiently stabilized to give their informed consent to participate in the study and to understand task instructions (three to seven days after admission). The diagnostic interview, the SANS and the SAPS were administered by one of the authors, whose interrater reliability of these measures had been established on another sample at the UCLA Clinical Research Centre for Schizophrenia ($r = 0.85$).

The psychological tests were administered in two sessions on two consecutive days, after assessment of the patients' symptoms by the other author, who was blind to the positive/negative symptoms of the patients (determined using the SANS and the SAPS). The SANS and the SAPS were administered on day 1; the WAIS on day 2; and the other cognitive tests on day 3, in the order described above.

The assessments of symptoms and cognitive functioning were repeated for each subject six months after the initial assessment. At follow-up, symptoms were assessed on day 1 and cognitive functioning on day 2. The subjects' premorbid functioning was assessed at admission to hospital and outcome was assessed at follow-up.

Since previous research (Addington and Addington 1991) has shown that at both periods the negative symptoms (anhedonia, flat affect, alogia, avolition/apathy, attentional impairment) were strongly correlated, while the positive symptoms (hallucination, delusions, formal thought disorder, bizarre behavior) appeared to be separate measures, the summary score for negative symptoms and the individual positive symptom scores were used in the correlational analysis. The protocol for this study was approved by the Joint Hospital Ethics Committee of the University of Calgary and Foothills Hospital, Calgary.

RESULTS

A correlational analysis showed that a higher dose of medication (chlorpromazine equivalent) was significantly related to lower IQ ($r = -0.34$, $p < 0.05$) but not to any of the other cognitive tests. Dose of medication and symptoms have been shown to be unrelated in this sample (Addington and Addington 1991). In this study, the dose of medication was not related to the subject's level of premorbid functioning or outcome.

The male subjects had poorer premorbid functioning than the female subjects ($t = 3.33$, $p < 0.01$). Number of previous admissions was not associated with either premorbid func-

Table 1

Relationship between symptoms and premorbid functioning and outcome (Spearman correlations)

	Admission		Follow-up	
Symptoms	Premorbid functioning	Outcome	Premorbid functioning	Outcome
Negative symptoms	0.44[a]	−0.45[a]	0.49[a]	−0.53[b]
Hallucinations	0.16	−0.14	−0.13	−0.21
Delusions	0.07	0.01	−0.11	−0.50[a]
Bizarre behavior	−0.12	−0.02	−0.12	−0.27
Thought disorder	−0.07	0.12	−0.04	−0.34[c]

[a]$p < 0.01$, [b]$p < 0.001$, [c]$p < 0.05$

tioning or outcome. The subject's age at first admission to hospital was unrelated to either premorbid functioning or outcome.

An examination of symptoms shows that negative symptoms, but not positive symptoms, were related to poor premorbid functioning at both periods. Negative symptoms at both admission and follow-up were significantly associated with poor outcome. However, poor outcome was also associated with the presence of positive symptoms at follow-up (see Table 1).

In an earlier article (Addington et al 1991), the data on the cognitive functioning for this sample were reduced by principle axis factor analysis to three factors, and three tests which were retained as three distinct measures. This was done because of the sample size (N = 38) and the large number of correlational statistical tests that would have to be conducted if the cognitive tests remained as individual variables. The first factor appeared to be a measure of verbal reasoning and concept formation. All of the scores from the WCST (perseverative errors, total errors, total number of categories) clustered on this factor, as did verbal IQ. The second factor appears to be a measure of visual-spatial ability (immediate and delayed recall of the visual memory tasks of the Wechlser Memory Scale, the copying of the Rey figure, and performance IQ). The third factor seems to be a measure of visual and verbal memory (immediate and delayed recall of the verbal memory tasks of the Wechlser Memory Scale, the recall of the Rey figure). The three tests that remained as distinct measures were the Jones-Gotman Design Fluency Test, the Newcombe Word Fluency and the Chicago Word Fluency.

An examination of cognitive functioning revealed that factor 1 (verbal reasoning and concept formation) was significantly associated with premorbid functioning at both admission to hospital and follow-up and with outcome at follow-up. Poor performance on the Newcombe Word Fluency Test was significantly associated with poor outcome at both times (see Table 2).

DISCUSSION

Consistent with the findings of other studies (Andreasen and Olsen 1982; Breier et al 1991; Pogue-Geile and Harrow 1984; 1986) poor premorbid functioning and poor outcome were significantly associated with negative symptoms. Even though negative symptoms improved from the acute stage of the illness to a period of relative remission (Addington and Addington 1991), these associations were significant during both the acute phase of the illness and the period of remission. Therefore, patients with schizophrenia who have poor social and socio-sexual functioning prior to the onset of the illness present with more severe negative symptoms during the illness and have poorer current social functioning. Negative symptoms and social functioning deficits may be influenced by some shared factors which tend to occur most often concurrently. Furthermore, as suggested by Keefe et al (1989), poor premorbid functioning may predispose an individual with schizophrenia to manifest features of the deficit syndrome.

Alternatively, in this study, positive symptoms at admission and follow-up were unrelated to poor premorbid functioning. Although positive symptoms present in the acute phase were unrelated to outcome, positive symptoms that remained into a period of relative remission were prognostically important. This is consistent with other findings (Breier et al 1991; Pogue-Geile and Harrow 1986).

This study supports the hypothesis that the prognostic importance of positive symptoms in schizophrenia differs between the period spent in hospital and after discharge. Both positive and negative symptoms make additive contributions to the prediction of a global outcome. In this study, only delusions and thought disorders were related to poor outcome. The relationships between outcome and hallucinations and bizarre behavior, although weak, were much stronger than at admission. The incidence of bizarre behavior in this sample was rare and may account for the weak association. It is unclear why the association with delusions was stronger

Table 2

Relationship between cognitive functioning and premorbid functioning and outcome (Spearman correlations)

	Admission		Follow-up	
Cognitive factors	Premorbid functioning	Outcome	Premorbid functioning	Outcome
Factor 1 – verbal reasoning and concept formation	0.33[a]	– 0.01	0.44[c]	– 0.37[a]
Factor 2 – visual-spatial ability	– 0.03	0.12	0.04	0.16
Factor 3 – memory	– 0.09	0.18	0.04	0.07
Newcombe Word Fluency	– 0.05	0.61[b]	– 0.06	0.49[c]
Chicago Word Fluency	– 0.21	0.21	– 0.10	0.11
Jones-Gotman Design Fluency Test	– 0.02	0.05	– 0.21	0.28

[a]$p < 0.05$, [b]$p < 0.001$, [c]$p < 0.01$

than that with hallucinations. Continual delusions make it more difficult to function at an adequate social level than hallucinations.

Premorbid functioning was related to poor functioning on measures of verbal reasoning and concept formation at both times. Poor performance on these same cognitive measures during remission was related to poor outcome. These results support the hypothesis that specific cognitive deficits are part of a deficit syndrome and that these deficits continue into remission and are consistent with continued poor functioning. This factor of verbal reasoning and concept formation was derived from the verbal IQ score and three scores from the WCST (perseverative errors, errors and categories achieved). Breier et al (1991) found that perseverative errors on the WCST were associated with the levels of negative symptoms and poor social functioning at follow-up. The association deficits on measures of frontal lobe functioning and premorbid functioning have been reported elsewhere (Walker and Lewine 1988). Premorbid functioning was not associated with memory or with visual-spatial ability.

Low scores on the outcome scale were related to poor performance on the Newcombe Word Fluency Test. The Newcombe is a measure of verbal fluency and may also be related to frontal lobe functioning. It has been shown to be significantly associated with negative symptoms at both the acute and remitted stage of the illness (Addington et al 1991).

The extent to which the conclusions drawn from this study can be generalized is limited by the nature and size of the sample. Another limitation is the fact that premorbid functioning was assessed only in terms of social and socio-sexual functioning; there was no measure of premorbid cognitive functioning, such as the National Adult Reading Test or the Wide Range Achievement Test. Furthermore, the effects of neuroleptic medications are inextricably confounded and are unclear in this study. This study cannot determine whether medication affects cognitive performance or whether cognitive deficits and the need for a higher dose of medication are both results of a more severe form of the illness.

One of the difficulties in examining premorbid functioning is determining whether it is part of the premorbid personality, a vulnerability to the disorder or part of the prodromal period, an issue which this study cannot address. Regardless, individuals with schizophrenia who present with a history of poor premorbid functioning tend to later demonstrate poor social functioning, more severe negative symptoms and increased cognitive deficits. This finding is supported elsewhere (Breier et al 1991; Keefe et al 1989).

The results of this study are supported elsewhere in the literature. However, it demonstrates the relationships among poor premorbid functioning, poor outcome, negative symptoms and specific cognitive deficits in the same sample of patients with schizophrenia and examines these relationships both at admission and during a period of relative remission. As a result, it strongly supports other results from cross sectional studies.

The results support Dworkin's observation (Dworkin et al 1990) that poor cognitive functioning and premorbid functioning are associated, but that these two dimensions are not interchangeable. Social functioning or asociality should be examined separately from negative symptoms and not as a negative symptom. Further research may look specifically at different aspects of outcome and social functioning. Certain aspects may be related to cognitive functioning and not to symptoms, and vice versa. Further attention should be given to the manner in which residual positive symptoms affect outcome.

Future studies should investigate possible gender differences in the variables examined in this study. In this study, the male subjects had poorer premorbid functioning than the female subjects. They also exhibited higher levels of flat affect and anhedonia. The idea that males may present with a form of the illness that has poorer premorbid functioning, more negative symptoms and poorer social functioning is not new (Goldstein and Tsuang 1990).

In summary, results of this study suggest that associations between poor premorbid functioning and negative symptoms and between poor premorbid functioning and deficits on measures of verbal reasoning and concept formation are stable from the acute phase of the schizophrenic illness to a phase of relative remission. In addition, poor outcome is predicted not only by negative symptoms but also by positive symptoms that remain in a period of relative remission. Poor outcome is also related to cognitive deficits on measures of frontal lobe functioning.

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