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Twelve-month psychosis-predictive value of the ultra-high risk criteria in children and adolescents

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ABSTRACT

Objective: The validity of current ultra-high risk (UHR) criteria is under-examined in help-seeking minors, particularly, in children below the age of 12 years. Thus, the present study investigated predictors of one-year outcome in children and adolescents (CAD) with UHR status.
Method: Thirty-five children and adolescents (age 9–17 years) meeting UHR criteria according to the Structured Interview for Psychosis-Risk Syndromes were followed-up for 12 months. Regression analyses were employed to detect baseline predictors of conversion to psychosis and of outcome of non-converters (remission and persistence of UHR versus conversion).
Results: At one-year follow-up, 20% of patients had developed schizophrenia, 25.7% had remitted from their UHR status that, consequently, had persisted in 54.3%. No patient had fully remitted from mental disorders, even if UHR status was not maintained. Conversion was best predicted by any transient psychotic symptom and a disorganized communication score. No prediction model for outcome beyond conversion was identified.
Conclusions: Our findings provide the first evidence for the predictive utility of UHR criteria in CAD in terms of brief intermittent psychotic symptoms (BIPS) when accompanied by signs of cognitive impairment, i.e. disorganized communication. However, because attenuated psychotic symptoms (APS) related to thought content and perception were indicative of non-conversion at 1-year follow-up, their use in early detection of psychosis in CAD needs further study. Overall, the need for more in-depth studies into developmental peculiarities in the early detection and treatment of psychoses with an onset of illness in childhood and early adolescence was further highlighted.

1. Introduction

Psychoses are one of the most severe disorders in children and adolescents (CAD) (Gore et al., 2011). Their poor outcome generally correlates positively with the durations of untreated psychosis (DUP) and illness (DUI) (Marshall et al., 2005). Outcome is even worse in early-onset psychosis (EOP), with the first episode starting before the age of 18 years (Rabinowitz et al., 2006).

1.1. Early-onset psychoses

Compared with adult-onset psychosis (AOP), the poorer outcome of EOP might not be intrinsic, but due to a significantly longer DUP (Schimmelmann et al., 2007, 2008). Furthermore, clinically, EOP often presents slightly differently compared with AOP (Gochman et al., 2011; Tiffin and Welsh, 2013). Thus, the challenges of early detection and treatment of first signs of the emerging disorder may be different in EOP and also in AOP with an illness onset in childhood and early adolescence compared with AOP that has an onset in late adolescence and adulthood (Schimmelmann and Schultze-Lutter, 2012; Schimmelmann et al., 2013a, 2013b).

1.2. Early detection of psychosis in children and adolescents

Two approaches for an early detection of psychoses currently prevail: the "ultra-high risk" (UHR) (Yung et al., 1998), mainly relying on attenuated psychotic symptoms (APS) and the "basic symptoms" (Schultze-Lutter et al., 2012). The alternative UHR criteria, which comprise the attenuated psychotic symptom (APS) criterion, the brief intermittent psychotic symptom (BIPS) criterion, and the genetic risk and

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functional decline (GRFD) criterion, were originally developed with the explicit aim of detecting an imminent risk for psychoses, i.e., persons at risk for developing a first-episode within the next 12 months (Schultze-Lutter et al., 2015). In contrast to the UHR criteria, the criteria based on basic symptoms, i.e., the cognitive-perceptive basic symptoms, (COPER) criterion and the cognitive disturbances (COGDIS) criterion (Schultze-Lutter et al., 2012), were developed to detect the risk for psychosis as early as possible in the development of the illness, ideally before functional impairments have appeared (Schultze-Lutter et al., 2015).

A recent meta-analysis showed pooled conversion rates in UHR samples that increased from 9.6% at 6 months to 37.0% at >4-year follow-up, with significantly lower conversion rates in 12- to 18-year-olds (Schultze-Lutter et al., 2015). Lower conversion rates in CAD might not be surprising as current risk criteria were developed and validated in predominately adult samples (age ≥ 16 years; Schultze-Lutter et al., 2015; Yung et al., 1998).

CAD studies reporting high prevalence of (attenuated) psychotic symptoms (hallucinations) in the general population further indicated age-related peculiarities of UHR symptoms (Schimmelmann et al., 2013a, 2013b). These seem to decrease throughout adolescence (Kelleher et al., 2012b; Brandizzi et al., 2014; Schimmelmann et al., 2015) and remit spontaneously in about three quarters of CAD (Bartels-Velthuis et al., 2011).

Thus, it was recently argued that the validity of current risk criteria needs to be examined in and possibly adapted to CAD populations (National Institute for Health and Clinical Excellence NICE, 2013; Schimmelmann and Schultze-Lutter, 2012; Schimmelmann et al., 2013a; Schultze-Lutter et al., 2012, 2015).

1.3. Aims of the study

To address this need, we investigated predictors of 1-year outcome in CAD at increased risk of psychosis in terms of both predictors of conversion to psychosis and of outcome of non-converters (remission and persistence of UHR criteria versus conversion).

2. Methods

2.1. Participants

The sample consisted of 35 patients (aged 9–17-years, n = 7 (20%) each age 9–11 and 16–17) with suspected EOP at the Child and Adolescent Neuropsychiatry Unit of the Children Hospital Bambino Gesù in Rome from 2012 to 2013 (Table 1). Inclusion criterion was the presence of any UHR criterion (Yung et al., 1998): APS, brief intermittent psychotic symptoms (BIPS) and/or genetic risk plus functional deterioration (GRFD). Exclusion criteria were: past or present psychosis, traumatic brain injury or any known neurological disorder, and current drug or alcohol abuse. A history of drug use was permitted if symptoms had also been present in drug-free periods. Participants were followed-up for 12 months.

The study was approved by the Ethics Committee of the Children Hospital Bambino Gesù. All participants provided written informed assent and their parents/legal guardians, written informed consent.

2.2. Assessments

UHR criteria and negative, disorganization, and general symptoms were assessed with the Structured Interview for Psychosis-Risk Syndromes (SIPS; McGlashan, 2001). It was also used to assess past or present psychosis at baseline and follow-up, defined by the presence of any positive symptom rated '6' that is seriously disorganizing or dangerous and/or persists for more than 7 days. The type of psychosis was diagnosed using DSM-IV (American Psychiatric Association, 1994).

Mental disorders were assessed using the Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997); alcohol and drug use using sections J and L of the Composite International Diagnostic Interview (CIDI; McGlashan, 2001). Functioning was rated globally on the Childhood Global Assessment Scale (CGAS; Shaffer et al., 1983) and differentially on the Global Functioning: Social (GF:Social; Auther et al., 2006) and the Global Functioning: Role (GF:Role; Niendam et al., 2006) scales. Baseline verbal IQ was assessed with the Wechsler Intelligence Scale for Children (WISC-III; Wechsler, 1991).

Table 1
Sociodemographic and clinical characteristics of ultra-high risk (UHR) patients at baseline (n = 35).

Age: mean (sd); Mdn (range)	13.8 (2.1); 13.8 (9–17)
Sex, male: n (%)	18 (51.4)
1st- or 2nd-degree relative with psychosis: n (%)	4 (11.4)
Verbal IQ: mean (sd); Mdn (range)	87.2 (17.3); 91 (53–129)
Education (in years): mean (sd); Mdn (range)	8.4 (2.2); 8 (3–12)
Urbanicity level, more than 2500 citizens: n (%)	25 (71.4)
Duration of mental problems (in months): mean (sd); Mdn (range)	28.1 (28.2); 12 (2–120)
SIPS sum scores: mean (sd); Mdn (range)	
Total SIPS	43.1 (14.6); 42 (12–80)
Positive subscale (SIPS-P sum)	12.2 (5.2); 13 (0–24)
Negative subscale (SIPS-N sum)	14.5 (6.4); 16 (1–29)
Disorganization subscale (SIPS-D sum)	6.5 (3.5); 6 (1–14)
General psychopathology subscale (SIPS-G sum)	9.9 (4.3); 10 (1–18)
UHR criterion: n (%)	
Any attenuated psychotic symptom (APS)	29 (82.9)
By unusual thought content/delusional ideas (P1 = |3–5|)	20 (57.1)
By suspiciousness/persecutory ideas (P2 = |3–5|)	27 (77.1)
By grandiosity (P3 = |3–5|)	5 (14.3)
By perceptual abnormalities/hallucinations (P4 = |3–5|)	18 (51.4)
By disorganized communication (P5 = |3–5|)	13 (37.1)
Any brief intermittent psychotic symptom (BIPS)	5 (14.3)
By unusual thought content/delusional ideas (P1 = 6)	1 (2.9)
By suspiciousness/persecutory ideas (P2 = 6)	1 (2.9)
By grandiosity (P3 = 6)	0
By perceptual abnormalities/hallucinations (P4 = 6)	3 (8.6)
By disorganized communication (P5 = 6)	0
Any genetic risk plus functional decline (GRFD)	4 (11.4)
By 1st-degree relative with psychosis	3 (8.5)
By schizotypal personality disorder according to SIPS	1 (2.9)
Main axis-I DSM-IV disorder by K-SADS-PL: n (%)	
Any depressive disorder	18 (51.4)
Any behavioral disorder	7 (20.0)
Any anxiety disorder	2 (5.7)
Any obsessive–compulsive disorder	5 (14.3)
Any other disorder	3 (8.6)
C-GAS: mean (sd); Mdn (range)	48.6 (4.3); 50 (37–55)
GF:Role: mean (sd); Mdn (range)	4.0 (0.7); 4 (3–5)
GF:Social: mean (sd); Mdn (range)	4.1 (0.6); 4 (3–5)
Cannabis use: n (%)	
Never	34 (97.2)
Last (regular) use >1 month ago	1 (2.9)
Current psychopharmacological medication: n (%)	
Any antidepressant	1 (2.9)
Any benzodiazepine	1 (2.9)
Any antipsychotic	0

SIPS: Structured Interview for Psychosis-Risk Syndromes (McGlashan, 2001); *C-GAS*: Childhood Global Assessment Scale (Shaffer et al., 1983); *GF:Role*: Global Functioning: Role (Niendam et al., 2006); *GF:Social*: Global Functioning: Social (Auther et al., 2006); *K-SADS-PL*: Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present and Lifetime Version (Kaufman et al., 1997).

2.3. Data analyses

Using SPSS 21, predictors of psychosis-conversion were assessed by logistic regression analyses; predictors of UHR status remission and persistence versus conversion by ordinal logistic regression analyses. Predictors were sociodemographic characteristics (age, gender, education,