

Adolescents with their first episode of schizophrenia spectrum psychosis: a comparison with adolescents suffering from other severe mental disorders

Emma Reponen, Juha Väänänen, Riittakerttu Kaltiala-Heino

Abstract

Studies of first-episode schizophrenia spectrum psychosis in adolescence in naturalistic, non-selected treatment settings are rare. Our aim was to compare adolescents hospitalized for first-episode schizophrenia spectrum psychosis with those hospitalized due to other disorders in order to recognize symptom profile, family and treatment-related characteristics specifically associated with schizophrenia spectrum psychosis, and to also recognize features in the early phases of contact with psychiatric services in order to predict the subsequent development of schizophrenia spectrum psychosis. In a well-defined catchment area all adolescents hospitalized due to first-episode schizophrenia spectrum psychosis (diagnosis codes F20-F29 in ICD-10) and a control for each subject were identified. Structured retrospective chart review was carried out. Adolescents with a first-episode psychosis presented not only with positive psychotic symptoms but also more frequently with suicidal behaviours, with somewhat fewer family adversities but more parental mental disorders, and with longer hospitalizations and heavier medication, suggesting lower functional level and more persistent symptoms. In the very early phases of their treatment histories, the two groups differed only slightly. Predicting future psychosis among child and adolescent psychiatric patients is important but extremely challenging. Across developmental years, symptom presentation at early contact has little predictive value for later diagnosis.

Introduction

Schizophrenia spectrum disorders (F20-F29) are among the most challenging mental disorders as regards symptoms, treatment and prognosis. Psychosis is defined as a severe mental disorder characterized by losing the sense of reality with core symptoms of disorganized thought processes, delusions and hallucinations. The long-term and recurrent course of the disease means that these conditions are also significant for public health. Schizophrenia is a psychotic disorder with a long-term and recurrent course. Symptoms of schizophrenia are divided into positive (hallucinations, delusions, diffuse speech and behaviour) and negative (emotional flatness, unexpressive speech, passivity, anhedonia) (1).

The lifetime prevalence of schizophrenia is assumed to be around 1% and the prevalence of all psychotic disorders somewhat higher, with some variation noted between studies and populations (2, 3). Studies on the prevalence of psychoses among adolescents are rare. It appears that rapid physical and mental development in youth exposes adolescents to mental disorders that vastly increase in prevalence from childhood to adolescence (4, 5). All psychotic disorders are rare up to the age of 13 years, but show a marked increase in prevalence between ages 15-17 with the peak ages of onset for these disorders between 15 and 30 years (6, 7).

The age of onset is associated with the prognosis of schizophrenia, earlier onset being associated with poorer outcome (8). Early-onset (< 18 years) schizophrenia spectrum disorders are characterized by significant morbidity and mortality (9, 10). Young people with schizophrenia tend to be predominantly male, experience an insidious onset, and to have severe negative symptoms and greater cognitive impairments than patients with onset in adulthood (10, 11). Follow-up studies suggest that the majority of patients with early-onset schizophrenia are chronically impaired and may have greater functional and social impairment than those with adult-onset schizophrenia (9-11).

Patients with adolescent-onset psychosis are also likely to encounter longer delays in receiving treatment for their psychosis than adult patients (8). Longer duration of untreated psychosis has been associated with poorer outcome (12). Treatment among adolescents is delayed probably because of ambiguities associated with psychotic disorders in adolescent patients and clinicians' reluctance to make a diagnosis of psychosis during adolescence (8).

Psychotic disorders in adolescents are diagnosed using the same criteria as adults. However, misdiagnosis of early-onset schizophrenia is a common problem in community settings, likely due to the symptom overlap between schizophrenia and other childhood psychiatric disorders, and the challenge of assessing the validity of reports of psychotic children and youths (10, 13, 14). For example, the vast majority of children referred to a national study of childhood-onset schizophrenia in the USA did not meet the diagnostic criteria for schizophrenia, but instead presented with a mixture of developmental delays, mood lability and subclinical psychotic symptoms (14). Psychiatric comorbidity is common among adolescents and a specific disorder may have such multiform symptoms that meet the criteria for several other disorders (15).

Schizophrenia spectrum psychosis is usually preceded by a prodromal phase, when the patient's functional level declines but psychotic symptoms are not yet apparent (16-18). In young people it is especially difficult to distinguish schizophrenia spectrum disorder in the early phase. Early symptoms are multiform, and the rapid mental development as well as considerable developmental differences between individuals during adolescence makes it more difficult to assess these disorders (17). Atypical characteristics related to early-onset psychosis detected in earlier research have been described, for example, as the dominance and greater severity of primary negative symptoms which may mask the more obvious psychotic symptoms (8). In young people the predominance of negative symptoms may make it difficult to distinguish, for example, psychosis from severe depression.

A sizeable group of children with complex developmental disorders and transient psychotic symptoms fall outside the current syndrome boundaries for psychotic disorders, but may nevertheless suffer from a variant of early-onset schizophrenia with some special features, such as earlier age of onset of psychotic symptoms and more serious depression (19). These patients share with very early-onset schizophrenia patients a pattern of premorbid developmental difficulties, a decline in cognitive ability and increased rate of schizophrenia spectrum disorder in first-degree relatives.

Another challenge in diagnosing psychosis in youths is that many adolescents displaying psychotic symptoms may not actually have a psychotic disorder. Although hallucinations or delusions are a characteristic of schizophrenia spectrum psychosis, psychotic symptoms may be present in other illnesses, like affective disorders, neurological conditions, acute intoxication and even in mentally healthy young people (6, 20-22). In post-traumatic conditions, short-term periods with brief hallucinatory experiences and rapid mood swings are common (21).

Psychotic symptoms are reported more commonly in early than in late adolescence but with increasing age these symptoms become increasingly predictive of diagnosable psychopathology. It is possible that hallucinatory and delusional experiences fall within the normal spectrum of experience during childhood but may be expected to cease in the course of development (20). Nevertheless, only a fraction of people with severe psychotic-like symptoms will develop an actual psychotic disorder (3, 22). However, the majority of adolescents reporting psychotic symptoms do have a diagnosable psychiatric disorder and these symptoms have been found to demonstrate a strong relationship with more severe psychopathology, indicating a high risk of multiple and more severe disorders (20).

Psychosis in adolescents has been studied less than in adults. Much of the research on early-onset schizophrenia spectrum psychosis is based on selected samples in treatment centres where patients undergo various screening procedures. To understand the natural course of early-onset schizophrenia spectrum disorder, it is important to study adolescents with psychoses in settings treating unselected patients. In this study we expected to have a representative sample of the adolescent population with severe mental disorders, since all adolescents in the Pirkanmaa Hospital District in need of psychiatric hospital care are treated in the same hospital, thus reducing socioeconomic and other confounding factors to a minimum.

Materials and methods

Site of the study

Tampere University Hospital provides all the adolescent psychiatric inpatient care for the inhabitants of a catchment area of 22 municipalities including both urban and rural areas. The 13- to 17-year-old population numbers about 28,000 (<http://tilastokeskus.fi/til/vaerak/index.html>). During the study period, adolescents aged 13 to 17 years old could be admitted to two wards with 12 beds each.

Data collection

All the admissions to the adolescent psychiatric wards of Tampere University Hospital in the period of 2001-2006 were identified in hospital databases. Adolescents diagnosed with schizophrenia spectrum psychosis (F20-F29 in ICD 10) for the first time

in their lives, during a hospitalization within the period of the data collection, were included in the study as psychosis group patients. Previous hospitalizations with other diagnoses were allowed. The next patient with no schizophrenia spectrum diagnosis to be hospitalized after each schizophrenia spectrum psychosis patient was included in the study as a control. If an adolescent was already included in the study, the next patient admitted was included in the data so that nobody was included in the study more than once. A retrospective chart review with a structured data collection form was involved. The data collection did not involve personal interviews or surveys with the patients. The study was duly approved by the ethics committee of Pirkanmaa Hospital District.

The study group

As each adolescent was included in the study only once, the final study sample comprised 218 adolescent patients of whom 106 were diagnosed with schizophrenia spectrum psychosis for the first time in their lives and 112 with other diagnoses.

Measures

Sociodemographic characteristics collected were age, sex and family situation (living with parent(s)/with foster parent(s)/in child welfare institution/independently). Previous treatment history was recorded whether or not the adolescent had been treated in specialized child and adolescent psychiatric community care (yes/no/unclear according to case histories) or inpatient care (yes/no/unclear). If the adolescent had previously lived and been treated in another hospital district, exact details of previous treatment history were not always to be found in the medical records of the study unit. When unclear, previous treatment was for the analyses coded "no".

Information recorded relating to the present hospitalization were the referring agent (primary care, GP/child or adolescent psychiatrist/other medical specialist), mode of referral (voluntary/involuntary), dates of admission and discharge, and involuntary detainment order (yes/no).

Symptoms displayed by the adolescents were collected from the referral and the medical records written during the index hospitalization. Twenty-one core symptoms of adolescent inpatients were recorded (yes/no) on a checklist (see Table 1). The list was originally developed as an aid in admission situations and is currently being used in clinical work in the study clinic as well as in research (23, 24).

Adverse family life events or conditions were recorded with the help of a structured 10-item checklist (see Table 2). The list was originally developed as an aid in admission situations and has been used in the study clinic and elsewhere both in clinical work and research (23, 24). Adverse family life events/conditions were recorded from referral and/or medical records written during the index hospitalization. Length of stay was calculated from dates of admission and discharge.

Psychiatric diagnoses were collected as given/confirmed at discharge by the senior adolescent psychiatrist (J.V.) in charge of the study unit according to the ICD-10. Diagnoses used in the analyses are classified as follows: substance abuse related disorders (F10-F19), schizophrenia spectrum disorders (F20-F29), mood disorders (F30-F39), anxiety disorders (F40-F49), somatoform disorders (F50-F59), personality disorders (F60-F69), mental retardation (F70-F79), developmental disorders (F80-F89), conduct disorders (F90-F99), non-psychiatric (somatic) diagnosis and Z-codes.

Medications given during hospitalization and prescribed at discharge were recorded. Medications were classified by therapeutic category level as follows: antipsychotics, antidepressants, antiepileptics, anxiolytics and hypnotics.

Similar information was collected of the subjects' first ever psychiatric inpatient treatment when appropriate.

Statistical analyses

Frequencies of the features studied are given. Sociodemographic characteristics, previous treatment, referring agents, symptoms, diagnoses and adverse family life events and conditions, medications prescribed and length of stay were compared between those diagnosed with schizophrenia spectrum psychosis at index inpatient period and those with other diagnoses using cross-tabulations with chi-square statistics and t-test or Mann-Whitney test where appropriate. Age and sex adjusted associations were studied using logistic regression, entering diagnosis (F20-F29 / other) as the dependent variable, and sex, age and the variables studied each in turn as independent variables. Age and sex adjusted Odds Ratios (OR) with 95% confidence intervals (OR, 95% CI) are given for risk of psychosis diagnosis according to sociodemographic characteristics, treatment characteristic, psychiatric symptoms and family adversities. Statistical significance was basically set at level of $p < 0.05$ but adjusted with Bonferroni correction for multiple testing regarding symptoms and family adversities.

Table 1. Symptoms displayed by adolescent psychiatric inpatients diagnosed with schizophrenia spectrum psychosis (F20-F29) and controls with no diagnosis of schizophrenia spectrum psychosis, % (N), odds ratio (OR) with 95% confidence interval (CI).

Symptom	Schizophrenia spectrum psychosis (N=106)	No schizophrenia spectrum psychosis (N=112)	p	OR (95% CI)	p (controlled for age and sex)
suicidal ideation and talk	50.9 % (54)	58 % (65)	0.29	0.73 (0.42 -1.26)	0.26
suicide attempt	9.4 % (10)	15.2 % (17)	0.20	0.55 (0.24 -1.29)	0.17
self-harming behaviour¹	46.2 % (49)	30.4 % (34)	0.02	2.05 (1.14 -3.69)	0.02
positive psychotic symptoms¹	100 % (106)	21.4 % (24)	<0.005	NA	NA
depression	81.1 % (86)	80.4 % (90)	0.89	0.98 (0.48 -1.99)	0.95
manic behaviour	9.4 % (10)	5.4 % (6)	0.25	1.51 (0.50 -4.55)	0.47
non-physical aggression towards other people	18.9 % (20)	17.0 % (19)	0.71	1.31 (0.64 -2.70)	0.47
temper tantrums	11.3 % (12)	11.6 % (13)	0.95	1.04 (0.45 -2.44)	0.92
violent behaviour towards other people	24.5 % (26)	22.3 % (25)	0.70	1.34 (0.69 -2.61)	0.39
breaking and destroying objects	12.3 % (13)	11.6 % (13)	0.88	1.25 (0.53 -2.93)	0.61
inappropriate sexual behaviour	8.5 % (9)	11.6 % (13)	0.45	0.68 (0.28 -1.68)	0.41
alcohol abuse	36.8 % (39)	41.1 % (46)	0.52	0.81 (0.47 -1.41)	0.46
substance use	21.7 % (23)	13.4 % (15)	0.11	1.75 (0.85 -3.60)	0.13
truancy/school refusal	23.6 % (25)	33.0 % (37)	0.12	0.64 (0.35 -1.16)	0.14
property crimes	6.6 % (7)	13.4 % (15)	0.10	0.50 (0.19 -1.32)	0.16
eating disorder symptoms	23.6 % (25)	14.3 % (16)	0.08	1.84 (0.91 -3.70)	0.09
isolation	6.6 % (7)	1.8 % (2)	0.07	3.74 (0.74 -18.81)	0.11
impulse control problems	7.5 % (8)	12.5 % (14)	0.23	0.61 (0.24 -1.55)	0.30
running away	7.5 % (8)	17.0 % (19)	0.04	0.38 (0.16 -0.93)	0.03
anxiety (generalized, obsessivecompulsive, phobias, panic disorder symptoms)	20.8 % (22)	17.0 % (19)	0.47	1.26 (0.64 -2.50)	0.51
attention problems	3.8 % (4)	8.9 % (10)	0.12	0.40 (0.12 -1.31)	0.13
other	26.4 % (28)	18.8 % (21)	0.18	1.59 (0.83 -3.03)	0.16

¹ Differences statistically significant after Bonferroni correction for multiple testing are highlighted in bold.

Table 2. Family adversities among the adolescent inpatients diagnosed with schizophrenia spectrum psychosis (F20-F29) and controls with no diagnosis of schizophrenia spectrum psychosis, % (N), sex and age adjusted odds ratio (OR) with 95% confidence interval (CI).

	Schizophrenia spectrum psychosis (N=106)	No schizophrenia spectrum psychosis (N=112)	p	OR (95% CI)	p (controlled for age and sex)
parental substance use problems	16.0 % (17)	24.1 % (27)	0.14	0.59 (0.30 -1.17)	0.13
parental severe mental disorder	16.0 % (17)	11.6 % (13)	0.34	1.46 (0.67 -3.18)	0.35
parental divorce or separation	12.3 % (13)	17.9 % (20)	0.25	0.61 (0.28 -1.32)	0.21
family violence¹	6.6 % (7)	19.6 % (22)	0.005	0.30 (0.12 -0.75)	0.01
severe problems related to siblings	9.4 % (10)	13.4 % (15)	0.36	0.65 (0.27 -1.53)	0.32
bereavement	9.4 % (10)	10.7 % (12)	0.75	0.86 (0.36 -2.10)	0.75
parental severe somatic illness	4.7 % (5)	9.8 % (11)	0.15	0.45 (0.15 -1.34)	0.15
severe financial difficulties	5.7 % (6)	9.8 % (11)	0.25	0.54 (0.19 -1.52)	0.25
(suspected) sexual abuse within the family	2.8 % (3)	6.3 % (7)	NA	0.37 (0.08 -1.54)	0.17
other	13.2 % (14)	19.6 % (22)	0.20	0.59 (0.28 -1.24)	0.16

¹ Differences statistically significant after Bonferroni correction for multiple testing are highlighted in bold.

Results

Sociodemographics, pathway to care and index treatment

Of the study cohort (N = 218), 141 (64.7%) were girls and 77 (35.3%) were boys. Their age ranged from 10 to 18 years, mean (standard deviation, SD) 15.8 (1.31) years. Of the adolescents, 32.1% were referred to the index treatment by doctors in primary health care, 57.4% by child or adolescent psychiatrists and 10.6% by other medical specialists. Prior to hospitalization, 76.6% of the adolescents were living with parent(s), 7.8% with foster parent(s), 8.7% in child welfare institutions and 6.9% independently (in boarding schools, communes, with partners, etc.).

Of the cohort, 76.6% had previously been treated in specialist adolescent (or child) psychiatric services, 26.6% had been hospitalized before, and of those, 57.9% had been treated in adolescent psychiatry units, 40.4% in child psychiatry units and only one person had been treated in an adult psychiatric unit. Of the adolescents, 35.8% had been referred involuntarily and 18.8% detained involuntarily. Mean (SD) length of stay was 77.78 (108.6) days, median 45.5 days. Variation of the length of stay was considerable.

Adolescents with a schizophrenia spectrum diagnosis did not differ from the control inpatients regarding age, sex and living arrangements before the index hospitalization. Adolescents in the schizophrenia spectrum psychosis group were more frequently referred to the index inpatient care by child or adolescent psychiatrists (63.9% vs. 50.9%), but less commonly referred by primary care practitioners (28.3% vs. 35.7%) or non-psychiatric specialties (7.5% vs. 13.4%, $p = 0.04$). Involuntary referral was equally common among subjects and controls, but those with a schizophrenia spectrum diagnosis were more commonly detained involuntarily than the controls (76.7% vs. 23.5%, $p < 0.05$).

Controlling for age and sex did not alter the associations of referring agent, living conditions or involuntary detainment with group membership.

Medication

During hospitalization 85.3% of the adolescents were treated with antipsychotics, 23.4% with antidepressants, 5.5% with antiepileptics, 55.0% with anxiolytics and 56.4% with hypnotics. At discharge 74.8% of the adolescents were prescribed antipsychotics, 15.1% antidepressants, 5.0% antiepileptics, 6.4% anxiolytics, 2.3% hypnotics and 0.5% stimulants. Adolescents diagnosed with schizophrenia spectrum psychosis were more frequently prescribed antipsychotics during treatment than those with other diagnoses (99.1% vs. 72.3%, $p < 0.05$). Moreover, anxiolytics (74.5% vs. 36.6%, $p < 0.05$) and hypnotics (68.9 vs. 44.6%, $p < 0.05$) were more often prescribed to adolescents in the psychosis group. At discharge, those diagnosed with schizophrenia spectrum psychosis were more often on antipsychotics (98.1% vs. 53.6%, $p < 0.05$) and anxiolytics (10.5% vs. 2.7%, $p = 0.02$). Adolescents in the psychosis group were less often on antidepressants (6.7% vs. 23.2%, $p < 0.05$). These associations between medication and group membership persisted after controlling for age and sex. Length of stay was longer among adolescents diagnosed with schizophrenia spectrum psychosis than those diagnosed with other diagnoses (99.4 days vs. 57.4 days, $p < 0.05$).

Family adversities

Most common adverse family life events or conditions were parental substance abuse problems (20.2%), divorce (15.1%), severe mental disorders of parents (13.8%) and domestic violence (13.3%) (Table 2). There were no statistically significant differences between the study groups as regards adverse family life events or conditions with the exception of domestic violence, which was present more often among adolescents with other than a schizophrenia spectrum diagnosis (19.6% vs. 6.6%, $p < 0.05$) (Table 2). However, there was a trend for all events or conditions to be more common among those with other diagnoses although no statistically significant differences were detected. The only exception was severe mental disorders in parent(s), recorded in the histories of 16.0% of those in the schizophrenia spectrum psychosis group vs. 11.3% of the others ($p = 0.34$). Among those diagnosed with schizophrenia spectrum psychosis, 55.7% ($N = 59$) had at least one family adversity recorded in their case files and among those with other diagnoses 63.4% ($N = 71$) ($p = 0.25$). On average 0.95 family adversities were reported among adolescents diagnosed with psychosis and among those with other diagnoses 1.42. This difference was statistically significant ($p = 0.02$). Adjusting for sex and age did not change the findings regarding adverse family life events and group membership.

Symptom presentation and diagnostic distribution

The most common symptoms reported were depression (80.7%), psychotic symptoms (59.6%) and suicidal ideation (54.6%) (Table 1). Surprisingly, there were not many differences between the groups studied regarding symptoms recorded. Adolescents diagnosed with schizophrenia spectrum psychosis presented more often with self-destructive behaviour (self-cutting, etc.) and with positive psychotic symptoms than adolescents with other diagnoses. Running away at first seemed less common among the schizophrenia spectrum psychosis group than among the control group, but did not reach statistical significance after Bonferroni correction. Adjusting for age and sex did not alter the associations detected in bivariate analyses between the diagnosis and psychiatric symptoms (Table 1).

Among adolescents diagnosed with schizophrenia spectrum psychosis, the mean number of symptoms reported was 5.3 (when using the 21-item checklist, the item "other" was excluded from the analysis) and among adolescents with other diagnoses 4.6. The difference was statistically significant ($p = 0.01$, t-test). However, because all the adolescents in the psychosis group presented with positive psychotic symptoms, when

excluding positive psychotic symptoms from the analysis, both adolescents in the psychosis group and in the other diagnoses group presented, on average, with 4.3 symptoms.

The most common primary diagnoses at discharge were schizophrenia spectrum disorders (F20-F29) (45.4%), mood disorders (F30-F39) (26.6%) and conduct disorders (F90-F99) (12.8%) (Table 3). The psychosis group patients by definition all had a diagnosis in the F20-F29 group, but in seven cases this was not recorded as the first diagnosis. The comparison group adolescents most commonly presented with mood disorders (F30-F39) and conduct disorders (F90-F99).

Main diagnosis	Schizophrenia spectrum psychosis (N=106)	No schizophrenia spectrum psychosis (N=112)	All (N=218)
F10-F19	0	0.9 % (1)	0.5 % (1)
F20-F29	93.4 % (99)	0	45.4 % (99)
F30-F39	4.7 % (5)	47.3 % (53)	26.6 % (58)
F40-F49	0	10.7 % (12)	5.5 % (12)
F50-F59	0.9 % (1)	7.1 % (8)	4.1 % (9)
F60-F69	0	0	0
F70-F79	0	0	0
F80-F80	0	5.4 % (6)	2.8 % (6)
F90-F99	0.9 % (1)	24.1 % (27)	12.8 % (28)
other	0	4.5 % (5)	2.3 % (5)

Previous psychiatric treatment

Adolescents diagnosed with schizophrenia spectrum psychosis had less frequently been treated in specialist child and adolescent psychiatric services prior to the index hospitalization than had adolescents with other diagnoses (68.9% vs. 83.9%, $p = 0.03$). Of those diagnosed with schizophrenia spectrum psychosis 21.7%, and of those with other diagnoses 31.3% had been previously hospitalized ($p = 0.11$).

There were 58 patients with one or more previous hospitalizations: Ten patients with two and seven patients with three previous hospitalizations, and four patients had been hospitalized four times before the index period. Adolescents with a diagnosis of schizophrenia spectrum psychosis at index hospitalization had, on average, 1.31 hospitalizations (95% CI of 1.17-1.45, min 1, max 5, median 1) and adolescents in the control group 1.51 (95% CI of 1.34-1.68, min 1, max 5, median 1).

Age and sex distributions at first ever hospitalization did not differ between those later diagnosed with schizophrenia spectrum psychosis and those with other diagnoses at index hospitalization. At the beginning of the first ever hospitalization the age of the patients (N = 57, further information about the hospitalization period was missing for one patient) ranged from 6 to 17 years, mean (SD) 13.6 (2.84) years. Among those later diagnosed with schizophrenia spectrum psychosis, the mean age (SD) was 14.3 (2.86) years and those given other diagnoses 13.2 (2.79) years ($p = 0.08$). Of those who had previous hospitalizations, 38 (65.5%) were girls and 20 (34.5%) were boys. Of those diagnosed at index hospitalization with psychosis, 73.9% were girls, and of those given other diagnoses at index hospitalization, 60.0% were girls ($p = 0.40$).

Symptoms reported during the first ever hospitalization did not differ among those later diagnosed with schizophrenia spectrum psychosis and controls with the exception of illegal drug use, which was more common among those later diagnosed with schizophrenia spectrum psychosis (Table 4). Among adolescents diagnosed with a schizophrenia spectrum psychosis at index hospitalization the mean number of symptoms recorded at first ever hospitalization was 4.7 (when using the 21-item checklist, the item "other" was excluded from the analysis) and among adolescents with other diagnoses at index hospitalization it was 4.0. The difference was not statistically significant ($p = 0.167$) (Mann-Whitney-test).

The mean duration of the first lifetime hospitalization period was 48.4 days in the group at index hospitalization presenting with schizophrenia spectrum psychosis (95% CI of 21.8-75.0, min 1 day, max 238 days, median 25 days) and 105.7 days (95% CI of 35.0-171.3, min 1 day, max 1116 days, median 45.5 days) in the control group.

Table 4. Symptoms at first ever psychiatric hospitalization among adolescents diagnosed with schizophrenia spectrum psychosis (F20-F29) during index admission, and controls with no diagnosis of schizophrenia spectrum psychosis, % (N), odds ratio (OR) with 95% confidence interval (CI).

Symptom	Diagnosis at index admission				
	Schizophrenia spectrum psychosis F20-F29 (N=21)	No schizophrenia spectrum psychosis (N=34)	p	OR (95% CI)	p (controlled for age and sex)
suicidal ideation and talk	57.1 % (12)	55.9 % (19)	0.93	0.93 (0.29 -2.95)	0.90
suicide attempt	4.8 % (1)	8.8 % (3)	~1	0.24 (0.02 -3.52)	0.30
self-harming behaviour	47.6 % (10)	38.2 % (13)	0.49	1.39 (0.45 -4.35)	0.57
positive psychotic symptoms	42.9 % (9)	20.6 % (7)	0.08	2.64 (0.77 -9.03)	0.12
depression	85.7 % (18)	73.5 % (25)	0.34	2.21 (0.51 -9.53)	0.29
manic behaviour	0 % (0)	2.9 % (1)	~1	NA	~1
non-physical aggression towards other people	23.8 % (5)	23.5 % (8)	~1	1.01 (0.27 -3.75)	0.99
temper tantrums	14.3 % (3)	14.7 % (5)	~1	1.72 (0.27 -10.81)	0.56
violent behaviour towards other people	23.8 % (5)	17.6 % (6)	0.73	1.82 (0.40 -8.29)	0.44
breaking and destroying objects	14.3 % (3)	11.8 % (4)	~1	1.50 (0.26 -8.52)	0.65
inappropriate sexual behaviour	9.5 % (2)	8.8 % (3)	~1	0.75 (0.10 -5.62)	0.78
alcohol abuse	23.8 % (5)	11.8 % (4)	0.28	2.05 (0.47 -9.01)	0.34
substance use¹	23.8 % (5)	0 % (0)	0.01	NA	NA
truancy/school refusal	9.5 % (2)	20.6 % (7)	0.46	0.36 (0.06 -1.99)	0.24
property crimes	4.8 % (1)	8.8 % (3)	~1	0.27 (0.02 -3.79)	0.33
eating disorder symptoms	33.3 % (7)	20.6 % (7)	0.29	1.79 (0.52 -6.24)	0.36
isolation	4.8 % (1)	2.9 % (1)	~1	1.47 (0.08 -26.08)	0.79
impulse control problems	0 % (0)	5.9 % (2)	0.53	NA	~1
running away	9.5 % (2)	5.9 % (2)	0.63	1.06 (0.12 -9.76)	0.96
anxiety (generalized, obsessivecompulsive, phobias, panic disorder symptoms)	9.5 % (2)	17.6 % (6)	0.70	0.50 (0.09 -2.88)	0.44
attention problems	0 % (0)	8.8 % (3)	0.29	NA	~1
other	28.6 % (6)	29.4 % (10)	0.95	1.40 (0.37 -5.31)	0.62

¹ Differences statistically significant after Bonferroni correction for multiple testing are highlighted in bold.

Discussion

There were few differences in the symptom profiles between the adolescent inpatients with first-episode schizophrenia spectrum psychosis (F20-F29) and control inpatients with other severe mental disorders. Adolescents diagnosed with schizophrenia spectrum psychosis only presented more often with self-destructive behaviour and, as might be expected, positive psychotic symptoms. On the other hand, positive psychotic symptoms were also quite common among adolescents diagnosed with other than psychotic disorder. This is in line with earlier studies showing that positive psychotic symptoms are also prevalent in a wide range of non-psychotic psychopathologies in children and adolescents (20, 21).

Both groups presented with diverse, wide-ranging symptoms. In earlier studies of early-onset schizophrenia, patients have been highly symptomatic and significantly impaired across multiple domains. They have been severely ill, with high rates of psychotic symptoms, mood and anxiety symptoms, behavioural problems, social and functional impairment and cognitive deficits (10, 25, 26). Our findings underline that complex, diverse symptoms are characteristic for adolescent severe mental disorders at large. Hospitalized patients, in spite of the diagnosis, are those with the most varied symptom profiles and behavioural problems, and they present, for example, with more severe anxiety. It is further possible that some patients in the control group will also develop an actual psychotic disorder later since prodromal symptoms of psychosis are often non-specific (17).

Although the study groups did not differ much from each other as regards symptom profiles, adolescents diagnosed with psychosis were treated longer, they were more commonly treated involuntarily and were more commonly prescribed antipsychotic and anxiolytic medication. Further, adolescents with schizophrenia spectrum psychoses were more commonly referred by child or adolescent psychiatrists. This implies that adolescents with psychosis were more seriously disturbed at the time of the admission, their functioning was more severely impaired and they needed more specialized care and more intensive hospital care. Longer treatment period may also imply that the symptoms of the adolescents with schizophrenia spectrum psychosis were more severe, at least more tenacious or harder to control if not different regarding symptom profile than among those with other diagnoses.

In adolescent psychiatric outpatient settings mood disorders comprise one of the most common clinical problems (27, 28). Dysphoria, anxiety and behavioural disturbances are common findings in all mentally ill young people regardless of their diagnostic status (26). Likewise in our study depression was a common symptom in both groups. In spite of depression, antidepressants were not commonly used. It is possible that in the schizophrenia spectrum psychosis group alleviation of the psychotic symptoms by antipsychotics was expected to have a favourable impact on mood as well.

Adolescents with diagnoses other than schizophrenia spectrum psychosis presented with more numerous family adversities than the schizophrenia spectrum group. This may suggest that the symptoms of the adolescents with other diagnoses were more reactive than the symptoms of those with schizophrenia spectrum psychosis. The psychotic symptoms in the control group might even be dissociative symptoms, although it was not possible to reliably assess this possibility in case files and this remains a possibility to be considered in clinical work and research in the future. Our finding does not, however, support the idea that actual schizophrenia spectrum psychosis is connected to traumatic history but is more likely an endogenous phenomenon. The greater prevalence of severe mental disorders among parents in the schizophrenia spectrum group suggests a greater familial risk, even though the difference from the control group was not statistically significant. Unfortunately the diagnoses of the parents could not be obtained.

Premorbid abnormalities are common features of early-onset psychotic disorders. Among the most common early signs and symptoms in schizophrenia spectrum disorder reported in earlier studies are sleep disturbance, anxiety, anger/irritability, depressed mood, deterioration in functioning, social withdrawal, poor concentration, suspiciousness, loss of motivation and of drive and low energy (16, 18). Young people with schizophrenia have been shown to have higher rates of premorbid social withdrawal and global impairment and tend to have fewer friends. The social withdrawal and peer problems specific to young people with schizophrenia likely represent early manifestations of negative symptoms (21). In that regard, it was somehow surprising that symptoms reported during the first ever hospitalization period did not differ among those diagnosed later with schizophrenia spectrum psychosis and those diagnosed with other disorders, with the exception of illegal drug use, which was more common among those diagnosed later with schizophrenia spectrum psychosis. Moreover, adolescents with schizophrenia spectrum psychosis at index hospitalization had been treated less frequently in specialist child and adolescent psychiatric services. The first hospitalization period ever seemed to be shorter among those in the subsequent

psychosis group than those in the control group although the difference did not reach statistical significance. This suggests that in the very early phases of their disorder development, the future schizophrenia spectrum psychosis group adolescents had appeared even less severely disturbed than those hospitalized due to other than schizophrenia spectrum disorder at index hospitalization.

Illegal drug use being the only difference between the study groups at first ever hospitalization was an interesting finding. There is mounting evidence that early and regular use of cannabis is associated with subsequent increases in psychotic illness and may bring forward the onset of schizophrenia (29). Many studies have reported cannabis use disorder to be linked to a younger age of onset in first-episode psychosis (30). However, in some studies the opposite has been found (31, 32). One potential explanation is that younger (pre)psychotic adolescents are less likely to come into contact with cannabis than older adolescents (33). This may counteract the potential (neurotoxic) effect of cannabis use causing an earlier onset of psychosis. Unfortunately our data does not indicate whether the early drug use was specifically cannabis, but it is known from large adolescent health surveys that if Finnish adolescents experiment with or take any drug other than alcohol, cannabis and inhalants are more common than other substances (www.thl.fi/kouluterveyskysely).

Methodological considerations

The present study has the advantage of comprising all adolescents from a well-defined catchment area who required inpatient admission due to schizophrenia spectrum psychosis. No other inpatient service is available for this population, thus the material suffers no selection bias, neither among the index patients nor among the controls. The study was based on register data. It suffers no bias due to refusal to participate. The retrospective study design ensures that practices of interest were not influenced by the study. The material collected was readily available for all the cases, and it was recorded into the data in a structured way, which adds to the data quality. Symptoms and family risk factors were rated as present if clearly stated in the medical records. It is possible that the actual symptoms of the subjects were more numerous than recorded in the data. In case of uncertainty or no explicit comments on certain types of symptoms, they were rated as not present. The same concerns family risk factors. Symptoms and family adversities are, however, highly prioritized in adolescent psychiatric assessments, and they are likely to be carefully evaluated for all patients in clinical practice (34).

We compared adolescents hospitalized with first-episode schizophrenia spectrum psychosis (F20-F29) to adolescents hospitalized due to other severe mental disorders. Inpatient care is restricted in the study area to severe mental disorders and most severe situations requiring constant supervision. In our study, adolescents were diagnosed with schizophrenia spectrum psychosis for the first time in their lives and they were referred to hospital during the acute phase of their illness. This allowed us to study our patients in the very early phases of their psychotic disorder.

Diagnoses were recorded as given by the treating psychiatrists according to the ICD-10, which is the diagnostic classification officially used in Finland. While structured research diagnosis could have added to the reliability of the diagnostic information, it has nevertheless been shown that diagnoses made in Finnish specialist psychiatric health services are sufficiently reliable, particularly as regards the most severe diagnoses (35, 36). The diagnoses were all made or confirmed by the same senior adolescent psychiatrist (J.V.) competent in diagnostic procedures such as K-SADS (Schedule for Affective Disorders and Schizophrenia for school-aged children), SCAN (Schedules for Clinical Assessment in Neuropsychiatry), SCID (Structured Clinical Interview for DSM Disorders) and SIPS (Structured Interview for Prodromal Syndromes).

A limitation is that the study group was small, which may be a cause of type-II errors, particularly regarding the comparisons concerning the first ever hospitalization where the groups were even smaller. This study concerns adolescent-onset schizophrenia spectrum psychosis, and it may not be extrapolated to adult-onset schizophrenia, because the adolescents in the control group may, of course, later meet the criteria of schizophrenia spectrum psychosis.

Since the data collection period, the number of adolescent psychiatric beds has been reduced in the study hospital. This means that criteria for inpatient admission have become stricter. Thus, those when admitted will likely be more severely ill than at data collection time. This will likely hold true particularly regarding other disorders than schizophrenia spectrum. Practices with schizophrenia spectrum disorder are likely rather similar, as at the data collection time, partly based on preliminary findings from the data here reported, from which regional guidelines for treatment of adolescent-onset schizophrenia spectrum psychosis were written (37) and are still in use. Thus, differences between schizophrenia spectrum and other adolescent psychiatric inpatients may towards today have grown smaller still, even if they were already few in the presented data.

Findings based on retrospective chart review can only be as reliable as the charts. The structured data collection form used in the present study was planned with the knowledge of what detail can be found in psychiatric case files, and thus we could carry out a comprehensive review on case files on a chosen level. As the study was retrospective and we did not contact the patients, we do not have structured information of, for example, symptom self-rating scales that may not have been used systematically, and what is more, were at the time of data collection, not archived permanently. Nowadays, more detailed information such as symptom scales can be archived in electronic form. Thus, nowadays one could add to the data collection form some more detailed entries. However, the results presented here would hardly be changed due to this.

Conclusion

Adolescents hospitalized due to first-episode schizophrenia spectrum psychosis differ surprisingly little from those hospitalized due to other severe mental disorders. The few differences at first ever admission between those subsequently diagnosed with schizophrenia spectrum psychosis during adolescence and those diagnosed with other severe mental disorders offer specialists little help in the prevention of schizophrenia spectrum psychosis during adolescent years. Across developmental years, symptom presentation at early contact has little predictive value for later diagnosis.

References

1. van Os J, Kapur S. Schizophrenia. *Lancet* 2009; 374: 635-645.
2. Perälä J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsä E, Pirkola S, Partonen T, Tuulio-Henriksson A, Hintikka J, Kiesepää T, Härkänen T, Koskinen S, Lönnqvist J. Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Arch Gen Psychiatry* 2007; 64: 19-28.
3. van Os J, Hanssen M, Bijl RV, Vollebergh W. Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. *Arch Gen Psychiatry* 2001; 58: 663-668.
4. Newman DL, Moffitt TE, Caspi A, Magdol L, Silva PA, Stanton WR. Psychiatric disorder in a birth cohort of young adults: prevalence, comorbidity, clinical significance, and new case incidence from ages 11 to 21. *J Consult Clin Psychol* 1996; 64: 552-562.
5. Paus T, Keshavan M, Giedd JN. Why do many psychiatric disorders emerge during adolescence? *Nat Rev Neurosci* 2008; 9: 947-957.

6. McClellan J, Stock S, American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. *J Am Acad Child Adolesc Psychiatry* 2013; 52: 976-990.
7. Thomsen PH. Schizophrenia with childhood and adolescent onset: a nationwide register-based study. *Acta Psychiatr Scand* 1996; 94: 187-193.
8. Ballageer T, Malla A, Manchanda R, Takhar J, Haricharan R. Is adolescent-onset first-episode psychosis different from adult onset? *J Am Acad Child Adolesc Psychiatry* 2005; 44: 782-789.
9. McClellan JM, Werry JS, Ham M. A follow-up study of early onset psychosis: comparison between outcome diagnoses of schizophrenia, mood disorders, and personality disorders. *J Autism Dev Disord* 1993; 23: 243-262.
10. Werry JS, McClellan JM, Chard L. Childhood and adolescent schizophrenic, bipolar, and schizoaffective disorders: a clinical and outcome study. *J Am Acad Child Adolesc Psychiatry* 1991; 30: 457-465.
11. Hafner H, Nowotny B. Epidemiology of early-onset schizophrenia. *Eur Arch Psychiatry Clin Neurosci* 1995; 245: 80-92.
12. Norman RM, Malla AK. Duration of untreated psychosis: a critical examination of the concept and its importance. *Psychol Med* 2001; 31: 381-400.
13. Hlastala SA, McClellan J. Phenomenology and diagnostic stability of youths with atypical psychotic symptoms. *J Child Adolesc Psychopharmacol* 2005; 15: 497-509.
14. McKenna K, Gordon CT, Lenane M, Kaysen D, Fahey K, Rapoport JL. Looking for childhood-onset schizophrenia: the first 71 cases screened. *J Am Acad Child Adolesc Psychiatry* 1994; 33: 636-644.
15. Angold A, Costello EJ, Erkanli A. Comorbidity. *J Child Psychol Psychiatry* 1999; 40: 57-87.
16. Gourzis P, Katrivanou A, Beratis S. Symptomatology of the initial prodromal phase in schizophrenia. *Schizophr Bull* 2002; 28: 415-429.
17. McGorry PD, McFarlane C, Patton GC, Bell R, Hibbert ME, Jackson HJ, Bowes G. The prevalence of prodromal features of schizophrenia in adolescence: a preliminary survey. *Acta Psychiatr Scand* 1995; 92: 241-249.
18. Norman RM, Scholten DJ, Malla AK, Ballageer T. Early signs in schizophrenia spectrum disorders. *J Nerv Ment Dis* 2005; 193: 17-23.
19. Kumra S, Jacobsen LK, Lenane M, Zahn TP, Wiggs E, Alaghband-Rad J, Castellanos FX, Frazier JA, McKenna K, Gordon CT, Smith A, Hamburger S, Rapoport JL. "Multidimensionally impaired disorder": is it a variant of very early-onset schizophrenia? *J Am Acad Child Adolesc Psychiatry* 1998; 37: 91-99.
20. Kelleher I, Keeley H, Corcoran P, Lynch F, Fitzpatrick C, Devlin N, Molloy C, Roddy S, Clarke MC, Harley M, Arseneault L, Wasserman C, Carli V, Sarchiapone M, Hoven C, Wasserman D, Cannon M. Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. *Br J Psychiatry* 2012; 201: 26-32.
21. McClellan J, Breiger D, McCurry C, Hlastala SA. Premorbid functioning in early-onset psychotic disorders. *J Am Acad Child Adolesc Psychiatry* 2003; 42: 666-672.
22. Yung AR, Nelson B, Baker K, Buckley JA, Baksheev G, Cosgrave EM. Psychotic-like experiences in a community sample of adolescents: implications for the continuum model of psychosis and prediction of schizophrenia. *Aust N Z J Psychiatry* 2009; 43: 118-128.

23. Kaltiala-Heino R. Involuntary commitment and detainment in adolescent psychiatric inpatient care. *Soc Psychiatry Psychiatr Epidemiol* 2010; 45: 785-793.
24. Lindberg N, Sailas E, Kaltiala-Heino R. The copycat phenomenon after two Finnish school shootings: an adolescent psychiatric perspective. *BMC Psychiatry* 2012; 12: 91.
25. Frazier JA, McClellan J, Findling RL, Vitiello B, Anderson R, Zablotzky B, Williams E, McNamara NK, Jackson JA, Ritz L, Hlastala SA, Pierson L, Varley JA, Puglia M, Maloney AE, Ambler D, Hunt-Harrison T, Hamer RM, Noyes N, Lieberman JA, Sikich L. Treatment of early-onset schizophrenia spectrum disorders (TEOSS): demographic and clinical characteristics. *J Am Acad Child Adolesc Psychiatry* 2007; 46: 979-988.
26. McClellan J, McCurry C, Speltz ML, Jones K. Symptom factors in early-onset psychotic disorders. *J Am Acad Child Adolesc Psychiatry* 2002; 41: 791-798.
27. Biederman J, Faraone S, Mick E, Lelon E. Psychiatric comorbidity among referred juveniles with major depression: fact or artifact? *J Am Acad Child Adolesc Psychiatry* 1995; 34: 579-590.
28. Karlsson L, Pelkonen M, Ruutu T, Kiviruusu O, Heilä H, Holi M, Kettunen K, Tuisku V, Tuulio-Henriksson A, Törrönen J, Marttunen M. Current comorbidity among consecutive adolescent psychiatric outpatients with DSM-IV mood disorders. *Eur Child Adolesc Psychiatry* 2006; 15: 220-231.
29. Rey JM, Martin A, Krabman P. Is the party over? Cannabis and juvenile psychiatric disorder: the past 10 years. *J Am Acad Child Adolesc Psychiatry* 2004; 43: 1194-1205.
30. Barnes TR, Mutsatsa SH, Hutton SB, Watt HC, Joyce EM. Comorbid substance use and age at onset of schizophrenia. *Br J Psychiatry* 2006; 188: 237-242.
31. Baeza I, Graell M, Moreno D, Castro-Fornieles J, Parellada M, González-Pinto A, Payá B, Soutullo C, de la Serna E, Arango C. Cannabis use in children and adolescents with first episode psychosis: influence on psychopathology and short-term outcome (CAFEPS study). *Schizophr Res* 2009; 113: 129-137.
32. Schimmelmann BG, Conus P, Cotton S, Kupferschmid S, McGorry PD, Lambert M. Prevalence and impact of cannabis use disorders in adolescents with early onset first episode psychosis. *Eur Psychiatry* 2012; 27: 463-469.
33. Roxburgh A, Hall WD, Degenhardt L, McLaren J, Black E, Copeland J, Mattick RP. The epidemiology of cannabis use and cannabis-related harm in Australia 1993-2007. *Addiction* 2010; 105: 1071-1079.
34. Kaltiala-Heino R, Frojd S, Autio V, Laukkanen E, Narhi P, Rantanen P. Transparent criteria for specialist level adolescent psychiatric care. *Eur Child Adolesc Psychiatry* 2007; 16: 260-270.
35. Isohanni M, Mäkikyrö T, Moring J, Räsänen P, Hakko H, Partanen U, Koiranen M, Jones P. A comparison of clinical and research DSM-III-R diagnoses of schizophrenia in a Finnish national birth cohort. Clinical and research diagnoses of schizophrenia. *Soc Psychiatry Psychiatr Epidemiol* 1997; 32: 303-308.
36. Pihlajamaa J, Suvisaari J, Henriksson M, Heilä H, Karjalainen E, Koskela J, Cannon M, Lönnqvist J. The validity of schizophrenia diagnosis in the Finnish Hospital Discharge Register: findings from a 10-year birth cohort sample. *Nord J Psychiatry* 2008; 62: 198-203.
37. Väänänen JM, Hämäläinen P, Oksa R, Sillanpää A, Saarelainen S, Autere K, Viskari H, Roivas M, Ylitörmä M, Lappalainen A, Toivakka H. Ensipsykoosiin sairastuneen nuoren hoitoprosessi 3/2011. [http://pshp.fi/fi-FI/Sairaanhoitopiiri/Sairaanhoitopiirin_julkaisut/Julkaisusarja/Julkaisusarjan_julkaisut_2011\(51430\)](http://pshp.fi/fi-FI/Sairaanhoitopiiri/Sairaanhoitopiirin_julkaisut/Julkaisusarja/Julkaisusarjan_julkaisut_2011(51430)) [Retrieved 15 June 2016]

Emma Reponen, MD
University of Tampere, School of Medicine, Tampere, Finland

Juha Väänänen, MD, PhD
Tampere University Hospital, Department of Adolescent Psychiatry, Pitkäniemi, Finland

Riittakerttu Kaltiala-Heino, MD, PhD, professor
University of Tampere, School of Medicine, and Tampere University Hospital,
Department of Adolescent Psychiatry, Tampere, Finland

Correspondence:
riittakerttu.kaltiala-heino@uta.fi