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Childhood adversities and clinical symptomatology in first-episode psychosis

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ABSTRACT

In addition to severe traumatic experiences, milder, more common childhood adversities reflecting psychosocial burden may also be common in people with psychotic disorders and have an effect on symptomatology and functioning. We explored eleven negative childhood experiences and their influence on clinical symptoms among young adults with first-episode psychosis (FEP, $n = 75$) and matched population controls ($n = 51$). Individuals with FEP reported more adversities than controls. Specifically serious conflicts within the family, bullying at school, maternal mental health problems, and one's own and parents' serious illness during childhood were experienced by the patients more often than by controls. In the FEP group, the severity of adversity was associated with increased anxiety, manic, and obsessive-compulsive symptoms, but not with the severity of positive psychotic symptoms. Adversity produced a more pronounced effect on symptoms in male patients than in female patients. To conclude, in line with earlier studies of more chronic psychosis, a majority of the participants with FEP reported exposure to childhood adversities, with the FEP group reporting more adversities than controls. High levels of mood and anxiety symptoms in patients with FEP may be related to cumulative exposure to childhood adversities. This should be taken into account in the treatment for FEP.

1. Introduction

Negative childhood life events are risk factors for psychosis as well as other severe mental disorders. In WHO surveys, childhood adversities related to maladaptive family functioning were the strongest predictor of non-psychotic disorders (Kessler et al., 2010). A meta-analysis focusing on psychotic disorders found exposure to childhood adversities to be 2.7 times more common in psychosis patients than in healthy control subjects, adversities increasing the risk of psychosis at a 2.8 odds ratio (Varese et al., 2012b). Dose–response effects of childhood adversities on psychosis risk have also been reported (Trauelsen et al., 2015). In a recent review it was concluded that some psychotic disorders may be rooted in childhood adversities; however, adversities are neither sufficient nor necessary to cause psychotic disorders (Morgan and Gayer-Anderson, 2016).

The exposure to a death in the family increased the risk of psychosis in later life in a large population-based cohort study (Abel et al., 2014). Parental divorce or other long-term separation from a parent in childhood (Ajnakina et al., 2016; Morgan et al., 2007; Stilo et al., 2017) and childhood socioeconomic disadvantage (Wicks et al., 2010) have also been associated with an increased risk of adult psychosis. Negative family environment was associated with psychosis proneness in community samples from different countries (Wüsten and Lincoln, 2017).

Being a victim of school bullying has been found to be a risk factor for the development of psychotic symptoms in early adolescence (Kelleher et al., 2013; Schreier et al., 2009) and adulthood (Arseneault et al., 2010; Sourander et al., 2016) as well as a diagnosis of probable psychosis (Catone et al., 2015). Individuals with first-episode psychosis (FEP) have reported bullying victimization twice as often as controls, but bullying has been associated with psychotic-like symptoms even in the general population (Trotta et al., 2013).

Cognitive theories suggest that exposure to social adversities may lead an individual towards the development of cognitive schemas that view the world as threatening, and to attributing negative experiences

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to external factors (Howes and Murray, 2014). The biological mechanisms linking adversity and psychosis include HPA-axis dysregulation (Misiak et al., 2017). Schiavone et al. (2015) suggest that the reaction of the central nervous system to prolonged stressful events during childhood enhances the risk to psychosis. Specific traumatic events have also been associated with specific psychosis-related symptoms (Bentall et al., 2014; Misiak et al., 2017), emphasizing the need to a more detailed understanding of the relationship between childhood events and symptomology. Gender differences in the relationship between trauma and psychosis have been found, but the results have been mixed (Misiak et al., 2017).

In this study we focused on more common negative childhood experiences rather than severe traumatic events such as neglect or abuse. Previous studies have often concentrated on single severe traumas, and we wanted to see if these kinds of milder, often long-term stressors also play a role in psychosis. We use the term "adversities" in this paper to refer to the following negative childhood experiences: parental divorce, serious conflicts within the family, financial difficulties within the family, parents' frequent unemployment, parents' serious disease or disability, parental mental health and alcohol use-related problems, one's own serious or chronic illness, and bullying (Table 1). The set of experiences assessed in this study have been investigated previously in the Finnish general population surveys Health 2000 and Health 2011, and found to be associated with adult mental disorders, including anxiety, depressive, alcohol use, and comorbid disorders (Markkula et al., 2017; Pirkola et al., 2005), heavy drinking (Kestilä et al., 2008), and daily smoking (Kestilä et al., 2006) in early adulthood. The adversities are also associated with shorter telomere length (Kananen et al., 2010), which is a biological marker of stress exposure (Mathur et al., 2016). These individual studies have been conducted within a large longitudinal study of the Finnish population and the same questionnaire was now used in a FEP study.

The objectives of this study were to explore self-reported childhood adversities in FEP patients compared with controls and to examine whether some adversities were associated with specific clinical features. We hypothesized that more adversities would be reported by the FEP group compared to control participants, but the analyses between adversities and clinical features in FEP were more exploratory in nature.

2. Methods

2.1. Participants and study procedure

The patients participating in the Helsinki Psychosis Study (Keinänen et al., 2015; Mäntylä et al., 2015; Raij et al., 2015; Rikandi et al., 2017) were aged 18–40, with first psychiatric treatment contact for psychosis in hospitals and outpatient clinics of the City of Helsinki and Helsinki University Hospital between December 2010 and July 2016. As a criterion for inclusion, we defined psychosis as a score of at least 4 in the items assessing unusual thought content (delusions) or hallucinations in the Brief Psychiatric Rating Scale, Expanded version 4.0, BPRS (Ventura et al., 1993), corresponding to mild but definite delusions or hallucinations. Psychotic disorders that unarguably were substance-induced or caused by a general medical condition were excluded. Participants with FEP were interviewed with BPRS as soon as possible after they had commenced treatment and were able to give consent (baseline assessment). They were interviewed again after two and twelve months with BPRS and Structured Clinical Interview for the DSM-IV, Research Version, SCID (First et al., 2002). After the interview, the participants were asked to fill in a questionnaire with additional questions including questionnaire of childhood adversities.

A control sample was recruited from the population register from the same area with age and gender matched. They were assessed at baseline and at twelve months. Psychotic disorders were an exclusion criterion, as were any conditions preventing MRI, and chronic neurological or endocrinological diseases.

Only the baseline information has been used in the current article except from diagnosis information which was based on SCID interviews at 2 months and 12 months with all available information.

The study protocol was carried out in accordance with the Declaration of Helsinki. It was approved by the Ethics Committee of the Hospital District of Helsinki and Uusimaa, and by the institutional review boards of the National Institute for Health and Welfare, Helsinki, and the University of Helsinki. Both patients and controls gave written informed consent to participate in the study.

2.2. Measures

2.2.1. Interview

For the assessment of symptoms, we used the 24-item version of BPRS (Ventura et al., 1993) complemented by 3 domains (alogia, anhedonia-asociality and avolition-apathy) from the Scale for the Assessment of Negative Symptoms, SANS (Andreasen, 1989). Symptom severity was rated based on the past 7 days (current), but positive and disorganized symptoms were also rated from the worst period lifetime before the interview.

BPRS total score was calculated as a sum of items 1–24 (current ratings). The sum for BPRS positive symptoms was calculated as the sum of current hallucinations, unusual thought content, bizarre behavior, and conceptual disorganization item scores. Sum for BPRS

Table 1
Adverse childhood events in first-episode psychosis (FEP) and control groups. Frequency (%) or mean (SD), range.

	FEP, n = 75[a]	Controls, n = 51[a]	Group difference[b]
1. Did your family have long-term financial difficulties?	13/67 (19.4%)	6/45 (13.3%)	p = 0.401
2. Were your father or mother often unemployed although they wanted to work?	11/73 (15.1%)	3/50 (6.0%)	p = 0.120
3. Did your father or mother suffer from some serious disease or disability?	18/65 (27.7%)	5/49 (10.2%)	**p = 0.021**
4. Did your father have alcohol use-related problems?	16/69 (23.2%)	8/51 (15.7%)	p = 0.310
5. Did your mother have alcohol use-related problems?	5/73 (6.8%)	3/51 (5.9%)	p = 0.828
6. Did your father have any mental health problem, e.g., schizophrenia, other psychosis, or depression?	8/60 (13.3%)	3/49 (6.1%)	p = 0.204
7. Did your mother have any mental health problem, e.g., schizophrenia, other psychosis, or depression?	11/66 (16.7%)	2/49 (4.1%)	**p = 0.035**
8. Were there any serious conflicts within your family?	23/66 (34.8%)	7/48 (14.6%)	**p = 0.015**
9. Did your parents divorce?	19/74 (25.7%)	13/51 (25.5%)	p = 0.981
10. Were you yourself seriously or chronically ill?	8/66 (12.1%)	0/51	**p = 0.002**
11. Were you bullied at school?	31/69 (44.9%)	12/49 (24.5%)	**p = 0.023**
Sum of adversities 1–11	2.2 (2.0), 0–9	1.2 (1.6), 0–6	**U = 2542.5, p = 0.001**
Severity of adversity: factor score of adversities 1–10	0.26 (0.65), −0.47 to 2.04	−0.06 (0.53), −0.47 to 1.23	**U = 2524.9, p = 0.002**

[a] The frequency of yes-answers. Unsure answers considered as missing data.
[b] Specific adversities: Pearson Chi-square test or Likelihood ratio test. Continuous variables: Mann-Whitney test.

Table 2
Demographic and clinical information of the participants. Frequency (%) or mean (SD), range.

	FEP, n = 75	Controls, n = 51	Group difference[a]	FEP male, n = 49	FEP female, n = 26	Group difference[a]
Males	49 (65.3%)	34 (66.7%)	ns	–	–	–
Age	26.4 (6.0), 18.3–41.1	26.9 (5.6), 19.1–40.9	ns	25.9 (5.7), 18.5–40.3	27.4 (6.7), 18.3–41.1	ns
Inpatient	46 (61.3%)	–	–	32 (65.3%)	14 (53.8%)	ns
Schizophrenia spectrum[b]	49 (65.3%)	–	–	33 (67.3%)	16 (61.5%)	ns
BPRS total score	43.4 (10.3), 24–73	25.8 (3.0), 24–37	U = 3698.5, p < 0.001	41.4 (9.8), 24–64	47.3 (10.2), 29–73	U = 835.0, p = 0.027
BPRS positive symptoms, current	6.2 (4.0), 0–16	0.1 (0.3), 0–2	U = 3506.5, p < 0.001	5.5 (3.9),0–14	7.4 (4.0),0–16	ns
BPRS positive symptoms, worst	11.9 (3.2), 5–21	0.1 (0.6), 0–4	U = 3825.0, p < 0.001	12.0 (3.1), 5–17	11.6 (3.3), 6–21	ns
BPRS negative symptoms	5.5 (3.5), 0–13	0.2 (0.8), 0–5	U = 3584.5, p < 0.001	5.6 (3.5),0–13	5.3 (3.5),0–12	ns
SOFAS	40.5 (8.8), 20–70	86.2 (6.9), 67–95	U = 2.5, p < 0.001	39.8 (9.0), 20–70	41.7 (8.5), 30–60	ns
GAF	36.1 (7.7), 3–65	82.5 (9.5), 55–95	U = 2.5, p < 0.001	36.3 (8.6), 3–65	35.7 (5.9), 30–50	ns
PSSS-R	43.1 (11.1), 13–60	52.2 (7.4), 31–60	U = 982.5, p < 0.001	42.5 (10.8), 13–60	44.2 (11.8), 23–60	ns
BDI	11.9 (10.3), 0–44	2.9 (5.2), 0–31	U = 3181.0, p < 0.001	10.0 (8.6), 1–40	15.5 (12.2), 0–44	U = 823.5, p = 0.038
BAI	15.9 (12.4), 0–49	3.1 (3.5), 0–14	U = 3312.0, p < 0.001	13.4 (11.3), 0–49	20.7 (13.2), 0–45	U = 859.5, p = 0.013
OCI-R	14.2 (10.7), 0–54	3.6 (3.8), 0–16	U = 3063.5, p < 0.001	12.7 (10.3), 0–42	17.1 (10.9), 0–54	ns
Sense of Mastery	19.6 (4.8), 9–28	23.8 (3.0), 18–28	U = 844.5, p < 0.001	20.4 (4.8), 11–28	18.1 (4.4), 9–25	ns
AUDIT	7.5 (6.7), 0–30	6.3 (4.3), 0–19	ns	9.5 (6.7),0–30	3.7 (4.7),0–15	U = 268.5, p < 0.001
MDQ	5.6 (3.9), 0–13	2.1 (3.0), 0–11	U = 2959.5, p < 0.001	5.5 (3.6),0–13	5.9 (4.3),0–13	ns

BPRS, Brief Psychiatric Rating Scale. SOFAS, Social and Occupational Functioning Assessment Scale. GAF, Global Assessment of Functioning. PSSS-R, Perceived Social Support Scale Revised. BDI, Beck Depression Inventory. BAI, Beck Anxiety Inventory. OCI-R, Obsessive-Compulsive Inventory – Revised. AUDIT, Alcohol Use Disorders Identification Test. MDQ, Mood Disorders Questionnaire. ns, nonsignificant.

[a] Dichotomic variables: Pearson Chi-square test or Likelihood ratio test. Continuous variables: Mann-Whitney test.

[b] Schizophrenia spectrum diagnoses include Schizophrenia (n = 26), Schizophreniform disorder (n = 20), and Schizoaffective disorder (n = 3). The rest were diagnosed with other psychosis, including Psychotic disorder NOS (n = 13), Bipolar I disorder (n = 5), Major depressive disorder with psychotic features (n = 3), Brief psychotic disorder (n = 3), Delusional disorder (n = 1), and Substance-induced psychotic disorder (n = 1).

negative symptoms was calculated as the sum of blunted affect, alogia, anhedonia, and avolition.

SCID interview (First et al., 2002) was used to assess the diagnoses. Medical records from mental health treatment were available and were used to complement information on symptoms provided by the patients in the SCID interview. In addition, Social and Occupational Functioning Assessment Scale (SOFAS) and Global Assessment of Functioning (GAF) (American Psychiatric Association, 2013) were scored based on structured questions on functioning.

2.2.2. Questionnaire

After the baseline interview childhood adversities were explored by a questionnaire used in Finnish population-based surveys (Kestilä et al., 2006; Pirkola et al., 2005). Participants were asked to answer “no”, “yes”, or “unable to answer” to 11 questions about their childhood before the age of 16 years. “Yes” answers for the 11 experiences (Table 1) were calculated, unsure answers being considered as missing data.

Additionally the questionnaire included the following measures, each of which is a well-known instrument in wide international use with well-reported psychometric properties. Perceived Social Support Scale Revised, PSSS-R (Blumenthal et al., 1987), measures social support with 12 questions using a 0–4 Likert scale. Alcohol Use Disorders Identification Test, AUDIT (Saunders et al., 1993), measures problems with alcohol use in the last 12 months with 10 questions. Each of the questions has a set of responses to choose from, each response having a score ranging from 0 to 3 or 0–4. Beck Depression Inventory, BDI (Beck et al., 1961) measures current depressive symptoms with 21 statements on a 4-point severity-rating scale. Beck Anxiety Inventory, BAI (Beck et al., 1988) measures anxiety symptoms over the past 7 days with 21 items using a 4-point severity-rating scale. Obsessive-Compulsive Inventory – Revised, OCI-R (Foa et al., 2002), assesses obsessive-compulsive symptoms in the preceding month with 18 items on a scale from 0 to 4. Mood Disorders Questionnaire, MDQ (Hirschfeld, 2002), assesses lifetime manic symptoms. To assess manic symptoms dimensionally, MDQ was used as a sum score of 13 part A symptom items answered as yes/no, which is a commonly used measure in research (Baryshnikov et al., 2015). Sense of Mastery was used to measure positive mental health (sense of having control over the forces that affect one's life) (Pearlin et al., 1981). It has seven items and four responses to choose from.

2.3. Analyses

A factor score indicating the severity of adversity was formed with item factor analysis created with Mplus (Muthén and Muthén, 2012). One dimensional item factor analysis using the weighted least square (WLSMV) estimator (tetrachoric correlation matrix) of all 11 items showed that item 11 (bullying) was very weakly related to the overall factor. The analysis was therefore rerun with variables 1–10. Fit indices were marginally adequate (CFI = 0.94, RMSEA = 0.07), which indicates that the items measure a mostly unidimensional phenomenon. The fit did not improve with removing the second poorest item number 10 ("own illness") and it was included in the final solution. Factor scores were estimated with the Expected A Posteriori algorithm for use in further analyses. The factor score is referred to as the “severity of adversity”.

Spearman correlations between the severity of adversity and continuous scales were calculated using IBM SPSS Statistics for Windows, version 24 (IBM Corp., 2016). Group differences of binary variables were analyzed with Pearson Chi-square test or Likelihood ratio test and of continuous variables with the Mann-Whitney U-test. Finally, concerning symptoms that were significantly correlated with the severity of adversity in the patient group, linear regression models were performed to assess if the severity of adversity remained significantly associated with the symptoms when age and gender were controlled for.

All statistical tests were two-tailed and a value of $p < 0.05$ was considered significant.

3. Results

The study sample consisted of 75 FEP participants and 51 controls, whose demographic and clinical information is presented in Table 2. Patients showed significantly higher clinical symptoms than controls in all the measures, except for AUDIT, which measures problems with alcohol use. Of note, none of the FEP patients or controls received a

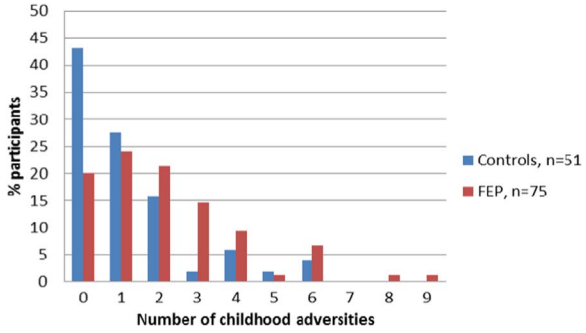

Fig. 1. Number of reported childhood adversities among patients with FEP and controls.

diagnosis of posttraumatic stress disorder in the SCID interview.

In the FEP group females had significantly higher BPRS total scores and depression and anxiety scores than males, and men had higher scores in AUDIT (Table 2).

3.1. Reported adversities

Of the participants with FEP, 60 (80.0%) reported at least one childhood adversity whereas the same was true for 29 (56.9%) controls (Pearson Chi-Square $p = 0.005$). The frequencies of individual adversities are reported in Table 1.

The number of experienced childhood adversities was significantly higher in the FEP group than in controls (Fig. 1). There were no gender or age differences, and patients with a schizophrenia spectrum diagnosis and other psychosis did not differ in severity of adversity patients (see Table 2 for information of the diagnostic groups).

3.2. Adversities and symptomatology

Table 3 shows correlations between the severity of adversity and scales of symptoms and functioning. In the FEP group only manic symptoms (MDQ) were associated with the severity of adversity in females, whereas in males associations were found with manic symptoms, BPRS total score, anxiety (BAI), depression (BDI), obsessive-compulsive symptoms (OCI-R), and problems with alcohol use (AUDIT).

Adversity question 11 concerning bullying was not included in the factor score and was examined separately. Bullying was not associated with symptoms in females, but those male patients who reported having been bullied reported higher depression ($U = 344.0$, $p = 0.011$) and anxiety ($U = 329.0$, $p = 0.030$) and lower sense of mastery ($U = 143.0$, $p = 0.025$).

We report the correlations between adversities and clinical scales separately for the two diagnostic groups in Supplementary Table 1. In those with schizophrenia spectrum diagnosis, severity of adversity was associated with higher anxiety symptoms, manic symptoms, and obsessive-compulsive symptoms, and in those with other psychotic disorder, with just manic symptoms.

Among controls, severity of adversity or bullying was not associated with the clinical scores in females. In men, however, higher severity of adversity was associated with lower functioning and mastery and higher anxiety symptoms, manic symptoms, and obsessive-compulsive symptoms (Table 3). Bullying was associated with lower SOFAS ($U = 63.0$, $p = 0.026$) and higher depression ($U = 172.0$, $p = 0.025$) in male control participants.

The correlations of the symptom/functioning scales with each other can be seen in Supplementary Table 2 (FEP) and Table 3 (controls).

Next, to control for effects of age and gender, a series of linear regression analyses were performed in the patient group, with the symptom scores that were positively correlated with the adversities among patients (BAI, OCI-R, and MDQ scores) individually as dependent variables. The predictor was the severity of adversity when age and gender were controlled for. In Table 4, it can be seen that in each model, the severity of adversity continued to be associated with all three symptom categories, however gender was also a significant predictor of both anxiety and obsessive-compulsive symptoms, but not of manic symptoms. Controlling for antipsychotic medication (chlorpromazine equivalent) did not change the results (data not shown).

3.3. The effect of specific adversities in the FEP group

We then investigated whether specific adversities contributed to the differences in BAI, OCI-R, and MDQ scores. Of the adversities that were more common among patients than controls (parental disease or disability, maternal mental health problem, conflicts within the family, person's own long-term illness, bullying at school), we found that reporting own illness or maternal mental health problem were not associated with the specific symptoms. Females showed no associations with the rest of the specific adversities either. In males, parental disease

Table 3
Clinical variable Spearman correlations with the severity of adversity.

	FEP						Controls					
	All, $n = 75$		Male, $n = 49$		Female, $n = 26$		All, $n = 51$		Male, $n = 34$		Female, $n = 17$	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
BPRS total score	0.18	0.114	**0.30**	**0.037**	0.07	0.726	[a]					
BPRS positive symptoms, current	0.14	0.235	0.14	0.341	0.16	0.427						
BPRS positive symptoms, worst	−0.17	0.156	−0.18	0.208	−0.20	0.316						
BPRS negative symptoms	0.05	0.669	0.13	0.355	−0.16	0.434						
SOFAS[b]	−0.09	0.462	−0.17	0.252	0.11	0.604	−0.24	0.090	−0.33	0.056	−0.13	0.632
GAF[b]	−0.04	0.741	−0.04	0.764	0.03	0.887	**−0.30**	**0.035**	**−0.35**	**0.042**	−0.18	0.490
PSSS-R[b]	−0.13	0.250	−0.16	0.279	−0.02	0.940	−0.20	0.152	−0.21	0.245	−0.28	0.285
BDI	0.15	0.193	**0.35**	**0.014**	−0.22	0.286	**0.35**	**0.012**	0.32	0.069	0.39	0.123
BAI	**0.36**	**0.002**	**0.57**	**< 0.001**	0.06	0.762	0.24	0.091	**0.44**	**0.009**	−0.11	0.676
OCI-R	**0.42**	**< 0.001**	**0.55**	**< 0.001**	0.30	0.149	0.16	0.276	**0.45**	**0.009**	−0.40	0.110
Sense of mastery[b]	−0.09	0.439	−0.25	0.094	0.14	0.499	**−0.34**	**0.019**	**−0.46**	**0.008**	−0.16	0.548
AUDIT	0.17	0.147	**0.29**	**0.040**	−0.07	0.739	0.07	0.623	0.12	0.493	−0.02	0.946
MDQ	**0.45**	**< 0.001**	**0.48**	**0.001**	**0.43**	**0.030**	**0.31**	**0.026**	**0.55**	**0.001**	−0.15	0.557

r, correlation coefficient. *p*, significance value. SOFAS, Social and Occupational Functioning Assessment Scale. GAF, Global Assessment of Functioning. PSSS-R, Perceived Social Support Scale Revised. BDI, Beck Depression Inventory. BAI, Beck Anxiety Inventory. OCI-R, Obsessive-Compulsive Inventory – Revised. AUDIT, Alcohol Use Disorders Identification Test. MDQ, Mood Disorders Questionnaire.

[a] Due to low levels, BPRS (Brief Psychiatric Rating Scale) symptoms were not analyzed in the control group.

[b] Higher scores indicate better mental health.

Table 4
Linear regression models.

	Independent					
	Severity of adversity		Age		Gender	
Dependent	Beta[a]	p	Beta	p	Beta	p
BAI	0.303	**0.006**	−0.161	0.141	0.319	**0.004**
OCI-R	0.324	**0.004**	−0.181	0.105	0.250	**0.024**
MDQ	0.421	**< .001**	−0.049	0.659	0.082	0.450

BAI, Beck Anxiety Inventory. OCI-R, Obsessive-Compulsive Inventory – Revised. MDQ, Mood Disorders Questionnaire.
[a] Standardized Coefficients Beta.

or disability during childhood was linked to patients' anxiety (U = 245.5, p = 0.030) and obsessive-compulsive symptoms (U = 275.5, p = 0.002). In addition, serious conflicts within the family were associated with more severe obsessive-compulsive symptoms (U = 387.0, $p < 0.001$), anxiety (U = 337.5, p = 0.009), and manic symptoms (U = 380.0, $p < 0.001$). As reported above in 3.2, bullying was associated with anxiety in males.

4. Discussion

We report the association of negative childhood experiences with first episode psychosis and a large variety of symptoms related to it. Furthermore, we examined the gender differences in these associations. Childhood stressful experiences make up a psychosocial burden that may play a separate or additional role in the neurodevelopmental etiology of psychosis. These events can affect the clinical picture and impose specific demands for treatments of the psychotic disorder.

4.1. Adversities experienced in the FEP group

The majority (80%) of the participants with FEP reported exposure to childhood adversities and patients reported more adversities than controls, with no gender differences. These results are comparable to earlier studies on severe forms of maltreatment. In a Danish study 89% of FEP patients reported at least one childhood trauma (Trauelsen et al., 2015) and in individuals with early psychosis in Australia over three quarters reported exposure to abuse or neglect (Duhig et al., 2015). However, it should be pointed out that instead of severe forms of maltreatment, our questionnaire assessed negative life events during childhood and should be viewed as a measure of childhood stress or psychosocial burden.

Compared to controls the individuals with FEP in our sample were especially exposed to their own or family members' serious illness during their childhood, maternal mental health problems, and serious conflicts within the family. School bullying was also more common in the FEP group than among controls, which is consistent with a previous study of FEP patients from the UK (Trotta et al., 2013). A previous Finnish longitudinal cohort study found that exposure to bullying at age 8 years was a risk factor of psychotic and mood disorders in early adulthood (Sourander et al., 2016). In a large Finnish population study, bullying at school was associated with adult anxiety, depressive, and alcohol use disorders (Pirkola et al., 2005). Interestingly, the childhood adversities experienced more in the FEP group than in the control group were almost the same ones that were specifically associated with the development of adulthood mental disorders in the Finnish population study using the same adversity questionnaire (Pirkola et al., 2005). These were conflicts within the childhood family, being bullied at school, parental mental health problems, and one's own serious medical illness.

4.2. Adversities and symptomatology

Severity of childhood adversities was linked with affective symptoms and anxiety, but not with the severity of positive psychotic symptoms in the FEP group. Among controls, adversities were associated with mood symptoms and lower social functioning and sense of mastery.

In previous literature, adverse and traumatic experiences have been linked to the positive symptom dimension in FEP and schizophrenia in many studies (Ajnakina et al., 2016; Bentall et al., 2014; Duhig et al., 2015; Lopes, 2013; Misiak et al., 2016; Ruby et al., 2017; Wang et al., 2013; Üçok and Bıkmaz, 2007). However, in the current study, childhood adversities were not associated with positive symptoms, possibly because the adversities assessed here were of different nature than the ones assessed in most previous studies. The adversities were neither associated with negative symptom scores, which is in line with earlier results on severe childhood trauma (Üçok and Bıkmaz, 2007).

Overall, our results are consistent with earlier findings suggesting an association of childhood trauma with increased depressive, anxiety, and stress symptoms in early psychosis (Duhig et al., 2015). Anxiety symptoms are common in individuals with psychotic disorders (Bosanac et al., 2016) and an association between trauma experiences (neglect and abuse) and anxiety has been found in schizophrenia patients (Li et al., 2015). In our study, only males showed higher depressive and anxiety symptoms with respect to adversities. Our results also indicated that serious parental disease or disability during childhood may be especially linked to increased anxiety in males with FEP. Conflicts within the childhood family were also associated with lifetime manic and anxiety symptoms among males with psychosis. In previous research, inter-parental conflict has been found to be associated with depression and anxiety in adolescents generally (Yap et al., 2014).

The adversities were associated with manic symptoms both in the FEP and control groups suggesting a similar association at the subclinical as well as clinical level. The association was present in both patients with schizophrenia spectrum and other psychotic disorder. Mania was also the only symptom that was associated with adversities across both genders in the FEP group; the association between adversity and anxiety and obsessive-compulsive symptoms was different in females and in males, whereas manic symptoms were associated with adversities in the same way among both genders. van Nierop et al. (2015) reported that a mixture of depressive, anxiety, mania, and psychotic symptoms were associated with childhood trauma (neglect, abuse, and peer victimization) both in the general population and in mental health patient samples. Conversely, in bipolar disorder, childhood trauma is associated with more severe clinical presentation, such as psychotic features (Aas et al., 2016), supporting the connection between mania, psychosis, and trauma. Many patients reported manic symptoms in the current sample, but it is notable that, used dimensionally, MDQ does not assess bipolar disorder specifically, but overlaps with borderline personality features (Baryshnikov et al., 2015; Zimmerman et al., 2010). The emergence of borderline personality has been associated with early life adversity in previous literature (Brüne, 2016; Newnham and Janca, 2014). Further, Moffa et al. (2017) reported an association between bullying and mood instability (as assessed with borderline personality items) in the general population. In conclusion, one could speculate that the experienced childhood adversities may add the risk for emotional instability detected in borderline personality among individuals with first-episode psychosis.

Negative childhood events (and especially serious parental disease or disability and conflicts within the childhood family) were related to obsessive-compulsive symptoms in males. In a Dutch study, psychosis patients with co-occurring obsessive-compulsive symptoms presented a more severe clinical picture and the authors discussed that the possible mechanisms could be increased sensitivity to stress, negative affectivity, and dysfunctional coping (Schirmbeck et al., 2016). An association between obsessive-compulsive disorder and psychosis has been

established, indicating a shared etiological pathway (Cederlöf et al., 2015; Meier et al., 2014).

Severity of adversity was associated with alcohol use in male patients. In a study conducted with individuals with schizophrenia in the USA, adverse childhood events – including parental mental illnesses and parental divorce among other adversities – related to poor functioning and substance abuse (Rosenberg et al., 2007). In the current study, adversities were not associated with functioning scores in the FEP group, contrary to a previous review (Cotter et al., 2015). Functioning tended to be rather poor in all patients at the baseline assessment and the lack of variance may partly explain why no correlation with childhood adversities was found.

In male patients, associations were found with more severe symptomatology in many measures. Similar gender differences could be seen in the control group, suggesting that the childhood negative events might have different effects on mental health depending on gender in the general population also. Previous results concerning gender-specific effects of adversity or trauma have been mixed. Some studies have found like we that men may be more vulnerable to the effects of childhood trauma, but opposite results have also been reported (Misiak et al., 2017). There were more men than women in our sample, possibly partly explaining the more numerous statistically significant results among men. However, similar gender differences could be seen both in patient and controls.

4.3. Strengths and weaknesses

The strengths of this study include participants with first-episode psychosis with a careful symptom scoring as well as a matched control group. Broad clinical assessment was available for both groups. The number of childhood adversities among controls in the current sample was comparable with the number of adversities reported in the large Health 2000 survey in Finland (Kananen et al., 2010), indicating that the control participants in the current sample represented the general population well.

An item factor analysis solution was used instead of summing up the adversities, offering a statistically better measure for assessing the effect of accumulating childhood adversity, as the different adversities assessed in the questionnaire do not necessarily measure the same phenomenon with the same value. Bullying was handled separately as it did not load with the same dimension as other, more family-related childhood adversities. However, the timing, severity, and burden of the experiences were not assessed. The number of participants reporting each adversity was rather small. Furthermore, retrospectively self-reported adverse experiences are not necessarily completely reliable, as people with psychiatric disorders may seek explanations for their difficulties from early experiences. Reporting adverse childhood experiences may be influenced by mental health (Colman et al., 2016), although childhood reports have been found to have good validity in psychosis patients (Fisher et al., 2011). In addition, our FEP patient sample had at baseline had a relatively short period of mental illness.

Correlational analyses must be interpreted with caution, as both the adversities and clinical scales are heterogeneous and correlated with each other (Supplementary Tables 2 and 3). Moreover, multiple testing was not controlled for in this exploratory study; the possible association between clinical features in FEP and stressful psychosocial circumstances in childhood has not been widely studied. However, if the false discovery rate had been controlled for using the Benjamini–Hochberg procedure (Benjamini and Hochberg, 1995), most of the associations would have remained the same – the biggest change being that the associations between clinical measures and adversities in controls (Table 3) would have not remained significant.

Causal relationships cannot be drawn from these results as adverse experiences and vulnerability to psychosis may cluster to the same individuals. For instance, bullying can be triggered by individual characteristics and family factors, such as schizotypal features or parental mental illness, that are related to psychosis risk (Arseneault et al., 2010). Rather than being isolated events, negative childhood experiences additionally elevate the risk of re-victimization in later life (Cotter et al., 2016; Stevens et al., 2017). The adversities assessed in the current study may co-occur with more severe trauma, which may explain some of the associations found. Moreover, additional mediating factors between trauma and symptoms may exist, for example, dissociative symptoms (Perona-Garcelan et al., 2012; Varese et al., 2012a).

Some of the adversities assessed were concerned with parents' problems. No comprehensive information of genetic risk was available, parents themselves were not assessed, and the severity of parental mental health problems could not be taken into account. Furthermore, there are complex relationships between psychosis, parental mental health problems, and childhood adversities. Parental mental health problems may be associated with psychotic disorders by increased genetic risk (Cross-Disorder Group of the Psychiatric Genomics Consortium et al., 2013). Parental mental health problems predispose to both psychotic disorders (Mortensen et al., 2010) and to negative childhood experiences (Bee et al., 2013; O'Donnell et al., 2015).

It is of note that the adversities assessed here may partly be associated with the psychotic disorder itself. Of the seven participants reporting own serious illness during childhood, all had FEP. Four of them reported somatic illnesses in the interview, e.g. childhood asthma and diabetes. It cannot be ruled out that responding to the question "When you think about your growth years, were you seriously or chronically ill?" in the questionnaire, some of the respondents referred to psychiatric problems originating in childhood.

4.4. Conclusions

In line with earlier studies in persons with chronic psychosis, self-reported adverse experiences during childhood (0–16 years) were more frequent in participants with FEP compared to controls, with a majority of the patients reporting exposure to childhood adversities. The occurrence of several adverse events was typical of individuals with FEP but less so in controls. While a single adversity may not add risk, it is perhaps the accumulation of negative experiences that is associated with psychosis.

Instead of affecting positive psychotic symptoms, chronic childhood stress may affect the level of functioning via internalizing symptoms and stress susceptibility, consistent with the impact of early-life stress on the HPA-axis and its association with mood and anxiety (Albrecht et al., 2017; Juruena, 2014). In the psychosocial treatment of FEP, it is important to pay attention to negative life events that may underlie affective symptoms. In addition, gender differences should be considered when examining the effects of childhood adversities on some clinical symptoms such as anxiety and obsessive-compulsive symptoms in FEP patients.

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Conflict of interest

ML has received financial compensation for an interview from Oy H.

Lundbeck Ab/Otsuka Pharma Scandinavia AB in 2016. All other authors declare that they have no conflicts of interest.

Authors' contributions

Authors OM, TK and JS designed the original study protocol. ML, TM, ER, and MT-H participated in collecting the data, and JS was responsible for DSM-IV diagnoses. ML undertook the statistical analysis and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2017.08.070.

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