Prospective Diagnosis of the Initial Prodrome for Schizophrenia Based on the Structured Interview for Prodromal Syndromes: Preliminary Evidence of Interrater Reliability and Predictive Validity

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Objective: This study was conducted to determine the interrater reliability and predictive validity of a set of diagnostic criteria for the prodrome of the first episode of schizophrenic psychosis when based on the Structured Interview for Prodromal Syndromes.

Method: The subjects were patients referred for evaluation because of a suspected schizophrenia prodromal syndrome. For the reliability study, two to four raters independently diagnosed 18 patients on the basis of face-to-face or videotaped interviews. For the validity study, 6- and 12-month outcome data were collected for 29 patients.

Results: Agreement in differentiating prodromal from nonprodromal patients was 93%. The prodromal features had converted to schizophrenic psychosis for 46% of the prodromal patients at 6 months and for 54% at 12 months.

Conclusions: In small groups of subjects, these diagnostic criteria for the schizophrenic prodrome and the Structured Interview for Prodromal Syndromes showed promising interrater reliability and predictive validity.

Prospective diagnostic criteria for the prodrome of the first episode of schizophrenic psychosis are intended to distinguish prodromal syndromes from psychosis and other clinical phenomena. Our group modified earlier criteria that identified patients with a 40% risk of becoming psychotic within 1 year (1) to produce the Criteria of Prodromal Syndromes (2). Like the earlier criteria, the Criteria of Prodromal Syndromes consist of three sets of criteria for prodromal features and a psychosis criteria set. The first three criteria sets identify patients as prodromal on the basis of attenuated positive symptoms, brief intermittent psychotic symptoms, or genetic risk plus functional deterioration; patients meeting one or more of the criteria sets for prodromal features but not the psychosis criteria are defined as prodromal. Two of the three criteria sets focus on positive symptoms because retrospective data (3) suggest that positive symptoms begin later than negative symptoms in the prodromal phase and crescendo in the last year before onset. Modifications incorporated into the Criteria of Prodromal Syndromes (e.g., referencing a new rating scale, requiring recent onset or change) were intended to increase the reliability of identification of positive symptoms and to improve identification of patients at imminent risk for schizophrenic psychosis.

To gather information needed to apply the Criteria of Prodromal Syndromes, we developed the Structured Interview for Prodromal Syndromes (4). The goal of this project was to field test the reliability and predictive validity of the Criteria of Prodromal Syndromes when based on the Structured Interview for Prodromal Syndromes.
TABLE 1. Six- and 12-Month Outcomes of 29 Patients Evaluated for Suspected Schizophrenia Prodromal Symptoms, by Baseline Status on the Structured Interview for Prodromal Syndromes

<table>
<thead>
<tr>
<th>Baseline Diagnostic Status</th>
<th>6-Month Outcomea,b</th>
<th>12-Month Outcomea,c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Psychotic</td>
<td>Prodromal</td>
</tr>
<tr>
<td>Prodromal</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Neither psychiatric nor prodromal</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

a Psychotic outcome refers to schizophrenic psychosis. Significant relationship of diagnostic status at baseline to outcomes at 6 months and at 12 months (2×3 Fisher's exact tests, both p<0.0001).

b Significant relationship of diagnostic status at baseline to outcomes dichotomized as psychotic versus prodromal/neither (p<0.004) and as psychotic/prodromal versus neither (p=0.0001) (2×2 Fisher's exact tests).

c Significant relationship of diagnostic status at baseline to outcomes dichotomized as psychotic versus prodromal/neither (p<0.002) and as psychotic/prodromal versus neither (p<0.00012) (2×2 Fisher's exact tests).

The criteria for remission included the absence of any positive symptoms. Reliability was achieved with patients who meet the criteria for attenuated schizophrenia; the interview has excellent interrater reliability with patients who meet the criteria for prodromal schizophrenia. Table 2 shows that six (46%) of the 13 developed schizophrenic psychosis by 6 months, and the rate was 54% at 12 months. Initial diagnostic status was significantly associated with diagnostic outcome (Table 1 and Table 2).

Further evidence that the patients who did not develop schizophrenic psychosis were correctly diagnosed is that none received antipsychotic medication. Two patients’ prodromal symptoms remitted. No initially nonprodromal patient developed schizophrenic psychosis, but two met the criteria for prodromal syndrome 12 months later.

Discussion

The reliability data suggest that raters can use the Structured Interview for Prodromal Syndromes to apply the Criteria of Prodromal Syndromes in making diagnostic judgments regarding the presence of the prodrome for schizophrenia; the interview has excellent interrater reliability with patients who meet the criteria for attenuated positive symptoms. Reliability was achieved with patients.
relevant to the intended use of the instrument: those referred because of suspected prodromal syndrome. Caution is indicated because of the small study group. In addition, these results were achieved among a small group of raters at one site who had trained and worked together intensively with this diagnostic group. Future studies are needed to determine whether these results can generalize.

The significant association between initial diagnoses and outcomes based on the Structured Interview for Prodromal Syndromes strongly supports the predictive validity of the Criteria of Prodromal Syndromes for patients meeting criteria for attenuated positive symptoms. The rate of conversion from prodrome to schizophrenic psychosis in the present study is similar to that observed with the earlier criteria (1). Longer follow-up is needed to determine whether patients with false positive diagnoses (either remaining prodromal or remitting) continue to be at risk for conversion. The Criteria of Prodromal Syndromes can also result in false negative diagnoses. This result is not surprising, since the present criteria are not intended to detect all prodromal patients but, rather, prodromal patients at relatively imminent risk of conversion to schizophrenic psychosis. Patients with subthreshold symptoms are invited to return for a repeat interview if their symptoms worsen.

The validity data must also be interpreted with caution. The study group was small, some eligible patients did not participate in follow-up, and the interviewers who made the follow-up diagnoses were not blind to the initial diagnoses. Another limitation is that the participants were primarily patients who met the criteria for attenuated positive symptoms. Future studies with larger study groups should investigate predictive validity in patients meeting the criteria for brief intermittent psychotic symptoms and for genetic risk plus functional deterioration. Other data relevant to validity, including the course of symptoms among patients remaining prodromal, the occurrence of other DSM-IV axis I and axis II disorders, and concordance of measures from other domains of measurement, such as cognitive functioning, remain to be analyzed.

Despite the preceding caveats, these initial reliability and validity results support the use of the Criteria of Prodromal Syndromes and the Structured Interview for Prodromal Syndromes in additional studies with patients suspected of having prodromal changes.

References

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