Schizophrenia Research xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Attenuated psychotic symptoms in children and adolescent offspring of patients with schizophrenia

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ARTICLE INFO

Article history:
Received 10 December 2016
Received in revised form 20 July 2017
Accepted 24 July 2017
Available online xxxx

Keywords:
Psychosis
Psychopathology
Schizophrenia
Offspring

ABSTRACT

Objective: To compare the offspring of patients with SZ (SZoff) with those of a community control group (CC-off) to determine the variables associated with attenuated psychotic symptoms (APS), general symptomatology and functioning that may help to differentiate those at genetic risk for SZ.
Methods: 41 SZ-off and 107 CC-off aged 6–17 years were included. The Structured Interview for Prodromal Symptoms (SIPS), scored on the Scale of Prodromal Symptoms (SOPS), was administered by a child psychiatrist blinded to parental diagnoses, together with other clinical and functional scales.
Results: The SZ-off group presented higher scores in positive ($p = 0.000$), negative ($p = 0.012$), and disorganized ($p = 0.009$) subscale scores, as well as in the total score ($p = 0.001$) on the SOPS when compared with the CC-off group. Other scales indicated significant emotional ($p = 0.028$), behavioral ($p = 0.000$) and peer-related problems ($p = 0.025$), lower performance at school ($p = 0.025$) and increased dysfunction score ($p = 0.005$) in the SZ-off group. Logistic regression analysis revealed lower socioeconomic statuses (OR: 0.92, 95%CI: 0.87–0.97) and higher SOPS positive subscale scores (OR: 2.41, 95%CI: 1.31–4.42) in the SZ-off group.
Conclusions: SZ-off presented significantly more APS and higher mean scores in psychopathological scales than CC-off, together with increased dysfunction scores. These early warning signs and follow-up for those at genetic high risk for schizophrenia will provide useful information about symptom progression, facilitating early intervention to improve short and long-term outcomes in youths with a positive family history.

1. Introduction

Schizophrenia (SZ) is a severe mental disorder with a strong genetic component, in which offspring of patients have a higher incidence of schizophrenia spectrum disorders and other mental illnesses when compared with offspring of unaffected parents (Gottesman et al., 2010; Rasic et al., 2014).

Observations of behavioral, neuropsychological, and brain structural and functional abnormalities in offspring of patients with SZ (SZ-off) strongly suggest that early signs of the disorder may originate during the postnatal period and continue during infancy and into adolescence (Keshavan et al., 2008). Studies of child and adolescent SZ-off may provide an opportunity to characterize premorbid psychopathology (Maziade et al., 2008) and potential neurobehavioral markers of risk for the disease (Cornblatt et al., 1999; Keshavan et al., 2005). These neurobehavioral markers include increased frequency of cognitive and neurological abnormalities (Niemi et al., 2005; Schubert and McNeil, 2005) and premorbid adjustment deficits (Niemi et al., 2005).

Regarding attenuated psychotic symptoms (APS), previous studies have focused on groups at high clinical risk of psychosis, using the Structured Interview for Prodromal Symptoms (SIPS) (Miller et al., 2003) and the Scale of Prodromal Symptoms (SOPS) to assess prodromal states. Conversion to psychosis in groups at high clinical risk has been associated with symptoms included in the positive (unusual thought content and suspicion/paranoia), disorganization (bizarre thinking), and general (sleep disturbances) subscales of the SIPS (Cornblatt et al., 2003; Meyer et al., 2005; Cannon et al., 2008). Although groups at high clinical risk may include individuals identified on the basis of familial risk criteria, to the best of our knowledge, few studies (de la Serna et al.,

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http://dx.doi.org/10.1016/j.schres.2017.07.050
0920-9964/

2011; Bhojraj et al., 2011; Tandon et al., 2012) have used structured interviews to assess APS in cohorts exclusively composed of individuals at high genetic risk for developing a psychotic disorder. In a different cohort, De la Serna et al. (2011) reported higher SOPS scores in the positive, disorganized, general and total subscales among child and adolescent offspring and siblings of patients with SZ when compared with a control group. Tandon et al. (2012) studied child and adolescents first- and second-degree relatives of patients with SZ using the positive and disorganization SOPS subscales and two subscales of the Wisconsin Schizotypy scale (perceptual aberration and magical ideation), and created a composite index that provided high specificity and sensitivity for predicting the likelihood of developing a psychotic disorder over a 2-year period. In a neuroimaging study, Bhojraj et al. (2011) assessed adolescent and young first- and second-degree adult relatives of patients with SZ at baseline and 1 year follow-up. They reported that positive, negative, disorganization, and general prodromal symptoms worsened over time in those at high risk. However, we are unaware of any other study evaluating APS symptoms using the SIPS/SOPS among the child and adolescent offspring of patients with SZ.

Other clinical characteristics are also important, and previous studies (Amminger et al., 2000; Keshavan et al., 2003; Niemi et al., 2003; Niemi et al., 2005; Glatt et al., 2006; De la Serna et al., 2011) using different scales have reported that a broad range of symptomatology emerges during childhood, adolescence, and early adulthood. Higher frequencies of nonspecific non-psychotic diagnoses in SZ-off have been reported: Niemi et al. (2005) determined more emotional symptoms before school age (7 years) and greater social inhibition at school age (7–17 years). Other sympthomatology as higher frequency of depression and anxiety (Amminger et al., 2000), greater difficulties in social and school adjustment (Niemi et al., 2003) and more problems with peers (Glatt et al., 2006) are also reported in previous stydies. Other studies have also reported higher frequencies of disruptive behavior disorders, attention deficit hyperactivity disorder (ADHD), conduct disorder, and oppositional defiant disorder in SZ-off compared with controls (Keshavan et al., 2003; de la Serna et al., 2011).

We aimed to compare APS and other clinical variables (emotional, relational, and general functioning) in SZ-off with those in the offspring of community controls (CC-off). Our aim was to identify variables that may help to differentiate SZ-off from CC-off. We hypothesized that SZ-off would have higher APS scores, more behavioral and emotional problems, and poorer functioning.

2. Methods

2.1. Sample

The study was conducted in two Child and Adolescent Psychiatry Departments in Spain, Hospital Clinic of Barcelona and Hospital Gregorio Marañón of Madrid, and was approved by the Ethical Review Boards of each participating hospital. A complete description of the methodology and recruitment criteria has been provided elsewhere (Sanchez-Gistau et al., 2015). Psychiatrists of adult units were asked to identify SZ probands with offspring aged 6–17 years, and to enquire whether they agreed to be contacted for the study. The rest of the assessments were conducted in the child and adolescent psychiatry departments of the Hospital Clinic of Barcelona and Hospital Gregorio Marañon of Madrid. The final sample consisted of 34 parents with a diagnosis of SZ and 41 offspring (SZ-off, n = 41). The exclusion criteria for affected parents consisted of intellectual disability and drug or medically-induced psychosis. A community control parent group was recruited through advertisements posted in primary health care centers and community locations within the same geographical area as the patients. In addition to the same exclusionary criteria for SZ parents, a history of bipolar disorder or SZ (either personal or of a relative) was deemed exclusionary for control parents. We enrolled 65 control families (CC-off, n = 107). Exclusion criteria for the CC-off and SZ-off included intellectual disability, head injury with loss of consciousness, or other severe neurological conditions.

Lifetime diagnoses were present in 58.5% of SZ-off and 17.8% of CC-off. The most prevalent diagnoses in SZ-off group were ADHD (46.3%), followed by anxiety disorders (17.1%), disruptive behavior disorders (14.6%), mood disorders (4.9%), and other psychiatric disorders (4.9%). In the CC-off group, the most prevalent diagnosis were ADHD (7.5%), anxiety (5.6%), mood disorders (4.7%), other psychiatric disorders (3.7%), and disruptive behavior disorders (1.9%) (Sanchez-Gistau et al., 2015).

2.2. General assessment

2.2.1. Clinical diagnosis

Parents or primary caregivers were interviewed about their children, and participants were assessed directly by trained child psychiatrists or psychologists who were blind to parental diagnoses, using the Spanish version of the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997). Socioeconomic Status (SES) was calculated according to the Hollingshead and Redlich scale (Hollingshead and Redlich, 1958). For offspring, the highest SES among biological parents was considered.

2.2.2. Structured interview for APS

The SIPS (Miller et al., 2003), Spanish translation by Lemos et al. (2005), is designed to evaluate prodromal symptoms of schizophrenia that are scored on the SOPS. The SOPS is a 19-item scale designed to assess the severity of prodromal symptoms via four subscales: positive symptoms (e.g., unusual thinking and perceptual disturbances), negative symptoms (e.g., anhedonia and flat affect), disorganized symptoms (e.g., conceptual disorganization), and general symptoms (e.g., depression and problems with role functioning). Each item is rated on a scale of zero (not present) to six (extreme or psychotic intensity). Items scored from three to five are considered prodromal.

2.2.3. Other psychopathology scales

- The Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982) assesses functioning in certain developmental goals at different life stages. The scale considers different age ranges: childhood (to 11 years), early adolescence (12–15 years), late adolescence (16–18 years), and adulthood (≥19 years). Each item is scored from zero to six, with zero indicating the best level of adjustment. The areas explored are sociability and withdrawal, peer relationships, school achievement, adaptation to school, and ability to establish socio-affective and sexual functioning.
- The Global Assessment of Functioning Scale (GAF) (Endicott et al., 1976), which measures the severity of symptoms and the level of functioning, and is scored from 0 to 100.
- The Strengths and Difficulties Questionnaire (SDQ), Parent Version (Goodman et al., 1998) assesses five areas: hyperactivity, behavioral problems, problems with peers, prosocial behavior, and emotional problems. Parents respond to 25 questions about their children's behavior using three-point Likert scales.
- The Hamilton Depression Rating Scale (HDRS) (Hamilton, 1967) is a 17-item scale administered to evaluate the severity of depressive symptoms during the previous week. Each item can be scored according to the severity of the depressive symptoms.
- The Young Mania Rating Scale (YMRS) (Young et al., 1978) is an 11-item scale developed to evaluate the severity of mania symptoms during the previous 48 h. Each item is scored depending on symptom severity.

Please cite this article as: Noguera, A., et al., Attenuated psychotic symptoms in children and adolescent offspring of patients with schizophrenia, Schizophr. Res. (2017), http://dx.doi.org/10.1016/j.schres.2017.07.050