Correlations of Premorbid Adjustment in Schizophrenia With Auditory Event-Related Potential and Neuropsychological Abnormalities
[Brief Reports]

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Abstract

Objective: The authors examined the relationship between premorbid adjustment in schizophrenia and event-related potential data and neuropsychological data obtained after onset of the illness. Method: They interviewed 13 male veterans with chronic schizophrenia, 12 normal comparison subjects, and their first-degree relatives and also obtained objective data from the patients’ school records and charts. They used interview and objective data to score the Cannon-Spoor Premorbid Adjustment Scale. Patients and comparison subjects were also given event-related potential tests, the Wisconsin Card Sorting Test, and the Wechsler Memory Scale-Revised. Results: Worse premorbid adjustment in the
schizophrenic patients was significantly associated with a marked reduction of the N2 component amplitude of the auditory event-related potential measured over the left temporal and central regions, but it was not associated with the P3 component amplitude. Worse Premorbid Adjustment Scale scores were significantly associated with more perseverative errors on the Wisconsin Card Sorting Test and worse performance on the visual memory span task of the Wechsler Memory Scale. Conclusions: Premorbid adjustment may predict the severity of specific neurophysiological and neuropsychological abnormalities in schizophrenia.

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Premorbid adjustment in schizophrenia is of interest because it may help reduce the heterogeneity of the disorder and because it may have predictive value. Elsewhere [1], we reported that premorbid adjustment correlated with psychosocial outcome in terms of the severity of current clinical state, negative symptoms, and a lower level of current independent functioning.

In this paper we examine the relationship between premorbid adjustment and postdiagnosis neurophysiological and cognitive variables. We hypothesized that poor premorbid adjustment would be associated with 1) diminished P3 and N2 event-related potential components and 2) worse neuropsychological performance on measures of executive functions and of spatial working memory, which have been reported to be abnormal in schizophrenia [2,3].

METHOD

Thirteen right-handed male veterans who met DSM-III-R criteria for chronic schizophrenia were recruited. They had a mean age at onset of 22.1 years (SD=3.4), a mean duration of illness of 16.1 years (SD=7.1), and a mean percentage of time hospitalized of 39.1% (SD=27.6%), and their verbal IQs were not less than 75. Twelve normal subjects were chosen to be similar to the schizophrenic patients, as described elsewhere [2]; they were selected for having no history of mental illness in themselves (clinically screened by a psychiatrist [J.J.L.]) or in their first-degree relatives. All subjects provided written informed consent.

We developed a standardized semistructured interview and used it in combination with detailed chart synopses and school records to score the Premorbid Adjustment Scale of Cannon-Spoor et al. [4]. This interview was administered to all 25 subjects, to the first-degree relatives of all 12 normal comparison subjects, and to the first-degree relatives of eight of the 13 schizophrenic patients. Interrater reliability for these measures has been high. A detailed description of our methodology is presented elsewhere [1].

An auditory oddball paradigm was used to elicit the N2 and P3 components to infrequent target tones [2]. N2 and P3 were measured from event-related potentials recorded at the vertex electrode (CZ) and lateral electrode sites (T3 and T4): P3 was measured from the target event-related potential, and N2 was measured from the difference event-related potential, generated by subtracting the frequent from the target event-related potential [2]. We found that N2 and P3 amplitudes were lower in patients with schizophrenia than in similar normal comparison subjects (p<0.01) but that latencies did not differ between groups [2].

We assessed neuropsychological performance in areas of spatial working memory and executive
functions using, respectively, the visual memory span subtest of the Wechsler Memory Scale-Revised [5] and the Wisconsin Card Sorting Test [6]. The Wisconsin Card Sorting Test provided four measures of performance: 1) number of categories achieved, 2) number of correct responses, 3) number of errors, and 4) number of perseverative errors.

A repeated measures analysis of variance was used to test group differences in mean Premorbid Adjustment Scale scores; this analysis was followed by planned comparisons with univariate t tests. Relationships between Premorbid Adjustment Scale scores and event-related potential component amplitudes and neuropsychological test scores were assessed by using Spearman’s rank order correlation [7].

RESULTS

Overall, the schizophrenic patients had significantly poorer Premorbid Adjustment Scale scores than the normal comparison subjects (F=18.06, df=1, 21, p<0.001). We also took an average score for the three earliest age periods, excluding the adulthood and general periods of the Premorbid Adjustment Scale [4], as recommended by Kelley et al. [8]. This eliminated the ambiguity between premorbid versus morbid effects during the adulthood period. We found that premorbid adjustment, measured by the mean score, was significantly poorer among schizophrenic patients (mean=0.44, SD=0.15) than among the normal comparison subjects (mean=0.26, SD=0.08) (p=0.001). For data reduction purposes, we chose this as our overall Premorbid Adjustment Scale variable for subsequent correlations.

As shown in Figure 1, worse (higher) overall Premorbid Adjustment Scale scores in our schizophrenic patients were associated with a marked reduction (a less negative deflection) of the N2 component. Overall Premorbid Adjustment Scale scores were significantly correlated with left temporal and central N2 amplitude (T3: r_s =0.60, N=13, p=0.03; CZ: r_s =0.60, N=13, p=0.03), but not with right temporal N2 amplitude (T4: r_s =0.31, N=13, p=0.30). We also found that Premorbid Adjustment Scale scores did not significantly correlate with the P3 component.

![Figure 1](image-url)
As also shown in Figure 1, worse schizophrenic Premorbid Adjustment Scale scores were associated with worse performance on the Wechsler Memory Scale-Revised visual memory span task and with more perseverative errors on the Wisconsin Card Sorting Test ($r_s = -0.83$, $N = 11$, $p = 0.002$ [two-tailed]; $r_s = 0.51$, $N = 11$, $p = 0.05$ [one-tailed]). None of the three other Wisconsin Card Sorting Test scores (number of categories achieved, number of correct responses, or number of errors) was significantly associated with Premorbid Adjustment Scale scores among the schizophrenic patients.

**DISCUSSION**

Despite the retrospective nature of our premorbid data, a current electrophysiological measure, auditory N2 amplitude, previously reported to be reduced in schizophrenia [2], showed strong left temporal and central region correlations with premorbid adjustment scores in schizophrenic patients. Conversely, P3 amplitude was not correlated with any premorbid measure. We have previously found that N2 amplitude reduction correlated clinically with worse outcome and anatomically with reduced limbic and...
neocortical gray matter volumes in the temporal lobe [2]. Together with the current finding of its association with worse premorbid adjustment, this suggests that N2 amplitude reduction may reflect psychobiological abnormalities that precede the onset of overt psychotic symptoms and that persist after treatment. Furthermore, our data on P3 are compatible with the failure of Friedman et al. [9] to find P3 abnormalities in children at risk for schizophrenia. Finally, the N2 component has been reported to index processes associated with sustained attention and working memory operations involved in stimulus classification [10]. Neuropsychological deficits in similar cognitive processes may be characteristic of some individuals at high risk for the development of schizophrenia [11].

Our additional finding of an association between premorbid adjustment and visual memory span suggests a possible premorbid impairment in spatial working memory in schizophrenia because poor performance on the visual memory span task of the Wechsler Memory Scale-Revised may reflect such a difficulty. Similarly, the significant association we found between poor premorbid adjustment and a greater number of perseverative errors on the Wisconsin Card Sorting Test may also be related to a working memory impairment and to attentional deficits that, perhaps, predate disease onset [11].

In conclusion, taken together with our previous report [1], which primarily revealed associations between premorbid adjustment and psychosocial outcome in schizophrenia, this report, showing associations between premorbid adjustment and the severity of biological (i.e., neurophysiological) and cognitive abnormalities, strengthens the evidence for the predictive value of premorbid adjustment in schizophrenia.

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