Prevalence of psychiatric illness in childhood-onset schizophrenia subjects

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Abstract

Childhood-onset schizophrenia (COS) refers to schizophrenia with onset of psychotic symptoms prior to a child’s 13th birthday. Optimal treatment likely includes family-based services supplementing antipsychotic pharmacotherapy. However, family-based services can require adjustment based on parental psychopathology; there has been little literature exploring the frequency or type of psychopathology seen in parents of COS cases. This report includes the results of a structured psychiatric evaluation on 80 parents of a COS case with comparison to a sample of 304 parents. Having a child with psychosis and being of minority racial/ethnicity status increased risk for psychiatric illness. Psychotic disorders (15% vs. 5%), mood disorders (54% vs. 27%), anxiety disorders (30% vs. 18%), and substance use disorders (49% vs. 31%) were all increased in the parents with a psychotic child. Psychiatric illness is common in parents of a child with COS and will need to be considered as family-based services for COS are developed.

Introduction

Childhood-onset Schizophrenia (COS) is defined by the same Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria as its adult counterpart, differentiated only by onset prior to a child’s 13th birthday.1 COS can be reliably diagnosed using a variety of semi-structured interviews, including the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Versions, when administered by a trained clinician.2 COS remains a rare condition occurring at about 1/50th of the rate of adult-onset schizophrenia. However, studies in comparative neuropsychiatry,3 physiology,4 neuroimaging,5 genetics,6 and neuroanatomy,7 have shown COS to be predictive of and continuous with adult schizophrenia spectrum disorders. COS may indeed present a more severe form of schizophrenia with a more debilitating course,8,9 making early treatment interventions a priority.10 Studies in children and adolescents diagnosed with other neuropsychiatric illnesses, such as major depression and bipolar mood disorder, have begun to look at rates of parental mental illness and its potential effects on treatment.11–13 For example, treatment models that utilize family focused therapy in conjunction with other modalities have recently been found to be effective in treating bipolar youth and their families.14 Such treatment modalities require the participation of either a well-functioning family or identification of parental psychopathology with relevant interventions to improve the day-to-day function especially in the domains of communication, social function, and parenting skills.15 For COS, antipsychotic pharmacology has been the primary treatment modality; however, there is also a more recent move to incorporate wrap-around models of family psycho-social interventions with intensive family case management and multi-systemic therapy models.16,17 However, the function of a COS-affected child’s family, the role of parental psychiatric illness, and their resulting implications on more comprehensive treatment models that require family participation are not well-studied or understood. Adoption studies have found that families with significant levels of dysfunction tend to lead to a poorer prognosis in children who are already genetically susceptible to though not yet diagnosed with schizophrenia.18 While the link between family dysfunction and mental illness has not been made in the family functioning scale utilized by Tienari et al.,19 many of the scale’s domains overlap with common clinical characteristics of a variety of Axis I mental illnesses. It would be reasonable to consider that the Axis I diagnoses of members of a family of a COS-child affects the child’s treatment and long term prognosis. Previous studies that examine parental phenotypes of COS children have tended to approach the topic from a genetic or inheritability standpoint and rarely look beyond psychotic diagnoses or physiological findings in first-degree relatives.19

This study takes the first steps in developing a more complete picture of the family functioning of COS-affected children by examining the frequency of a variety of Axis I psychiatric illnesses present amongst the parental caretakers of COS-affected children compared to the frequencies in parents in a normal population sample. It is hoped that such information will contribute to a better understanding of the nature and extent of psychiatric interventions needed to optimize comprehensive treatment plans for schizophrenic children.

Materials and Methods

Participants

The Colorado Childhood-onset Schizophrenia Research Program recruits children with childhood-onset schizophrenia and their families for research into physiological correlates, genetics, and treatment of COS children. These children are referred by community providers who have already identified potential warning signs of schizophrenia in these children. At the time of this study, approximately 134 children had been recruited and screened, 89 of whom met DSM-IV criteria for schizophrenia or schizoaffective disorder and were either under 13 years of age at the time this diagnosis was made or had met the criteria before age 13 based on history provided by their parents and/or mental health providers. The biologic parents of all the referred children, regardless of their child’s ultimate diagnosis, were asked to participate in additional screening measures as to their own mental health history. Eighty parents, representing 50 families, completed a diagnostic interview (Figure 1). Parent participants were also the primary caretakers of the children in all cases in this study. The mean age of the participating parents of COS-affected children is
39.6±7.6 years. Of the 80 participating parents, 86% were Caucasian non-Hispanic, 6% were Hispanic, 4% were African American, and 4% were of other or unknown ethnicity. A comparison group of 161 new mothers and 143 new fathers were recruited from a major metropolitan birth registry. Only parents age 24 years or older were included in this study to compensate for the fact that all COS-parents were at least 24 years of age. Individuals with minority ethnicity or lower socio-economic status are least likely to participate in research studies. Over-recruitment from zip codes with higher percentages of minority and low socio-economic status resulted in a participating sample reflective of the general population. The demographic composition of the 304 control parents was 71% Caucasian non-Hispanic, 18% Hispanic or Latino, 3.6% African American and 6.6% mixed, unknown, or other ethnicity. Demographic information is summarized in Table 1. All child probands provided assent and all parents provided consent as monitored by a local Institutional Review Board.

Diagnostic procedure

Diagnoses of COS were best-estimate DSM-IV diagnoses based on both the parental and the child versions of the Kiddie Schedule for Affective Disorders and Schizophrenia- Present and Lifetime Versions administered by experienced clinicians with advanced degrees (M.S.W., D.O., and M.D.), and, when available, medical records and/or discussion with referring clinicians. A robust effort was made to separate primary psychotic symptoms from post-traumatic symptoms, and notable trauma was rare in COS diagnosed subjects. Children who were ultimately diagnosed with schizophrenia or schizoaffective disorder were held to the strict DSM-IV criteria that the perceptual distortion must occur throughout the day for several days or several times a week for several weeks and not just limited to a few brief moments or the nature of their delusions to be so bizarre as to be distressful and far from the spectrum of normal childhood fantasy. The members of all COS families were then asked to participate in further structured interviews and diagnosed for Axis I psychiatric illness again based on DSM-IV criteria, this time using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) administered by trained clinicians.20 The SCID-I provides for high inter-rater reliability and diagnostic accuracy, particularly when performed by trained clinicians.21 Likewise, the 304 control group participants were also interviewed with the SCID-I for Axis I diagnoses based on DSM-IV criteria. As the best predictor of future psychiatric illness is a history of psychiatric illness, an individual was assigned a diagnosis if they had ever met criteria for that diagnosis (lifetime diagnoses). Diagnoses were non-hierarchically assigned and were best estimate diagnoses based on the results of structured interviews.

Data analysis

Treatment service needs for children may depend on the presence of any parental psychopathology. The presence or absence of psychosis in their child was used, along with potential confounding variables of parental age, gender, and race/ethnicity in a step-wise regression. If parental psychiatric illness is present, treatment service needs may vary dependent on which illness the parent has (e.g. a family with a parent with a substance use disorder may have different treatment needs that a family with a parent with a primary mood disorder). Because many psychiatric disorders occur at low rates even in non-vulnerable populations, diagnoses were collapsed into 4 categories: mood disorders (which did not include schizoaffective disorder), psychotic disorders (which did include schizoaffective disorder), substance use disorders, and anxiety disorders. The presence or absence of psychosis in their child was used, along with potential confounding variables of parental age, gender, and race/ethnicity in a step-wise linear regression for each of these diagnostic categories. Treatment service needs may also vary with degree of comorbidity. The number of diagnostic categories in which a subject met diagnostic criteria was utilized as rough assessment of comorbidity.

Finally, differences in frequencies of specific Axis I diagnoses between parents with a child with schizophrenia and a comparison group were examined. The absolute number of parents diagnosed with any particular Axis I diagnosis was predicted to be low for many illnesses and differences between groups may be difficult to detect; thus, this last analysis was exploratory. A Fischer’s Exact test between parents with and without a child with schizophrenia was done separately for each gender.

Results

The most common age range for childhood-onset children to enroll in this project is 7-10 years of age. Consistent with this finding, both fathers (42.5 years vs. 33.5 years, t=6.9, P<0.001) and mothers (37.8 years vs. 31.8 years, t=6.9, P<0.001) of a child with childhood-onset schizophrenia were 6-to-9 years older than their control counterparts who were parents of a newborn infant. The parents of a child with schizophrenia were more likely to be of majority racial/ethnic status (86.3% Caucasian Non-Hispanic vs. 71.4% Caucasian Non-Hispanic).

Subjects referred with possible psychotic symptoms n=134

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Subjects with COS Schizophrenia or Schizoaffective Disorder n=89

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Schizophrenic COS Subjects with One or Both Parents Interviewed n=50

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Schizophrenic COS Subjects’ Total Parents Interviewed n=80

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Mothers interviewed n=48

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Fathers Interviewed n=32

Figure 1. Breakdown of participants. COS, childhood onset schizophrenia.

Table 1. Demographic comparison of parents of childhood-onset schizophrenia-group and parents in Control Group.

<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>Control parents</th>
<th>COS parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age + standard deviation (years)</td>
<td>33±6</td>
<td>40±8</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian Non-Hispanic</td>
<td>217</td>
<td>71.4%</td>
</tr>
<tr>
<td>Other Race/Ethnicity</td>
<td>87</td>
<td>28.6%</td>
</tr>
</tbody>
</table>

COS, childhood onset schizophrenia.
sian non-Hispanic compared to 71.4% of the comparison group; Fischer’s exact = 0.006). Of the 80 parents of a child with schizophrenia, 57 (71%) have at least one Axis I diagnosis, compared to 153 of the 304 (50%) comparison parents. A linear regression identified racial/ethnicity minority status (β=0.34; P<0.001) and having a child with schizophrenia (β=0.16; P=0.001) as predictors of increased risk for an Axis I diagnosis. Rates of psychotic disorders (15% vs. 5%), mood disorders (54% vs. 27%), anxiety disorders (30% vs. 18%), and substance use disorders (49% vs. 31%) are higher in COS-parents than in comparison parents. A linear regression identified racial/ethnicity minority status and having a child with schizophrenia as significant predictors of greater risk in the parents for a mood disorder, an anxiety disorder, and a substance use disorder. Only having a child with schizophrenia was predictive of greater risk of the parent having a psychotic disorder. In a similar fashion, racial/ethnicity minority status and having a child with schizophrenia were predictive of meeting criteria for illness across categories. Parents with a child with schizophrenia met criteria for illness in an average of 1.6±1.3 categories versus 0.8±0.9 categories for parents in the comparison group. Parent age and parent gender were not significant predictors in any analysis.

The sample size was not large enough to justify statistical analysis on each specific diagnosis, but the rates of specific illnesses are presented in Figure 2. When broken down by gender, COS mothers tend to have higher categorical rates of psychotic disorders (17% vs. 5%), mood disorders (63% vs. 33%), and substance use disorders (44% vs. 26%) than the comparison group (Figure 3). COS-mothers also tend to meet DSM-IV criteria in more diagnostic categories. Sixty-seven percent of COS mothers had one or more categorical (psychotic, mood, substance, anxiety) Axis I diagnoses compared to 53% of control group mothers (Figure 4). Fathers of COS children have a higher categorical rate of mood disorders (41% vs. 16%) than their gender matched comparison group (Figure 5). COS-fathers also tend to meet DSM-IV criteria in more diagnostic categories. Seventy-eight percent of COS fathers had one or more categorical (psychotic, mood, substance, anxiety) Axis I diagnoses compared to 47% of control group fathers (Figure 6). Of the 31 COS children with both parents interviewed, 29 (94%) had at least one parent with a lifetime Axis I diagnosis; 17 (55%) had both parents affected.

**Discussion**

Fifty percent (50%) of the population-based
conclusion group of parents has a lifetime history of at least one Axis I diagnosis, consistent with what has been found in population surveys. Twenty-one (71%) percent of the parents of COS-children have a lifetime history of at least one Axis I diagnosis, a rate significantly higher than the comparison group.

Similar to previous work, psychic disorders are significantly more common in the parents of children with schizophrenia than they are in our comparison group (15% vs 5%). The increase in psychotic illness was significantly elevated in mothers (17% vs 5%, Fischer exact P<0.02), with a suggestion of a similar effect in fathers (13% vs 4%, P<0.07). Psychic relatives tend to under-participate in family studies of adults with schizophrenia, leading to underestimates of family member psychosis rates. This pattern may hold true for family members with severe non-psychotic illness as well. Amongst a theoretical potential of 178 biologic parents of the 89 COS children in our sample population, 80 parents and only 32 of them fathers, completed the SCID interview and assessment. It seems reasonable to suggest that parental mental illness rates affected the COS-parents participation, with less ill individuals being able to complete the SCID interview and assessment while the more ill parents would be lost to follow up. For fathers, this effect seems particularly noticeable and may partially explain the failure to find significantly increased psychosis rates in our paternal sample.

While previous studies have noted increased rates of psychotic illness in parents of COS-children, they were not designed to identify other Axis I illnesses. In general, depressive disorders and substance use disorders are the most prevalent Axis I diagnoses in parents of COS children, accounting for much of the pathology and much of the difference in rates of pathology relative to the comparison sample. Stress increases the frequency of both depressive disorders and substance use disorders. Having a child with a severe psychiatric illness is a major stress, thus it is unclear if the increased frequencies of depressive and substance use disorders in these parents are the result of having a child with psychosis, or whether they share risk factors with childhood psychosis. Another limitation is that the study was originally focused on genetic risk factors. The diagnostic interviews focused on lifetime diagnoses; current and resolved mental illness as a frequent component of their life or have at some point during their child’s illness.

### Conclusions

Previous studies of children and adolescents with bipolar disorder have demonstrated that prognosis closely correlates with measures of family functioning in areas of communication, expressed emotion, contingency planning, and psychoeducation. In turn, family functioning in these areas and others are likely influenced by parental as well as child mental illness. Of the COS children who had both parents participate (n=31), 94% had at least one parent with a lifetime Axis I diagnosis, and 55% had both parents with an Axis I diagnosis. Because of the ascertainment biases noted above, these frequencies are likely underestimates of the true COS-parental mental illness rates. Future areas of research may expand upon these findings to explore how parental illness affects family functioning and, in turn, how this affects COS patient’s prognosis, treatment adherence, treatment effectiveness, and outcome. Treatment modalities that rely on interventional with the entire family in a wrap-around, multi-systemic model need to incorporate comprehensive psychiatric evaluation and treatment of parents and caregivers.

### References

14. Miklowitz DJ, Otto MW, Frank E, et al. Intensive psychosocial intervention enhances functioning in patients with...


