Schizophrenia Research 181 (2017) 13–16

Contents lists available at ScienceDirect

Schizophrenia Research

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

A longitudinal study of adolescent psychotic experiences and later development of substance use disorder and suicidal behavior

Martin Cederlöf [a,*], Ralf Kuja-Halkola [a], Henrik Larsson [a,b], Arvid Sjölander [a], Per Östberg [c], Sebastian Lundström [d,e], Ian Kelleher [f], Paul Lichtenstein [a]

[a] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden
[b] School of Medical Sciences, Örebro University, Örebro, Sweden
[c] Division of Speech and Language Pathology, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Sweden
[d] Centre for Ethics, Law and Mental Health (CELAM), University of Gothenburg, Sweden
[e] Gillberg Neuropsychiatry Centre, University of Gothenburg, Sweden
[f] Department of Psychiatry, Royal College of Surgeons in Ireland, Ireland

ARTICLE INFO

Article history:
Received 2 July 2016
Received in revised form 30 August 2016
Accepted 30 August 2016
Available online 5 September 2016

Keywords:
Psychotic experiences
Substance use disorder
Suicide attempt
Epidemiology

ABSTRACT

Introduction: Psychotic experiences are associated with later substance use disorder and suicidal behavior, but individual psychotic experiences have not been examined in a longitudinal data set. Also, the potential dose–response relationship between these phenomena remains unknown.
Method: Cohort study including 9242 adolescents who participated in The Child and Adolescent Twin Study in Sweden (CATSS). At ages 15 and/or 18, seven psychotic experiences (auditory and visual hallucinations, and five delusions) were assessed via questionnaires. Outcomes at follow-up were physician-assigned diagnoses of substance use disorder and suicide attempts ascertained from the Swedish Patient Register. Associations were estimated with Cox regressions and expressed as hazard ratios.
Results: All psychotic experiences were associated with later substance use disorder and/or suicide attempts, with hazard ratios ranging from 1.6 to 3.0. A dose–response relationship was observed between psychotic experiences and later substance use disorder, and suicide attempt.
Discussion: Auditory and visual hallucinations as well as delusions in adolescence are associated with later development of substance use disorder and suicide attempt, and there is a dose–response relationship between the load of psychotic experiences and these adverse outcomes. Clinicians should assess subclinical hallucinations as well as delusions in psychiatric evaluations of adolescents.

1. Introduction

Substance use disorder and suicidal behavior represent major causes of preventable suffering, morbidity and death worldwide (World Health Organization, 2001), especially among individuals with schizophrenia (Bertolote et al., 2004). A few studies suggest that adolescents with psychotic experiences also have elevated risks of developing substance use disorder (Dhossche et al., 2002) and suicidal behavior (Kelleher et al., 2013; Fisher et al., 2013). Psychotic experiences, i.e., hallucinations and delusions, constitute the classic symptoms of schizophrenia, but are surprisingly common in the general population; a meta-analysis has shown that they are reported by ca 7% of adolescents (Kelleher et al., 2012) and a similar proportion of adults (Linscott and van Os, 2013). Even though psychotic experiences usually are of lower severity and impact than clinical psychosis, these phenomena may still prompt help seeking, be considered clinically relevant, and be subject to care (Kelleher et al., 2011; Horwood et al., 2008).

Most prior research into risks of later substance use disorder and suicide attempt has looked at limited range of experiences, e.g., by using auditory/visual hallucinations alone (Dhossche et al., 2002; Kelleher et al., 2013) delusional beliefs alone (Saha et al., 2011) or collapsing all types of experiences into one variable (Fisher et al., 2013). Two exceptions are the cross-sectional studies by Capra et al. (2015), who reported that perceptual abnormalities and persecutory ideation (but not bizarre experiences) predicted suicidality risk, and Koyanagi et al. (2015), who found that subtypes of psychotic experiences were associated with suicidal ideation and suicide attempt. Since the epidemiologic characteristics of psychotic experiences are more variegated than previously thought, influential researchers have called for more studies on the course and consequences of individual psychotic experiences. (McGrath et al., 2015; David, 2010). To sum up the current knowledge, adolescent psychotic experiences have prospectively been shown to

* Corresponding author at: Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Box 281, SE-171 77 Stockholm, Sweden.
E-mail address: Martin.Cederlof@ki.se (M. Cederlöf).

http://dx.doi.org/10.1016/j.schres.2016.08.029
0920-9964/

increase risk for suicidal behavior, and cross-sectional research suggests that subtypes of psychotic experiences might be differentially associated with suicide risk. However, there has been no prospective research to date to investigate this clinically important question, and we are also not aware of any prospective studies examining whether the risk of later substance use disorder or suicide attempt increases in a dose–response fashion by the number of reported psychotic experiences.

In the current study, we linked the Child and Adolescent Twin Study in Sweden (CATSS; Anckarsäter et al., 2011) to the National Patient Register (Ludvigsson et al., 2011) and conducted a prospective cohort study to examine how individual and aggregated psychotic experiences would associate with later diagnoses of substance use disorder or suicide attempt. The study was approved by the Regional Ethics Committee in Stockholm.

2. Method

2.1. Participants

Participants were born between 1994 and 1999 and came from CATSS, an ongoing longitudinal study targeting all twins born in Sweden since 1992. The sample comprised 9242 adolescents who participated in the CATSS-15 ($n = 8,247$) or CATSS-18 ($n = 4038$) studies. A total of 3033 adolescents participated in both studies. The response rate averaged 54% in the CATSS-15 and CATSS-18 studies.

2.2. Measures

2.2.1. Psychotic experiences

In CATSS-15 and CATSS-18, participants were asked seven questions specifically targeting current auditory hallucinations and visual hallucinations, and delusions of persecution, reference, control, special powers, and thought broadcasting. These items correspond very closely to a validated screening instrument for psychotic experiences (Kelleher et al., 2011). There were different response alternatives across ages of assessment, so all answers were dichotomized so that 1 score equaled 1 individual psychotic experience. A composite score variable was created by adding all seven psychotic experiences together. There were few individuals with four or more endorsed psychotic experiences, so these observations were lumped into a single category. The range of the composite score variable was thus 0 to ≥ 4.

2.2.2. Substance use disorder and suicide attempt

To get information about diagnoses of substance use disorder and suicide attempt, data from CATSS-15 and CATSS-18 were linked to the National Patient Register, which contains in- and outpatient diagnoses assigned by the treating physician. We used the following ICD-10 (inpatient and outpatient) codes for substance use disorder: F10–16 and F18–19, and suicide attempt: ×60–84, Y10–34. Diagnoses in the National Patient Register are generally valid (Ludvigsson et al., 2011), and for example schizophrenia and bipolar disorder have >90% agreement when compared with medical records and semi-structured interviews (Ekholm et al., 2005; Sellgren et al., 2011; Lichtenstein et al., 2006).

2.3. Statistical analyses

Associations were examined with Cox regressions with the end of coverage of the National Patient Register as censoring time (31st December 2014). Time to event was calculated from the date participants completed the CATSS-15 or 18 questionnaires. Individuals who were members of both the CATSS-15 and the CATSS-18 studies entered the study the date they completed the CATSS-15 questionnaire. Individuals with diagnoses of substance use disorder or suicide attempt prior to their (first) participation in the CATSS-15 or CATSS-18 studies were excluded from the analyses. Since twins in a pair are correlated, a robust sandwich estimator was used when calculating the confidence intervals. First, we examined the associations between individual psychotic experiences and substance use disorder and suicide attempt. Second, we assessed the potential dose–response relationship between the number of psychotic experiences and substance use disorder and suicide attempt, and used to log-rank test for trend of survivor functions across the four categories of psychotic experiences. Finally, we examined the associations between a composite score of psychotic experiences and the same outcomes.

Table 1
Sample characteristics.

	Sample
Characteristic	*n* (%)
	9.242 (100)
Sex	
Male	4.182 (45.3)
Birth year	
1994	1.661 (18.0)
1995	1.615 (17.5)
1996	1.844 (19.9)
1997	1.361 (14.7)
1998	1.463 (15.8)
1999	1.298 (14.0)
Follow-up time in years, median (range)	2.7 (0.1–5.8)
Frequencies of age 15/18 psychotic experiences	
Auditory hallucinations: "Sometimes I hear voices other people couldn't hear"	522 (5.6)
Visual hallucinations: "Sometimes I have seen something or someone that other people couldn't see"	1.322 (14.3)
Persecution: "Sometimes I have thought that I was being followed or spied upon"	3.711 (40.1)
Thought broadcasting: "Other people have read my thoughts"	2.953 (32.0)
Ideas of reference: "Sometimes I thought that I was being sent special messages through the television"	518 (5.6)
Having special powers: "I have special powers that other people don't have"	742 (7.3)
Being controlled by some special power: "Sometimes I felt that I was under the control of some special power"	1.145 (12.4)

3. Results

3.1. Sample characteristics

Table 1 shows sample characteristics. The median follow-up time was 2.7 years, with a range of 1 month to 5.8 years.

3.2. Individual psychotic experiences at ages 15 or 18 years, and later substance use disorder and suicide attempt

All psychotic experiences were associated with a subsequent diagnosis of substance use disorder and/or suicide attempt, with hazard ratios ranging from 1.6 to 3.0 (Table 2).

Table 2
Hazard ratios and 95% confidence intervals (CI) describing associations between individual psychotic experiences at ages 15 or 18 years, and later substance use disorder, and suicide attempt.

Age 15 or 18 years psychotic experiences	Later substance use disorder		Later suicide attempt	
	n (%)	HR (CI)	*n* (%)	HR (CI)
Auditory hallucinations	10 (1.9)	**2.8 (1.4–5.5)**	24 (3.8)	**2.5 (1.6–3.9)**
Visual hallucinations	22 (1.7)	**2.7 (1.7–4.5)**	33 (2.2)	**1.7 (1.2–2.6)**
Persecution	45 (1.2)	**3.0 (1.8–5.1)**	81 (1.8)	**1.6 (1.1–2.3)**
Thought broadcasting	28 (0.9)	1.5 (0.9–2.5)	67 (2.0)	**1.6 (1.1–2.3)**
Ideas of reference	5 (1.0)	1.4 (0.6–3.4)	17 (3.0)	**2.2 (1.2–3.9)**
Having special powers	10 (1.4)	1.9 (1.0–3.8)	19 (2.1)	**1.7 (1.1–2.8)**
Being controlled by some special power	12 (1.1)	1.5 (0.8–2.9)	32 (2.6)	**2.3 (1.5–3.5)**

Note: statistically significant associations, at 5% significance level, are bolded. HR = hazard ratio.