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Frequency and pattern of childhood symptom onset reported by first episode schizophrenia and clinical high risk youth

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ABSTRACT

Background: Psychosis prevention and early intervention efforts in schizophrenia have focused increasingly on sub-threshold psychotic symptoms in adolescents and young adults. Although many youth report symptom onset prior to adolescence, the childhood incidence of prodromal-level symptoms in those with schizophrenia or related psychoses is largely unknown.
Methods: This study reports on the retrospective recall of prodromal-level symptoms from 40 participants in a first-episode of schizophrenia (FES) and 40 participants at "clinical high risk" (CHR) for psychosis. Onset of positive and non-specific symptoms was captured using the Structured Interview for Prodromal Syndromes. Frequencies are reported according to onset during childhood (prior to age 13), adolescence (13–17), or adulthood (18+).
Results: Childhood-onset of attenuated psychotic symptoms was not rare. At least 11% of FES and 23% of CHR reported specific recall of childhood-onset of unusual or delusional ideas, suspiciousness, or perceptual abnormalities. Most recalled experiencing non-specific symptoms prior to positive symptoms. CHR and FES did not differ significantly in the timing of positive and non-specific symptom onset. Other than being younger at assessment, those with childhood onset did not differ demographically from those with later onset.
Conclusion: Childhood-onset of initial psychotic-like symptoms may be more common than previous research has suggested. Improved characterization of these symptoms and a focus on their predictive value for subsequent schizophrenia and other major psychoses are needed to facilitate screening of children presenting with attenuated psychotic symptoms. Accurate detection of prodromal symptoms in children might facilitate even earlier intervention and the potential to alter pre-illness trajectories.

1. Introduction

Schizophrenia and related psychotic disorders are serious disorders that can lead to long-term disability, particularly if untreated (Keshavan et al., 2003; Marshall et al., 2005; Frazier et al., 2007). Over the past 50 years, significant research effort has focused on the early detection of emerging psychosis in order to facilitate the identification of etiological mechanisms and earlier intervention. The examination of familial risk, based on presumed genetic contribution to psychotic disorders and accompanying neurodevelopmental markers, has made important progress (Keshavan et al., 2005). In recent years, efforts have expanded to consider clinical and behavioral high risk as well as familial risk, determined through symptom-based screening instruments such as the Structured Interview for Prodromal Syndromes (SIPS, Miller et al., 1999; McGlashan et al., 2001). These instruments query the onset and severity of newly emerging or worsening

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symptoms that may suggest a possible prodrome to, or more conservatively "clinical high risk" (CHR) for, a psychotic disorder.

Most primary psychotic disorders onset in late adolescence and early adulthood, with peak onset between ages 15 to 25 in males and 20 to 29 in females (Castle et al., 1993; Häfner et al., 1993). Since the prodromal period is thought to precede illness onset by 1 to 6 years (Yung and McGorry, 1996; Häfner et al., 1998; Köhn et al., 2004), screening measures for identification of prodromal symptoms have been developed primarily for adolescents and young adults. The predictive validity of attenuated psychotic symptoms in younger cohorts has yet to be determined. Given the developmental normalcy of magical thinking, grandiose and fantastical beliefs, concrete and more loosely organized thinking in young children, and the lower frequency of truly psychotic thinking, child responses to adolescent and adult screening instruments should be interpreted with caution (e.g., Woolley et al., 2004; Bartels-Velthuis et al., 2011). Poorly worded questions that exceed a child's comprehension can result in false positives (Breslau, 1987). That said, even carefully conducted screening and interviews have yielded high frequencies of psychotic-like experiences in children.

Indeed, Laurens et al. (2012) found that in a London community sample of 8000 children ages 9–11, almost two-thirds endorsed at least one "psychotic-like experience" (PLE). In a study by Yoshizumi et al. (2004), 21% of a Japanese general population sample of children ages 11–12 experienced hallucinations. Subgroups that experience PLEs in general adult populations share biological and environmental risk factors with schizophrenia (Kelleher et al., 2011a), suggesting a continuum of psychosis in the general population (van Os et al., 2008). Subclinical auditory hallucinations in childhood appear to be transitory in most cases, but similarly to PLEs in adults, correlate with developmental and behavioral problems, hinting that such a continuum may also be present in youth populations (Hlastala and McClellan, 2005; Bartels-Velthuis et al., 2010, 2011). Thus, accumulating evidence suggests that PLEs may be more common in childhood than previously recognized. Importantly, prevalence of PLEs does not equate with prevalence of prodromal syndromes. There is poor reliability between PLEs and prodromal syndromes identified through structured clinical interview with the SIPS and much lower prevalence rates of CHR syndromes relative to PLEs in both adults and children (Kelleher et al., 2011a, 2011b; Schultze-Lutter et al., 2013, 2014).

Childhood-onset schizophrenia is exceedingly rare, with an estimated prevalence rate of 1.8/10,000 (Häfner and Nowotny, 1995). Yet genetic, neuroanatomical, cognitive, motor, and social abnormalities during childhood have been repeatedly associated with adult onset of schizophrenia (Jones et al., 1994; Marenco and Weinberger, 2000; Rapoport et al., 2005; Woodberry et al., 2008; Thermenos et al., 2013). In retrospective research of the precursors to schizophrenia, Häfner et al. (1998) found that negative symptoms preceded positive symptoms in 70% of adult-onset cases. However, these early "premorbid" and "prodromal" abnormalities and symptom patterns tend to be nonspecific, associated with risk for mood disorders like depression or bipolar disorder as well as psychosis (Cannon et al., 1997; van Os et al., 1997). A better understanding of the predictive value of psychotic-like experiences (PLEs) during childhood may improve the specificity of risk identification in childhood cohorts and support earlier intervention efforts.

One strategy for understanding the potential implications of psychotic-like experiences in children is to identify the degree to which individuals with clinically significant psychotic-like symptoms or psychotic disorders report a childhood onset of these symptoms. Thus, the purpose of the current study was to identify the prevalence and pattern of prodromal-level symptom onset in childhood as reported by adolescents and adults either in a first episode of schizophrenia (FES) or with a CHR syndrome. Although we explored differences in childhood symptom onset between these two groups, the overall goal was to characterize childhood symptom onset in both groups to inform screening and early intervention efforts. To our knowledge, no previous studies have used the same method to query symptom onset in both groups.

2. Methods

2.1. Participants

The study sample was recruited for the Boston Center for Intervention Development and Applied Research (CIDAR) study entitled, "Vulnerability to Progression in Schizophrenia" (www.bostoncidar.org). Individuals ages 13–45 in a first episode of schizophrenia (FES, including schizophrenia, schizoaffective disorder, or schizophreniform disorder) or persons ages 13–35 meeting criteria for CHR were recruited from area hospitals, outpatient treatment settings, and the metropolitan Boston community through advertisements, formal outreach presentations, and word of mouth. Exclusion criteria included sensory-motor handicaps, neurological disorders, medical illnesses that significantly impair neurocognitive function, intellectual disability, education less than 5th grade if under 18 or less than 9th grade if 18 or older, lack of English fluency, DSM-IV-TR substance abuse in the past month or substance dependence, excluding nicotine, in the past 3 months, current suicide risk, and a history of electroconvulsive therapy within the prior 5 years.

CIDAR recruited a total of 44 FES and 45 CHR participants. Of these, we excluded from these analyses one CHR and four FES due to missing SIPS data, one CHR (from the CHR sample only) who converted to schizophrenia and was thus included in the FES sample, and three CHR who had no reported attenuated positive symptom onset (but were included in the CIDAR study on the basis of a presumed negative symptom syndrome or genetic risk and decline of functioning). Thus 40 CHR and 40 FES were included in these analyses. All participants provided written informed consent (or assent and parental consent in the case of minors). The institutional review boards at the Beth Israel Deaconess Medical Center, Cambridge Health Alliance, Harvard Medical School, Massachusetts General Hospital, the Veteran Affairs Boston Healthcare System, Brockton campus, and Brigham and Women's Hospital approved the study.

2.2. Clinical measures and procedures

FES status and clinical diagnoses for both groups were determined by diagnostic consensus based on a clinical interview with the Structured Clinical Interview for DSM IV-TR (SCID, Research Version, First et al., 2002) and available medical records. Prodromal symptoms and symptom onset were assessed with the Structured Interview of Prodromal Syndromes (SIPS; Miller et al., 1999; McGlashan et al., 2001; see von Hohenberg et al., 2013 for details on CHR criteria used in the CIDAR study). All clinical interviewers were trained on the SIPS by Yale University trainers (Drs. Tandy Miller and/or Barbara Walsh), and had to achieve accurate identification of CHR status for two videotaped interviews. Final determination of CHR status was determined by diagnostic consensus based on the Criteria of Prodromal Syndromes (COPS).

For inclusion in these analyses, participants had to provide sufficient recall of positive (attenuated psychotic) and nonspecific (negative, disorganized, or general) symptom onset via the 19 item SIPS (see Supplemental Table 1). For CHR participants the SIPS was the primary clinical interview for determining both eligibility and onset of PLEs. For FES participants the SIPS was a secondary interview, eliciting retrospective account of the onset of prodromal-level symptoms both for symptoms that had subsequently reached a psychotic level and for symptoms currently experienced at a "prodromal-level." Based on the difficulty eliciting retrospective self-report of symptom onset for which acutely psychotic patients might have little or no insight (e.g., P3 grandiosity and P5 disorganized speech), the CIDAR study decided to query only nine of the nineteen symptoms of the SIPS

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