Creating School-Age Versions of Semistructured Interviews for the Prodrome to Schizophrenia: Lessons From Case Reviews

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Abstract

There is an increasing emphasis on identifying individuals with schizophrenia earlier and earlier in their disease process, with the assumption that earlier identification translates into earlier treatment, which translates into improved outcome. Unfortunately, one age cohort, children under 13 years of age, have been excluded from this critical alteration in clinical intervention strategy, and its associated improved clinical outcome. One of the barriers to inclusion of younger children is the lack of knowledge about diagnostic issues related to attenuated psychotic symptoms in this age sample. This report focuses on our experience with evaluating attenuated psychotic symptoms in young children, in particular subthreshold hallucinations and delusions, using semistructured interviews. The inclusion of both Caregiver and Child report sections and the addition of concrete, detailed examples of clear conscience, non-stress-related subthreshold psychotic symptoms are likely to be necessary.

Keywords: childhood-onset schizophrenia, prodrome, diagnostic interviews.


Introduction

Schizophrenia is generally characterized as a neurodevelopmental disorder, in which the full clinical syndrome is assumed to be the result of abnormal alterations in brain development, perhaps years before the onset of the full clinical disorder (Weinberger 1987). This neurodevelopmental hypothesis has an important corollary; specifically, the earlier in the disease process treatment begins, the more likely the intervention is to stabilize or even normalize brain development, and therefore the greater the benefit of treatment. Although far from conclusive, a review of the available evidence supports that the earlier treatment begins after onset of the full clinical disorder, the better the long-term outcome (Wyatt and Henter 2001).

The past several years have seen a concerted effort to extend these clinical findings by initiating antipsychotic treatment even before the full clinical disorder is present. For schizophrenia, and other psychotic disorders such as bipolar mood disorder with psychotic features, the full clinical syndrome is often preceded by a period of subthreshold psychosis and thought disorder, termed the prodrome or at-risk mental state. A major advance in recent years is the development of structured diagnostic interviews, such as the Comprehensive Assessment of At Risk Mental States (CAARMS; Phillips et al. 2000) and the Structured Interview for Prodromal Syndromes (SIPS; Miller et al. 2002), to identify individuals in the late prodromal period. These interviews identify a group of ultra–high-risk subjects, where 41 to 54 percent convert to an Axis I psychosis within the following 12 months (Miller et al. 2002; Phillips et al. 2000). In an attempt to decrease the duration of untreated psychosis and improve long-term outcome (McGorry 2000), a number of double-blind treatment trials during the prodromal period are underway. Early results (McGorry et al. 2002) support the value of a 6-month antipsychotic regimen in decreasing conversion to psychosis over a 1-year period, although it remains to be seen if the improvement in outcome continues with longer followup.

The most common ages of onset for psychosis, and in particular schizophrenic psychosis, are late adolescence and early adulthood. Research protocols have generally focused on these ages of highest risk and have thus limited participation to subjects 12 years of age and older. Childhood-onset psychosis has been described in children as young as 4 years of age (Russell 1994; Spencer and Campbell 1994). Childhood-onset schizophrenia is similar to adolescent- and adult-onset forms of the disorder (Nicol-
son et al. 2000), with the prepsychotic phases of childhood-onset schizophrenia associated with significant impairment, psychiatric care, and pharmacological interventions (Alaghband-Rad et al. 1995; Schaeffer and Ross 2002). Although rare, childhood-onset psychosis is often more severe than adolescent- and adult-onset psychosis (Beitchman 1985; Alaghband-Rad et al. 1995) and creates a significant burden for affected children and their families. The ethical implications of treating false positives requires constant review of treatment trials; however, if a school-age prodrome has the high levels of current morbidity seen in adolescent patients (Peda et al. 2002), then involvement in treatment trials of school-age children vulnerable to psychosis may be warranted.

One of the factors hampering school-age enrollment in prodromal studies is the unknown applicability of relevant semistructured interviews to this age group. The prodromal period is identified in adolescents and young adults by (a) the onset of attenuated (either lower frequency or lower severity) positive symptoms or (b) an increase in general psychopathology in a genetically vulnerable individual. When considering the application of these criteria to school-age populations, at least three concerns can be raised: (1) children will be uncomfortable talking with unknown adults and thus will under-report; (2) children will both under-report (because they don’t understand the questions) and over-report (because they have difficulty separating real from nonreal), leading to higher levels of both false negatives and false positives; and (3) the types and pattern of symptoms will vary with age, and combinations of symptoms used to identify adolescents and adults as prodromal will not be applicable to school-age children. The purpose of this report is to use case examples to illustrate these issues, so that empirical studies can be designed.

Subject Pool

The Colorado Childhood-Onset Schizophrenia Research Program began in 1994 and was expanded to become the Colorado Childhood-Onset Psychosis Research Program in 1998. The Program is focused on genetic etiology (Buervenich et al. 2000; Leonard et al. 2002), physiological correlates (Ross et al. 1999; Ross 2003), developmental phenomenology (Ross and Compagnon 2001; Schaeffer and Ross 2002), and treatment (Schaeffer and Ross 2002) of children, ages 12 years and younger, with and vulnerable to psychosis. Children are referred to the Program because either (a) the treating clinician believes the child has a psychotic illness or (b) the child has a 1st degree relative with psychosis. The former group has a 4:1 male to female ratio; the latter group consists of approximately equal numbers of each gender. The average age of children referred to the program is 10 years of age, although children as young as 3 years of age have been evaluated. All children referred to the program are diagnosed using DSM–IV (American Psychiatric Association 1994) criteria, using a structured diagnostic interview (Kaufman et al. 1997). All children involved in the program have received the parent and child versions of the Kiddie-SADS-PL, although for children younger than 8 years of age, the child interview is limited to affective and psychotic symptomology. Over the last 6 months we have piloted the inclusion of a modified Comprehensive Assessment of At-Risk Mental States (Phillips et al. 2000) in the assessment battery (n = 8 subjects to date). Semistructured interviews are completed by experienced research clinicians with advanced degrees (M.S.W., D.O., or M.D.), and medical records are reviewed. Final diagnosis is a consensus diagnosis from the research team. Age at onset of symptoms is based on parental recall and review of medical records. All children given an Axis I diagnosis of a psychotic disorder are assessed using high-resolution cytogenetic screening and fluorescent in situ hybridization (FISH) for 22q11 deletion. To date, one child diagnosed with schizophrenia had abnormalities on high-resolution cytogenetic screening (a mosaic deletion distal to 16q22), and no child had 22q11 deletions.

This Program has developed into the regional referral center for childhood psychosis for the state of Colorado and portions of surrounding states. Over the past 8 years, we have completed structured interviews on approximately 130 subjects 12 years of age and younger, who were referred as children with or vulnerable to psychosis. Approximately 45 percent met diagnostic criteria for an Axis I psychotic disorder: schizophrenia, schizoaffective, bipolar mood disorder with psychosis, or major depression with psychosis. We take extensive effort to differentiate psychosis associated with post-traumatic stress disorder (PTSD) as a separate category, and only 5 to7 percent of our subjects given an Axis I psychotic disorder have a history of significant trauma.

Issue 1: Children Are Uncomfortable Talking With Unknown Adults and Thus Will Under-Report

Case A. This 5-year-old male is the offspring of a mother with bipolar-I disorder. He has a 2 1/2-year history of unusual behavior, including inserting foreign objects in his rectum, ingesting dirt, stabbing the family dog, and killing the pet hamster, as well as unprovoked frequent aggression. Child A has threatened his siblings with scissors, threatened his mother with a knife, and described, in detail, his plans for murdering his brother with a gun. There was a 1-month history of irritability and lethargy, but no sleep or appetite changes nor pressured speech. On Mental Status Exam, Child A was a cheerful young school-age child with good eye-contact, age-appropriate vocabulary, and bright but anxious affect. Affect and eye
contact remained cheerful and positive while Child A discussed his plans to murder his brother.

Direct questioning of Child A for psychotic symptoms produced responses that were not clearly psychotic. The majority of questions concerning the presence of positive symptoms from the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) received either a shrug of the shoulders, an initial response of “I don’t know,” or a disorganized response that related little to the question being asked. Conversely, when Child A’s mother was interviewed, she repeated a number of psychotic symptoms that Child A had repeatedly demonstrated across settings, including command auditory hallucinations to kill himself and his peers. At these times, he got mad and hit his mother if she said she couldn’t hear the voices. Child A had informed his mother of visual hallucinations where, when alone in the middle of a field, he would start trying to swing at “children that are trying to hit me.” Child A also reported to his mother grandiose delusions such as that “he can get the signal to change from red to green just by thinking it.” When these specific examples were repeated to Child A, he endorsed them.

Case B. Child B is an 8-year-old male, adopted at birth, who had been diagnosed with attention deficit hyperactivity disorder (ADHD) and dyslexia at the age of 6 and came to the clinic because of ineffectiveness of methylphenidate in reducing his symptoms. IQ is in the low normal range. He has been expelled from a succession of schools because of oppositional behavior, primarily refusing to do any schoolwork. Child B had ongoing difficulties with sustaining attention, was easily distracted, had difficulties with staying in his seat, showed impulsivity, made frequent careless mistakes, had difficulty listening to directions, and was forgetful in daily activities. In addition, Child B is notable for high levels of anxiety, with frequent concerns about whether he will arrive at places on time, and fears that his mother’s plane will crash anytime she travels. Child B’s behavior was much calmer when within eyeshot of his mother. There were no reports of trauma, or symptoms consistent with PTSD, depression, or mania. When questioned about psychotic symptoms, Child B’s parents reported that, at 4 years of age, he would complain of being afraid of ghosts, but that that had not occurred since that time. Since then there had been no history of hallucinations or delusions. In contrast, Child B provided a rich, and consistent over time, description of the ghosts that he saw “most of the time,” including during the interview. The ghosts had “red eyes,” could only be seen by him, and served to protect him from other individuals. The ghosts controlled and guided his behavior, were responsible for all “nice” behaviors by Child B, and provided him with answers to his homework. Child B frequently felt “things walking on me,” which he attributed to a variety of secret animals from a “private pet shop.” [Child B has no pets]. Child B believes that older students at school are constantly staring at and talking about him, and planning to kill him. Affect was flat, eye contact was intermittent, and Child B intermittently put his hands in his pants to masturbate throughout the exam.

Comment on Cases A and B. Many young children have difficulty conversing with unknown adults (strangers) and have difficulty with self-recognition of behavior as different from peers or outside of accepted norms. Information obtained directly from Child A would not have suggested a psychotic illness. In contrast, inclusion of a parental interview provided clear evidence supporting the diagnosis of a DSM-IV Axis I psychotic disorder. Most diagnostic interviews of younger children require parental report, and interviews for prodromal symptoms should follow this model. In our setting, with children under 12 years of age, parents are always interviewed before the children.

While Case A was notable for the importance of parental report in symptom extraction, Case B is an example of the importance of direct child interview. An interview with the parents alone would have led to a diagnosis of ADHD and generalized anxiety disorder, while inclusion of child report led to a diagnosis of schizophrenia. Jensen and colleagues (Jensen et al. 1999) have stressed the general value in most childhood psychiatric disorders of utilizing the “either/or” criteria in childhood assessment. Specifically, if either the child or the caregiver endorses a symptom, it should be considered as present, although the reliability of the responses should also be considered. Because of the rarity of childhood psychosis, the work of Jensen et al. did not specifically address psychotic symptoms; however, as illustrated by Children A and B, both child and caregiver interviews are necessary in evaluation of psychosis. Although symptoms endorsed by the child should be discussed with the caregivers to rule out alternative explanations, the either/or criteria should, in general, be extended to this diagnostic group.

Issue 2. Children Will Both Under-Report (because they don’t understand the questions) and Over-Report (because they have difficulty separating real from non-real), Leading to Higher Levels of Both False Negatives and False Positive Cases

Case C. The mother of this 8-year-old female reported that this child began, at age 4 years, to describe unusual experiences, like seeing a jaguar run next to the car (age 4), seeing colored spots in the air (age 6), or see-
ing big green worms (age 7). Child C also had, for several years, intermittently complained that adults in public places were watching her and insisted on wearing a box over her head for entire trips to the grocery store. In direct questioning of Child C, her responses to standard psychosis interview questions, such as “Do you hear voices that other people don’t hear?” or “Do you see things that other people don’t see?” were almost universally responded to in the negative. However, when specific examples were given, they were more likely to elicit positive responses. For example, “Have you ever heard people talking and looked around and nobody was there?” resulted in Child C discussing a woman’s voice calling her in the grocery store, or “Have you ever seen a ghost?” resulted in discussion of disembodied hands that follow her. Positive response content to psychosis questions, whether maternal or Child C report, were notable for a consistent pattern of low frequency events, occurring a few times per month or less.

**Case D.** Child D is a 7-year-old male who has been followed longitudinally in our Program, receiving structured diagnostic interviews at 4 years, 5 years, and 7 years of age. He is the offspring of a father who has schizoaffective disorder. Child D was exposed to domestic violence in the first 6 months of life and reportedly was shaken once at age 6 months. There has been no contact with the biological father since 6 months of age, and no history of notable trauma since that age. At all three time points, attention and impulsivity have been identified as concerning symptoms. Both Child D and his mother have denied, at all three time points, any symptoms consistent with anxiety disorders (including PTSD), mood disorders, or psychosis. While Child D appeared to understand and respond appropriately to aggression and depression questions, the direct questioning of Child D concerning psychotic symptoms was more problematic. Frequently, Child D would respond affirmatively to general questions concerning psychotic symptoms; however, a quizzical facial expression or an unusual response suggested incomplete understanding of the expression. For example, when asked if he ever heard or saw anyone talking to him that no one else could see or hear, he responded “Yes”; additional requests for clarification elicited “I hear your voice and I see you too.” Despite the problems with Child D’s comprehension of general psychotic questions, concrete examples, such as those described for Child C, were generally understood and associated with a negative response.

**Comment on Cases C and D.** Two of the three clusters of symptoms generally included in prodromal diagnostic schemas are based primarily on the presence of subthreshold positive symptoms (e.g., where hallucinations and/or delusions are present but are either not severe enough or not present often enough to meet diagnostic threshold). Thus, if prodromal schemas are to be applicable to school-age populations, subthreshold positive symptoms must be distinguishable from other forms of school-age hallucinations. Children have incomplete development of cognition, emotional understanding, social interpretation, and verbal skills and may be at risk of both under-reporting true prodromal symptoms as well as over-reporting normal phenomena such as imaginary companions or hypnagogic hallucinations (see Egdell and Kolvin 1972 for a review). Supporting the latter concern, hallucinations have been reported in 1 percent of outpatient (Garralda 1984a) and 5 percent of inpatient (Egdell and Kolvin 1972) child-psychiatry populations, while longitudinal follow up suggests that conversion to a psychotic illness in children with hallucinations is no greater than the general population (Garralda 1984b).

Breslau (1987) has suggested that the validity of positive psychotic symptoms can dramatically be improved with longer, more concrete questions. Children C and D provide examples of this phenomenon. Children with more severe psychosis, like Child B, respond affirmatively to psychosis questions even in the absence of specific examples, even if they have never been psychiatrically interviewed before. However, for Child C, where psychotic symptoms are subthreshold for a psychotic diagnosis, concrete examples of psychotic symptoms improved detection. Especially for children who may in the prodromal period, where psychotic symptoms are of lower severity, frequency, and duration, utilizing specific examples of each type of psychotic symptom may be necessary to elicit positive responses. This is true for children under 10 years of age and particularly true for children under 8 years of age. For children who have not themselves experienced psychotic symptoms, like Child D, there is an even greater difficulty comprehending psychosis questions. While general questions can lead to false positive responses, detailed concrete examples may improve comprehension and minimize false positives. Examples likely should also include a description of clear consciousness and presence of symptoms unrelated to acute stressors (Egdell and Kolvin 1972) and determine that the child believes that the hallucinations or delusions are held with at least reasonable conviction (Yung et al. 2003). There is a theoretical possibility that repetition of a number of concrete examples provided by the examiner might suggest that this is what the examiner wants to hear, resulting in over-reporting by non-psychotic children for secondary gain. Our experience with children below 12 years of age suggests that the frequency of this event is low, even with children who come from a family with psychosis.
Issue 3: The Types and Pattern of Symptoms Will Vary With Age and Combinations of Symptoms Used to Identify Adolescents and Adults as Prodromal Will Not Be Applicable to School-Age Children

Continuation of Case C. As discussed above, this 8-year-old female endorsed hallucinations and delusions, but only for short durations a few times each month. This child and parent were re-interviewed 4 months after the initial interview. Both parent and child gave a history of more frequent and severe psychotic symptoms. This increase in the pervasiveness of the psychotic symptoms was associated with greater capacity by Child C to endorse psychotic symptoms in response to a more general psychosis question.

Case E. Child E was first evaluated as a 10-year-old male while living with his maternal grandmother; both Child E’s mother and 12-year-old brother had schizophrenia. Child D had mildly delayed speech and motor milestones as an infant, met criteria for ADHD by 5 years of age, and, since the age of 7 years, “worries about everything,” including future performance and what others think of his behavior. There was no known history of trauma; care by the maternal grandmother was initiated at birth. Child E was brought in for evaluation because he had on three occasions, without obvious provocation, screamed and ran around the house frightened, believing a stranger was in the house trying to hurt him. Two of these events occurred waking up from a sound sleep in the middle of the night, one occurred during daylight hours. Child E reported a single episode of hearing voices for a few hours but being unable to make out what they said. Child E believed the voices must be his imagination playing tricks on him. No other hallucinatory or delusional symptoms were endorsed. No mood symptoms or substance use were present.

Over the following two months, Child E developed a case of severe trichotillomania and intermittent irritability. Six months after that, Child E heard multiple male voices conversing frequently, disrupting attention and thought processes, with the experiences associated with screaming, hiding under his desk, and running out of the classroom.

Comment on Cases C and E. Child C demonstrates the prospective 4-month progression from subthreshold to super-threshold psychosis consistent with what we have retrospectively reported for the prodromal period in school-age psychosis (Schaeffer and Ross 2002) and is similar to prospective reports in adolescent and older subjects (Rosen et al. 2002). Child E presents an alternative cluster of prodromal symptoms. While clear sub-threshold psychosis could not be established, a rapid increase in general psychopathology in a genetically vulnerable individual was followed by onset of super-threshold psychotic symptoms, consistent with one of the proposed adolescent presentations (Phillips et al. 2002). In at least some cases of school-age psychosis, onset is preceded by a prodromal period with symptomatic presentation similar to that identified for adolescents and adults.

Discussion

Most psychiatric disorders—including ADHD, depression, and psychosis—occur across the lifespan, from early school-age years to later adulthood. For many psychiatric disorders, symptom presentation is sufficiently similar in children, adolescents, and adults that the same or very similar diagnostic criteria can be used over almost the entire lifespan (American Psychiatric Association 1994). Empirical studies are necessary to establish if this pattern holds for the prodrome to psychosis diagnostic category. However, case review suggests that prodromal symptoms can be sensitively elicited in school-age children.

Despite the similarities across ages for symptom presentation in many neuropsychiatric disorders, the relationship between age and response to treatment is often more unpredictable. While treatment response to stimulants is remarkably similar in children, adolescents, and adults with ADHD, the effect of age on response to antidepressants in depression is more complex. Thus, it is inappropriate to assume that treatment trials in adolescents and adults can inherently be extended to younger children without empirical evidence. If treatment for neuropsychiatric disorders in children is to be empirically based, it is critical that children be included in treatment trials. However, to be included in treatment trials, age-appropriate diagnostic tools must be available. For identifying school-age children with the prodrome to psychosis, we suggest modification of current diagnostic tools, such as the CAARMS and SIPS. Initial modifications should include a more extensive list of example psychotic symptoms, which are detailed, concrete, which occur independent of acute stressors, and which occur during clear consciousness. In addition, the diagnostic tools should include both child and caregiver interviews. The either/or strategy for symptom assessment has proved useful in younger children for other symptom domains. Thus, for each symptom, the worst severity reported by either source should be considered as the severity level of record.

References


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