Schizophrenia Research 158 (2014) 1–6

Contents lists available at ScienceDirect

Schizophrenia Research

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

Predicting psychosis in a general adolescent psychiatric sample

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ARTICLE INFO

Article history:
Received 30 August 2013
Received in revised form 14 January 2014
Accepted 22 June 2014
Available online 9 July 2014

Keywords:
Prodrome
CHR
Psychosis
Conversion
Adolescent
SIPS

ABSTRACT

Introduction: Current psychosis risk criteria have often been studied on a pre-selected population at specialized clinics. We investigated whether the Structured Interview for Prodromal Syndromes (SIPS) is a useful tool for psychosis risk screening among adolescents in general psychiatric care.
Methods: 161 adolescents aged 15–18 with first admission to adolescent psychiatric services in Helsinki were interviewed with the SIPS to ascertain Clinical High-Risk (CHR) state. The participants were followed via the national hospital discharge register, patient files, and follow-up interviews. DSM-IV Axis I diagnoses were made at baseline and 12 months. Register follow-up spanned 2.8–8.9 years, and hospital care for a primary psychotic disorder and any psychiatric disorder were used as outcomes.
Results: CHR criteria were met by 54 (33.5%) of the adolescents. Three conversions of psychosis as defined by SIPS emerged during follow-up, two of whom belonged to the CHR group. The positive predictive value of the CHR status was weak (1.9%) but its negative predictive value was 98.0%. Using the DSM-IV definition of psychosis, there were five conversions, three of which were in the CHR group. In regression analyses, hospital admissions for primary psychotic disorder were predicted by positive symptom intensity in the baseline SIPS. In addition, CHR status and SIPS positive and general symptoms predicted hospitalization for psychiatric disorder.
Discussion: Psychosis incidence was low in our unselected sample of adolescent psychiatric patients. CHR status failed to predict SIPS or DSM-IV psychoses significantly at 12 months. However, in a longer follow-up, CHR did predict psychiatric hospitalization.

1. Introduction

Psychotic-like symptoms that are milder than in clinical psychotic disorders are common among adolescents (van Os et al., 2009; Yung et al., 2009) and are usually transitory in nature (Simon et al., 2009; Ziermans et al., 2011). However, these subclinical psychotic symptoms can also be predictive of later psychosis, especially when persistent (Dominguez et al., 2011) or when linked to negative symptoms and poor global functioning (Addington and Heinssen, 2012). Furthermore, psychotic experiences need clinical attention by themselves, as they are associated with increased risk for other mental disorders and psychiatric hospitalizations (Rössler et al., 2011; Werbeloff et al., 2012), even when they have not been considered as clinically relevant (van Nierop et al., 2012).

Recent studies suggest that it is often possible to identify an individual as having a high risk of psychosis before the onset of the first episode of psychosis (Addington and Heinssen, 2012). A recent meta-analysis found that the psychosis high-risk state, also called clinical high-risk state (CHR), is associated with a 36% risk for psychosis during a three-year follow-up, although the methods to define the high-risk state vary (Fusar-Poli et al., 2012).

CHR has been proposed as a valid diagnostic entity, distinct from other psychiatric disorders in terms of symptoms and functioning (Woods et al., 2009). CHR is associated with long-term impairment in social and role functioning (Addington et al., 2011) and disruptive symptoms, also among those CHR individuals who do not develop psychosis (Haroun et al., 2006). However, critical opinions have also arisen, concerning different at-risk criteria, the risk of false positives and the use of psychosis conversion as the only outcome (Larsen et al., 2001; Simon et al., 2011; Schultze-Lutter et al., 2013; Fusar-Poli et al., 2014).

The study population appears to have a large impact on how well the CHR status predicts later psychosis (Yung et al., 2008). Many prospective studies have been made in clinics specialized in treating patients with CHR (Cannon et al., 2008; Ruhrmann et al., 2010). These clinics choose their patients using different kinds of screening methods, or referral to the clinic may be based on the referring clinician's impression

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http://dx.doi.org/10.1016/j.schres.2014.06.028
0920-9964/

that the patient is at risk of psychosis. Not surprisingly, the proportion of the patients converting to psychosis is high (Fusar-Poli et al., 2014). Due to this pre-selection in high-risk research, the existing results linking CHR status to later psychosis cannot be generalized to all psychiatric patients.

The objective of this study was to investigate the validity of CHR in predicting psychosis in general adolescent psychiatric services.

2. Methods

2.1. Procedure and participants

The Helsinki Prodromal Study is a prospective study of psychosis risk among adolescent psychiatric patients in Helsinki, Finland (Lindgren et al., 2010). The study cohort included all consecutive new patients aged 15–18 years who presented to any public adolescent psychiatric clinic in Helsinki during a three-year period (1.1.2003 to 15.3.2004, and 15.3.2007 to 31.12.2008). At their first or second clinic visit, the adolescents were asked to fill in the Prodromal Questionnaire (PQ, Loewy et al., 2005), a validated 92-item self-report measure for screening prodromal symptoms. The only exclusion criterion for the study was a psychiatric treatment contact within the previous two years. In total, 683 adolescents were screened with the PQ; most were first-visit outpatients, 10.0% were inpatients. Their average age was 16.5 years and 66.5% were female.

The cutoff score for an in-depth assessment was 18 or more positive symptom items of the PQ as suggested by Loewy et al. (2012). There were 145 screen-positive and 538 screen-negative adolescents. All screen-positives were invited to the assessment and 114 agreed to participate, while a random sample of 87 screen-negatives was invited and 60 participated. For the participants, we administered the Structured Interview for Prodromal Syndromes (SIPS, Miller et al., 2003) and the Structured Clinical Interview for the DSM-IV, Clinician Version (SCID, First et al., 1996). The SIPS addresses negative, disorganization, general, and positive symptoms, which are rated on 19 SOPS scales (Scale of Prodromal Symptoms). The aim of the SIPS is to detect three kinds of CHR syndromes: Brief Intermittent Psychotic Syndrome (BIPS), Attenuated Positive Prodromal Syndrome (APS) and Genetic Risk and Deterioration Syndrome (GRD).

The adolescents gave written informed consent to participate in the study and their parents were informed. The study protocol was reviewed and approved by the institutional review boards of the National Public Health Institute (since January 1, 2009 the National Institute for Health and Welfare) and the Hospital District of Helsinki and Uusimaa, and was carried out in accordance with the Declaration of Helsinki.

The diagnostic assessments were ascertained by trained research staff in the Department of Mental Health and Substance Abuse Services at the National Institute for Health and Welfare (ML, MM, UM, TL, ST). In 2002, the research staff completed a three-day SIPS training workshop and achieved excellent interrater agreement (kappa = .97 for CHR status). Staff had been previously trained to high standards of reliability on the SCID by Professor Jaana Suvisaari, MD. The researchers were blind to the PQ scores of the participants. Most of the SIPS ratings were assigned by team consensus by watching videotaped interviews.

The final number of subjects who completed the whole study protocol was 174. Participants fulfilling the criteria for SIPS psychosis (n = 5) or lifetime DSM-IV psychosis (n = 8) were excluded from further analyses (see Fig. 1). Table 1 lists the characteristics of the remaining 161 study participants.

2.2. Follow-up information

The date of the SIPS interview was considered the baseline for all follow-up analyses. Follow-up information was gathered from three sources: The first information source was one-year follow-up assessment including SCID and SIPS interviews for a proportion (n = 58) of the participants. This data was mostly gathered in the second phase of the study (n = 55). See supplementary material for characteristics of those with and without follow-up SIPS.

Secondly, complete medical records were available for 157 (97.5%) participants from the total duration of their psychiatric treatment.

DSM-IV Axis I diagnoses were made separately for baseline (n = 161) and follow-up (1 year or less if the treatment had ended before that, n = 148) using all available data including medical records and follow-up assessment. Conversion to psychosis as defined by SIPS and DSM-IV was assessed. While making the baseline diagnosis, researchers were blind to any follow-up information.

Thirdly, psychiatric hospital admission data were collected from the Finnish hospital discharge register HILMO (Care Register for Health Care). The time window was from the initial interview till the end of 2011, giving a register follow-up time of 1025–3249 days [2.8–8.9 years; mean 2058 days (5.6 years); standard deviation 823 days]. The diagnostic system used in the register is ICD-10. Outcome variables derived from the register were primary psychotic disorders (F20, F22–F29, F30.2, F31.2, F31.5, F32.3, F33.3) and psychiatric hospital treatments.

2.3. Statistical analysis

Gender, participation rate, and screening outcome were taken into account using weights in all analyses (see supplementary material). The data were analyzed with R 3.0.1 (R Core Team, 2013) and its packages *survival* (Therneau, 2013) and *survey* (Lumley, 2012). All statistical tests were two-tailed, with α level set at 0.05.

SIPS and DSM-IV conversion at the one-year follow-up was calculated for the 148 subjects with adequate follow-up data. All available data including medical records and follow-up assessment was used. Following the SIPS definition, conversion to psychosis meant a positive symptom was rated six if 1) it had a frequency of $\geq$1 h/day four days/week during the past month or 2) it was a seriously disorganizing or dangerous symptom. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the CHR status were calculated as well as an adjusted Wald test of association (Thomas and Rao, 1987), which is an F-test.

Cox regression survival analysis was performed to assess the hazard ratio of hospitalization for 1) primary psychotic disorder, n = 149, and for 2) any mental disorder, n = 133. Those with such hospitalizations at baseline, or without permission to register follow-up, were excluded from the analyses. CHR status and symptom factors derived from the SIPS—formed earlier in our study (Lindgren et al., 2010)—were used as predictors of hospital treatment. Kaplan–Meier was used for survival curves. Gender was included as strata in all the regression analyses.

3. Results

3.1. Baseline data

Of the 161 participants, 54 (33.5%) met the criteria for at least one of the SIPS prodromal syndromes (CHR group); 51 met the criteria for APS, one for GRD, and two for both. Table 1 presents the characteristics of the CHR and non-CHR groups. Table 2 presents the DSM-IV baseline diagnoses of the participants. See supplementary material for the SIPS score means and standard deviations and data by gender.

3.2. Conversion to SIPS psychosis

During the one-year follow-up, three (2.0%) of the 148 subjects developed a psychotic disorder as defined by SIPS. All three were outpatients with a non-psychotic mood disorder diagnosis at baseline. Conversion to psychosis took place 25, 62, and 221 days after