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Does a Parent-Report Measure of Behavioral Problems Enhance Prediction of Conversion to Psychosis in Clinical High-Risk Adolescents?

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Abstract

Recent research on risk for psychosis has focused on youth who manifest subclinical signs that are often associated with the prodrome to psychosis. Standardized measures of prodromal symptoms have been shown to significantly enhance prediction of risk for conversion to an Axis I psychotic disorder. In the present study, a widely used parent-report measure of behavioral problems, the Child Behavior Checklist (CBCL) was administered to examine the clinical and diagnostic utility of the measure as an adjunctive screening instrument in the identification of at-risk youth. The CBCL, the Structured Interview for Prodromal Syndromes (SIPS), and other diagnostic measures were administered at baseline and at one year follow-up assessments to adolescents (n = 41) at clinical high-risk for the development of a psychotic disorder. Analyses were conducted to compare the 14 at-risk adolescents who subsequently converted to psychosis to the 27 who did not. Conversion to psychosis was defined as conversion to an Axis I psychotic disorder or affective disorder with psychotic features. Consistent with expectations, at one year follow-up, compared to the Non-Converted participants, the Converted participants manifested significantly higher scores on the prodromal symptom scales of the SIPS. There were, however, no differences in CBCL social and behavioral ratings as a function of conversion status. It is concluded that the CBCL does not show promise as an alternative or adjunctive predictor of conversion to psychosis in at-risk adolescents.

Keywords

Psychosis; Prodromal; High-Risk; Adolescents; Social Functioning; Behavioral Problems
1. Introduction

Social and behavioral precursors of psychosis are well documented in the literature (Cornblatt, 2002; Erlenmeyer-Kimling, 2000; Johnstone et al., 2000; Nuechterlein & Dawson, 1984; Olin & Mednick, 1996). The majority of individuals who succumb to psychotic disorders manifest prodromal signs of behavioral disturbance (Larsen, McGlashan, & Moe, 1996; Neumann, Grimes, Walker, & Baum, 1995). The general pattern of findings suggests that pre-psychotic youth are more socially isolated, withdrawn, emotionally labile, anxious, and aggressive than their healthy siblings and/or age-matched comparison subjects. They also have higher levels of impaired attention, which remain stable and elevated from childhood to adolescence, and are assumed to negatively affect social interactions leading to increased stress related to social situations (Cornblatt, Obuchowski, Schnur, & O’Brien, 1997; Amminger et al., 1999; Hans, Auerbach, Asarnow, Styr, & Marcus, 2000; Miller, Byrne, Hodges, Lawrie, & Johnstone, 2002; Ballon, Kaur, Marks, & Cadenhead, 2007). The divergence in developmental trajectories becomes more pronounced with age and is especially apparent in the adolescent period. Research findings also suggest that the behavioral expression of vulnerability to psychosis is characterized by sex differences, with males exhibiting more externalizing behavior problems, while females exhibiting more internalizing behavior problems (Walker, Weinstein, & Baum, 1995; Neumann et al., 1995; Gutt, Petresco, Krelling, Busatto, Bordin, & Lotufo-Neto, 2008).

Early studies of risk for schizophrenia and other psychoses focused on genetic high-risk samples (i.e., offspring of parents with psychotic disorders) to identify predictors of subsequent illness. More recently, the focus has shifted to clinical high-risk samples who manifest symptoms characteristic of the prodrome to psychosis. It has been shown that standardized diagnostic interviews for measuring prodromal symptoms and syndromes (such as schizotypal personality disorder (SPD) and attenuated positive symptoms (APS)), can enhance prediction beyond that achieved with genetic high-risk study designs. For example, a number of studies using standardized procedures for assessing prodromal signs have demonstrated that 25% to 45% of these individuals develop a psychotic disorder within 2 to 4 years of baseline assessment (Cannon et al., 2008; Klosterkotter, Hellmich, Steinmeyer, & Schultze-Lutter, 2001; Miller et al., 2003; Olsen & Rosenbaum, 2006). In particular, the Structured Interview for Prodromal Syndromes (SIPS) is an instrument that yields reliable ratings of APS, as well as other prodromal signs, and has been repeatedly shown to identify populations with high subsequent rates of conversion for psychosis (Cannon et al., 2008; Miller et al., 2003).

Given the importance of early identification of at-risk individuals for the development of preventive interventions for this population, the prediction of conversion to psychosis in clinical high-risk samples has now become a central focus of attention. In particular, investigators are attempting to determine whether prediction of risk for conversion can be enhanced beyond that obtained with standardized prodromal measures. One avenue to pursue this line of investigation is the adjunctive use of observer-report measures. This is important, because of potential limitations with self-report measures related to the clinical presentation of prodromal symptoms (e.g., poor insight, cognitive deficits, suspiciousness, disorganized communication). Ideally, such adjunctive measures would be valid, reliable, and easily administered in a clinical setting. The Child Behavior Checklist (CBCL) (Achenbach, 1991) is a parent-report measure of child behavioral problems that meets these criteria, in that extensive normative data have been published on the CBCL, and its reliability and validity are well established.

The purpose of the present study is to shed light on the clinical and diagnostic utility of the CBCL as an adjunctive screening instrument in the identification of at-risk youth. Although
the CBCL was not intended to predict specific clinical outcome, it has the potential to serve as an inexpensive adjunctive screening measure for identifying individuals likely to develop psychosis. Based on previous findings showing that greater functional declines are associated with conversion to psychosis among individuals who meet prodromal criteria (Yung et al., 2003; Cornblatt et al., 2007), it was hypothesized that at-risk adolescents who convert to psychosis will be rated by parents as exhibiting more pronounced social and behavioral problems on the CBCL when compared to those who do not convert to psychosis. It was also predicted that the differences between the groups will become more pronounced over time. In addition, it was expected that more severe SIPS/SOPS symptom ratings will predict conversion to psychosis in this clinical high-risk sample. The adolescent period is the focus of this study because it is characterized by a rapid increase in risk for psychosis onset, and it is likely to be a critical period for intervention (Walker, 2002).

2. Methods

The present sample is 41 at-risk adolescents, ranging in age from 12 to 18 years, who participated in a longitudinal study of risk for psychosis conducted at Emory University. Assessments were conducted in the research clinic at baseline and subsequently up to four years on an annual basis. As described below, 14 of the 41 participants in the present study developed an Axis I psychotic disorder or affective disorder with psychotic features within the study follow-up period. The majority (n = 8) of these conversions to psychosis occurred after the one year follow-up assessment. Demographic characteristics by conversion status are presented in Table 1.

For a detailed description of the methodology and data analyses approach, please see the online Supplementary Materials section.

3. Results

3.1. Conversion to Psychosis

Because contemporary findings from genetic research do not support specific etiological distinctions among psychotic disorders (Craddock, O’Donovan, & Owen, 2009; Ivleva et al., 2010), the outcome variable in the present study is Axis I psychotic disorder or affective disorder with psychotic features.

As noted above, of the 41 at-risk adolescents, 14 converted to an Axis I psychotic disorder in the 5 years since the inception of the study (initial assessment followed by four annual assessments). In this group six were diagnosed at the 1st year follow-up, five converted during the following year, and three converted in the 3rd year. This conversion rate of almost 35% in the study sample and time frame is in the range reported in previous longitudinal studies of clinical high-risk samples, in particular those using the SIPS (Cannon et al., 2008; Miller et al., 2003; Olsen & Rosenbaum, 2006). The Axis I psychotic disorders diagnosed in the Converted group were schizophrenia (n = 4), schizoaffective disorder (n = 5), bipolar I disorder with psychotic features (n = 4), and major depressive disorder with psychotic features (n = 1).

3.2. Cross-sectional comparisons

Analyses were first conducted to tests for demographic differences between Converted and Non-Converted adolescents. There were no significant age (t(39) = .88, p = .385) or sex differences (χ² = .36, p = .548) between the two groups.

The means and standard deviations for all SIPS/SOPS scales at baseline and at one year follow-up assessments are presented in Table 2. The two groups did not show significant
baseline differences in prodromal symptom severity as measured by the five SIPS/SOPS
composite scales. As shown in Table 2, however, there was a trend toward higher scores for
the Converted group on all but the scale Positive Symptoms. Consistent with expectations, at
one year follow-up the Converted group showed significantly higher scores on all SIPS/
SOPS scales compared to the Non-Converted group, except for the scale General
Symptoms. However, when this analysis was conducted without the medication covariates,
there were significant group differences for the scale General Symptoms.

The means and standard deviations for all CBCL individual scales at baseline and at one
year follow-up assessments are presented in Table 3. Contrary to the prediction for baseline
assessment, MANCOVA revealed no significant main effect for conversion status on the
CBCL individual or composite scales. Also, no significant main effect for medication was
found. A significant main effect of sex for Thought Problems, $F(1, 33) = 4.92, p = .034, \eta^2 = .13$, indicated higher scores for female at-risk adolescents. There were no significant
Conversion Status X Sex interactions.

Similar to the baseline findings, no significant main effect for conversion status was found
with the CBCL individual or composite scales for one year follow-up assessment. Also, no
significant main effect for any medication was found. A significant main effect of sex for
Aggressive Behavior, $F(1, 20) = 5.11, p = .035, \eta^2 = .20$, indicated higher scores for female
at-risk adolescents. There were no significant Conversion Status X Sex interactions.

The intercorrelations between prodromal symptoms and CBCL individual scales at baseline
and at one year follow-up assessments are presented in Table 4.

### 3.3. Temporal progression of SIPS/SOPS and CBCL ratings

Consistent with the prediction, repeated-measures ANCOVA of the SIPS/SOPS prodromal
scale ratings revealed a main effect for conversion status for all five prodromal scales:
General Symptoms, $F(1, 25) = 6.24, p = .019, \eta^2 = .20$, and Total Symptomatology, $F(1, 25) = 9.06, p = .006, \eta^2 = .27$. There was a significant Conversion Status X Time interaction for
the scales Positive Symptoms, Wilks’s $\Lambda = .81, F(1, 25) = 5.63, p = .026, \eta^2 = .18$, and
Total Symptomatology, Wilks’s $\Lambda = .80, F(1, 25) = 5.66, p = .026, \eta^2 = .19$, with Converted
adolescents showing significant increases in prodromal symptoms over time. Figures 1 to 5
illustrate the temporal progression of SIPS/SOPS prodromal symptom ratings from baseline
to one year follow-up assessment.

With respect to medications, the analyses yielded significant main effect for antipsychotic
medication for the scales Negative Symptoms, $F(1, 25) = 12.51, p = .002, \eta^2 = .34$, and
Total Symptomatology, $F(1, 25) = 6.08, p = .021, \eta^2 = .20$. Study participants not on
antipsychotic medication had lower symptom scores.

There was a significant Conversion Status X Sex interaction for the scales Negative
Symptoms, $F(1, 25) = 4.24, p = .049, \eta^2 = .15$, and Total Symptomatology, $F(1, 25) = 5.77, p = .024, \eta^2 = .19$. Univariate tests within sex for both prodromal scales revealed significant
differences only for males, in that Converted males showed higher Negative and Total
scores than Non-Converted males, whereas there were no differences between Converted
and Non-Converted females.

Contrary to the prediction, repeated-measures ANCOVA of the CBCL scale ratings revealed
no main effect for conversion status and no significant Conversion Status X Time
interactions for any of the CBCL individual or composite scales. Figures 6 and 7 illustrate
the temporal progression of CBCL composite scores – Total Competence, Internalizing Problems, and Externalizing Problems – from baseline to one year follow-up assessment.

There was a main effect for time for the individual scale Somatic Problems, Wilks’s Λ = .83, F(1, 25) = 4.65, p = .041, η² = .16, due to decrease in problems over time. Although the time effect was not significant for the remaining CBCL scales, the overall trend across scales was toward a decline of problems over time.

With respect to medications, the analyses yielded a significant Antipsychotics X Time interaction for the scale Activities, Wilks’s Λ = .78, F(1, 25) = 6.68, p = .016, η² = .22. This was due to a greater decrease in problems over time for those on antipsychotic medication, t (2) = −3.66, p = .033. A significant main effect for stimulant medication was found for the individual scales Attention Problems, F(1, 25) = 4.79, p = .039, η² = .16, Delinquent Behavior, F(1, 25) = 10.82, p = .003, η² = .31, Aggressive Behavior, F(1, 25) = 8.45, p = .008, η² = .26, and the composite scale Externalizing Problems, F(1, 25) = 5.79, p = .024, η² = .19. This significant effect was due to higher symptoms ratings for participants on stimulant medication. Also, there was a significant main effect for antipsychotic medication for the scales Withdrawn, F(1, 25) = 4.90, p = .037, η² = .17, and Thought Problems, F(1, 25) = 4.68, p = .041, η² = .16, and a significant main effect for antidepressant medication for the scale Thought Problems, F(1, 25) = 4.62, p = .042, η² = .16.

There was a significant Sex X Time interaction for the scales Thought Problems, Wilks’s Λ = .61, F(1, 25) = 15.31, p = .001, η² = .39, and Attention Problems, Wilks’s Λ = .84, F(1, 25) = 4.32, p = .048, η² = .15, with female adolescents showing significant decreases in problems over time. Also, a significant main effect of sex for the scale Aggressive Behavior, F(1, 25) = 6.36, p = .019, η² = .21, indicated higher scores for female at-risk adolescents.

4. Discussion

The purpose of this study was to determine whether parent-reported social and behavioral problems on the CBCL contributed to the prediction of conversion to psychosis in adolescents at clinical high-risk. The conversion rate to a psychotic disorder of almost 35% observed in the present sample is consistent with the range reported in previous studies (Cannon et al., 2008; Miller et al., 2003; Olsen & Rosenbaum, 2006). While conversion status was not related with baseline prodromal symptoms, consistent with expectations, at one year follow-up the Converted group manifested significantly higher scores on the prodromal symptom scales. Furthermore, consistent with predictions, a significant Conversion Status X Time interaction for the scales Positive Symptoms and Total Symptomatology indicated that at-risk adolescents who converted to psychosis showed increases in prodromal symptoms over time compared to those who did not. This finding supports the clinical and diagnostic utility of the SIPS/SOPS standardized measure in predicting conversion to psychosis in clinical high-risk samples. In addition, the finding that the two groups did not show significant baseline differences in prodromal symptoms supports the need for adjunctive measures to aid early detection of at-risk youth likely to develop psychosis. This is a high priority research domain, given the need for the development of novel prevention and early intervention approaches.

Contrary to predictions, however, there were no differences in parent-reported baseline CBCL scores as a function of conversion status, and no significant differences between Converted and Non-Converted youth in CBCL scores over the subsequent one year. Although not significant, there was a trend toward a decline of CBCL scores between baseline and follow-up assessments. There is variability within this general trend, with some
participants manifesting stable or increasing behavioral problems. The present results indicate that this variability does not map onto differences in psychotic outcome.

Given that this is the first study in the literature examining parent-reported social and behavioral characteristics in a prospective study of adolescents at clinical high-risk, direct comparison with other reports is not possible. Although the present results might be viewed as inconsistent with findings from other studies of clinical high-risk samples that report significant declines in social and cognitive functioning, and increases in depressive symptoms, anxiety symptoms, decreased attention, and disorganization as predictors of conversion to psychosis (Yung, Phillips, Yuen, & McGorry, 2004; Cornblatt et al., 2007; Ballon et al., 2007; Cannon et al., 2008; Woods et al., 2009), all of these earlier investigations relied primarily on self-report during diagnostic interviews. Thus, the present results point to the advantage of direct clinical assessment of prodromal symptoms (i.e., SIPS/SOPS), as opposed to informant’s reports, in predicting conversion.

Although parents typically observe their child in a variety of contexts, this may not outweigh the advantages of the clinical interview for obtaining symptom data that are predictive of conversion. The advantages of the clinical interview may be a function of both the probing questions it contains about perceptual, ideational and mood symptoms, as well as the clinical training of the rater. Consistent with this speculation, some earlier research on general clinical samples comparing the predictive power of structured diagnostic interviews with parent-reported behavior problems indicates that structured interviews have higher positive predictive power and greater validity (Wassenberg, Max, Koele, & Firme, 2004; Reitman, Hummel, Franz, & Gross, 1998). Also, it has been argued that while externalizing problems are more readily observable because the problem behaviors are directed toward others, internalizing problems are relatively poorly recognized by parents (Bird, Gould, & Staghezza, 1992; Sourander, Helstela, & Helenius, 1999). Parent-report CBCL ratings may not be sensitive to the subclinical positive symptoms, decreased expression and experience of emotion, social isolation, and decreased role functioning that precedes conversion to psychosis. In addition, mentally ill adolescents are likely to influence their family environment, which in turn may have an effect on the parent-report.

Of course, it is important to consider the possibility that the predictive power of the parent-report CBCL will improve when more long-term psychiatric outcome data are obtained and at-risk adolescents move closer to the age of conversion to psychosis. Compared to the mean age of clinical high-risk prodromal samples in other studies (mid to late teens/early twenties) (Yung et al., 2003; Yung, Phillips, Yuen, & McGorry, 2004; Klosterkotter et al., 2001; Woods et al., 2009), the present sample has a younger mean age (M = 14.24 years of age). Thus, adolescents in this study are just entering the highest risk period for onset of psychosis in late adolescence/early adulthood. Support for this possibility is provided by studies showing evidence for increased positive predictive power temporally closer to the onset of psychosis (Rackfield & McGlashan, 2004; Salokangas & McGlashan, 2008).

Although past research has indicated that the behavioral expression of vulnerability to psychosis is characterized by sex differences (Watt, 1978; Walker, Downey, & Bergman, 1989; Olin & Mednick, 1996; Done, Crow, Johnstone, & Sacker, 1994), no significant Conversion Status X Sex interactions were found in this study. The one sex difference observed in the present study is the finding of female at-risk adolescents showing higher scores on the CBCL scale Aggressive Behavior. This runs counter to the higher rate of aggressive behavior in males in the general population. However, the finding is in line with research evidence showing that female sex is a significant predictor of psychosis (McGorry et al., 2002) and may indicate that aggressive behavior is uniquely elevated in prodromal females, although it did not predict conversion in either sex in the present study.
In interpreting the present findings, it should be noted that limited statistical power due to a small sample size reduced the likelihood of detecting a significant difference in CBCL scores. Therefore, the evidence is insufficient to confirm a null finding. Future longitudinal high-risk studies with larger sample sizes may detect CBCL differences between at-risk youth who convert to psychosis and those who do not. Nonetheless, the present results indicate that the effect size for prediction of conversion with the CBCL is likely to be much smaller than that of the SIPS/SOPS prodromal ratings. Therefore, even if a larger sample of at-risk youth yielded a significant difference, it would not necessarily indicate adequate predictive power to justify the adjunctive use of the CBCL in predicting risk for psychosis conversion in clinical high-risk groups. This does not, of course, rule out the potential utility of the CBCL in identifying at-risk youth in the general population. Studies of general population samples may show that the CBCL is capable of differentiating among youth as a function of their risk for subsequent psychosis.

Also, it should be noted that the presence of participants taking psychotropic medications represents a methodological challenge (i.e., at-risk adolescents who manifest the most pronounced behavioral problems prior to baseline would be more likely to receive medications). While the present study was not intended to address questions about medication effects, the findings underscore that medication classes are differentially associated with behavior. Therefore, to better parse out the relationship between behavioral ratings and conversion to psychosis, psychotropic medications should be examined in future research on social and behavioral problems in clinical high-risk samples. In this connection, the inclusion of naturalistically prescribed medication covariates is a relative strength of this study in terms of generalizability of findings to the population of interest. Also, future research with larger samples may benefit from a regression approach, examining incremental improvements in prediction with the inclusion of additional measures. Another valuable approach might be to create positive (e.g., hallucination-like experiences, suspiciousness) and negative (e.g., social withdrawal) symptom domains from the respective CBCL items to determine, if parent-report of these specific constructs can enhance prediction. Finally, some participants in the study were receiving psychotherapy and other clinical care, which may have an impact on social and behavioral characteristics in this clinical high-risk sample.

In summary, the present findings did not provide evidence that a parent-report measure, the CBCL, is capable of differentiating at-risk adolescents who do and do not convert to a psychotic disorder. Thus, it does not appear that the CBCL has a potential clinical and diagnostic utility to serve as an adjunctive screening measure to enhance identification of those at-risk youth most likely to develop a psychotic disorder. Future research is needed to determine whether the CBCL holds promise for the identification of at-risk youth in the general population.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

**Acknowledgments**

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**References**


Figure 1.
SIPS/SOPS Positive Symptoms for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments
Figure 2.  
SIPS/SOPS Negative Symptoms for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments
Figure 3.
SIPS/SOPS Disorganization Symptoms for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments
Figure 4.
SIPS/SOPS General Symptoms for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments
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Figure 6.
CBCL Total Competence for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments
Figure 7.
CBCL Internalizing Problems and Externalizing Problems for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments
Table 1

<table>
<thead>
<tr>
<th></th>
<th>Converted</th>
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</tr>
<tr>
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<tr>
<td>Females</td>
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<td>(SD)</td>
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<td>(1.79)</td>
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Table 2
Mean Scores and Standard Deviations for Prodromal Symptoms for Converted and Non-Converted Adolescents at Baseline and at One Year Follow-Up Assessments

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<td>Positive</td>
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<td>2.45 (.94)</td>
<td>.39</td>
<td>36</td>
<td>.553</td>
<td>2.60 (.87)</td>
<td>1.48 (.91)</td>
<td>9.91</td>
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<td>Group Differences</td>
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<td>43.69 (7.74)</td>
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<td>37.69 (8.35)</td>
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<td>72.58 (10.17)</td>
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<td>64.17 (9.02)</td>
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<td>67.38 (12.58)</td>
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<td>59.75 (13.52)</td>
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<td>69.85 (8.25)</td>
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<td>63.58 (8.86)</td>
<td>65.19 (10.56)</td>
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<td>67.96 (8.31)</td>
<td>n.s.</td>
<td>62.92 (10.22)</td>
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<td>61.85 (8.55)</td>
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<td>62.67 (9.28)</td>
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<td>68.12 (13.23)</td>
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<td>60.92 (9.75)</td>
<td>65.00 (11.59)</td>
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▲ Note: high scores indicate more social competencies
Table 4

Intercorrelations between Prodromal Symptoms and CBCL Individual Scales at Baseline and at One Year Follow-Up Assessments

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**p ≤ .01
*p ≤ .05