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The impact of gender and childhood abuse on age of psychosis onset, psychopathology and needs for care in psychosis patients

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ABSTRACT

Gender is associated with several features of psychotic disorders, including age of illness onset, symptomatology, a higher prevalence of history of childhood sexual abuse (CSA) and needs for care. Childhood sexual abuse is associated with adverse mental health consequences but as there is a gender difference in stress reactivity, there may be a differential impact of CSA on psychopathology, age of psychosis onset and needs for care in First Episode Psychosis (FEP) patients. We hypothesized that a history of abuse would be associated with lowering of age of onset, increased symptomatology and more unmet needs in women but not men. A total of 444 FEP patients have been recruited within the context of the GET UP trial. Symptomatology has been assessed using the PANSS scale, needs for care with the CAN scale and childhood abuse with the CECA-Q scale. Childhood sexual abuse was more frequent among female patients [22.6% in women *vs* 11.6% in men (OR = 0.45, $p < 0.01$)], whereas there was no gender difference in the prevalence of childhood physical abuse (29.0% in women *vs* 31.7% in men). Childhood abuse was associated with higher levels of negative symptoms in both men and women, with a reduced age of onset in women only and little increase in needs for care in both men and women. Our results seem to suggest that childhood sexual abuse in female FEP patients may be linked to a more severe form of psychosis whose presentation is characterized by earlier age of onset and higher levels of negative symptoms and we can also speculate that gender-specific protective factors in women, but not in men, may be outweighed by the consequences of childhood abuse.

1. Introduction

There have been many studies investigating the impact of gender on psychosis, but few studies have examined the impact of gender on first episode psychosis (FEP). However, there is some evidence that at psychosis onset, gender is associated with age of onset (lower for male patients compared to females (Jackson et al., 2013)), symptoms (women having more positive symptoms than men; men presenting with more negative and disorganized symptoms than women (Hui et al., 2014)), and different needs for care (women showing more unmet needs in the domains of "functioning" (basic education, money, childcare, self-care, looking after the home) (Bertani et al., 2012) and "services" (information, telephone use, transport, and benefits compared to men (Ochoa et al., 2012))). Other gender differences include rates of childhood trauma, with women being more likely to have been exposed to sexual abuse and physical abuse during their childhood (Alvarez et al., 2011). Childhood traumatic experiences appear to be involved in the etiological path leading to the development of psychosis with postulated mechanisms that include the lowering of Brain Derived Neurotrophic Factor (BDNF) levels (Theleritis et al., 2014); the over-activation of the

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Hypothalamus Pituitary Adrenal (HPA) axis (Aas et al., 2011); a subclinical pro-inflammatory state (Dennison et al., 2012) and metabolic dysregulation (Misiak et al., 2015) which have been observed in FEP patients. However there has been less research on how childhood adversities impact on clinical features of psychosis. Most studies have involved samples of chronic adult patients, which suggest that a history of childhood trauma is associated with an increased severity in positive symptoms (Gallagher III and Jones, 2013), whereas the relationship with negative symptoms is more controversial (Alemany et al., 2013; Ruby et al., 2015). In FEP patients, childhood emotional abuse has been linked to an increased severity in positive symptoms (Ramsay et al., 2011), whereas childhood sexual abuse has found to be associated with and both positive (Ucok and Bikmaz, 2007) and negative symptoms (Burns et al., 2011).

As there is evidence of gender differences in stress reactivity to trauma (Riecher-Rössler et al., 2018), there may be a differential impact of childhood abuse on psychopathology, age of psychosis onset and needs for care in First Episode Psychosis (FEP) patients. There are only two studies to our knowledge examining this. Haug et al. (2015) found higher levels of anomalous self-experiences in female FEP patients exposed to childhood abuse compared to males. Misiak et al. (2016) found higher levels of auditory-verbal hallucinations in female FEP patients exposed to childhood abuse compared to males. The impact of childhood adversities on the age of psychosis onset has been investigated in samples of chronic adult patients. Two studies have found a positive association between earlier age of psychosis onset and childhood psychological abuse (Li et al., 2015; Alvarez et al., 2011). Hacioglu Yildirim et al. (2014), in a sample of female patients with schizophrenia, found that patients with a history of childhood sexual abuse were significantly younger than those without. One study has focused on how childhood trauma interacts with gender on age of psychosis onset (Kocsis-Bogár et al., 2018) and found that childhood physical abuse predicted an earlier age at psychosis onset only for female patients. To our knowledge no study has focused on the impact of gender and childhood traumatic experiences on needs for care in people with psychosis to date.

Thus, the impact of gender and childhood adversities on psychotic patients, especially FEP patients, is unclear. The present study therefore aims to: 1) explore gender differences in psychopathology, age of onset and needs for care in a large cohort of FEP patients; and 2) assess the combined effect of gender and traumatic experiences (physical and sexual abuse) on psychopathology, age of psychosis onset and needs for care. Given that both severe physical and sexual abuse appear to be associated with psychosis in female patients, that childhood sexual abuse is more frequently experienced by girls and that childhood sexual abuse has been reported to be associated with some features of psychosis at illness onset, our primary hypothesis was that women with FEP, compared with men, would have had higher levels of positive and negative symptoms and lower age of illness onset in people exposed to childhood sexual abuse. Due to the lack of information on the impact of gender and childhood abuse on needs for care of both chronic and FEP patients, for the formulation of our secondary hypothesis we relied on studies assessing gender differences in needs for care in FEP patients. We thus hypothesized that women with FEP, compared with men, would have had more unmet needs for care in the services and functioning domains in people exposed either physical or sexual abuse in their childhood.

2. Methods

2.1. Study design

Here we present secondary analyses of the GET UP PIANO trial. The GET UP PIANO trial has a pragmatic cluster randomized controlled design, which compares the effectiveness of Treatment As Usual (TAU) plus a multi-element psychosocial treatment for patients with FEP and their family members, *versus* TAU alone, as provided by Italian community mental health services. All the Community Mental Health Services in the GET UP catchment area (Veneto and Emilia-Romagna Regions and the cities of Florence and Bolzano) were are asked to refer all potential cases of psychosis at their first contact with the service over a period of 1 year. The Screening Schedule for Psychosis (Jablensky et al., 1992) has been administered to all patients as soon as possible after first service contact, Patients meeting all inclusion criteria have been invited to undertake standardized assessments as soon as possible once they achieve clinical stabilization. (Ruggeri et al., 2015). Based on the methodology adopted in the WHO Ten-Country study (Jablensky et al., 1992), inclusion criteria to ascertain FEP were: (1) age 18–54 years, (2) residence in catchment areas (Veneto and Emilia Romagna regions and cities of Milan, Florence and Bolzano), (3) presence of at least one of the following: hallucinations, delusions, qualitative speech disorder, qualitative psychomotor disorder, bizarre, or grossly inappropriate behaviour, or two of the following: loss of interest, initiative, and drive; social withdrawal; episodic severe excitement; purposeless destructiveness; overwhelming fear; or marked self-neglect, (4) first lifetime contact with Mental Health Services, prompted by these symptoms. Exclusion criteria were: (1) antipsychotic medication (>3 months) prescribed for an identical or similar mental disorder; (2) mental disorders due to general medical condition; (3) moderate-severe mental retardation per a clinical functional assessment; and (4) psychiatric diagnosis other than International Classification of Diseases (ICD)-10 for psychosis. A detailed description of the GET UP PIANO trial is available elsewhere (Ruggeri et al., 2015).

2.2. Measures

Age at psychosis onset together with other socio-demographic and clinical information has been collected by using an *ad hoc* schedule. Symptomatology has been assessed using the *Positive and Negative Syndrome Scale* (PANSS), a widely used assessment scale consisting of 30 items that covers positive symptoms, negative symptoms and general psychopathology; each item is rated on a Likert-type severity scale ranging from 1 (absent) to 7 (extreme) (Kay et al., 1987). The European version of the *Camberwell Assessment of Needs* (CAN-EU) has been used to measure the number of present needs of subjects per area and the number of unmet needs. This interview comprises 22 items grouped into five conceptual domains: health (psychotic symptoms, drugs, alcohol, safety to self, safety to others, psychological distress, and physical health); basic (accommodation, food, and daytime activities); social (sexual expression, social networks, and intimate relationships); service (information, telephone use, transport, and benefits) and functioning (basic education, money, childcare, self-care, looking after the home). Each item is rated on a scale of three conditions: 0 = no problem, 1 = absent or moderate problem due to the person receiving ongoing interventions (met need), 2 = actual serious problem and no interventions received (unmet need) (McCrone et al., 2000). Information on childhood trauma has been collected at baseline using the *Childhood Experience of Care and Abuse-Questionnaire* (CECA-Q), a measure of sexual abuse, parental physical abuse and lack of parental care (neglect and antipathy) occurred before the age of 17. It takes the form of a semi-structured interview, which aims to reflect objective features of early life experience with probing questions to ascertain details of context and time-sequence of experience (Bifulco et al., 2005).

2.3. Statistical analysis

Gender differences in socio-demographic characteristics at baseline were evaluated by Chi-square test (for marital status and working status), Fisher's exact test (for educational level, nationality and diagnosis) and test for independent groups (for age of onset). Differences among the 4 sub-groups (CECA-Q completers and non-completers, males and females, respectively) in age of onset were assessed by Analysis of

Table 1
Gender differences in socio-demographic characteristics.

	Females (n = 184)	Males (n = 260)	p-Value Chi-square, Fisher or *t*-test
Age at onset, mean (SD)	33.4 (10.2)	27.9 (8.5)	<0.001
Educational level, n (%)	(12 missing)	(10 missing)	
Low (primary-middle school)	69 (40.1%)	94 (37.6%)	0.61
High (secondary school, university)	103 (59.9%)	156 (62.4%)	
Marital status, n (%)	(11 missing)	(13 missing)	
Unmarried	102 (59.0%)	211 (85.4%)	<0.001
Married	54 (31.2%)	26 (10.5%)	
Widowed, separated, divorced	17 (9.8%)	10 (4.1%)	
Working status, n (%)	(10 missing)	(5 missing)	
Employed	60 (34.5%)	99 (38.8%)	0.03
Unemployed	51 (29.3%)	93 (36.5%)	
Housewife, student, retired, other	63 (36.1%)	63 (24.7%)	
Nationality, n (%)	(1 missing)	(4 missing)	
Italy	163 (88.6%)	227 (87.3%)	0.76
Other	21 (11.4%)	33 (12.7%)	
Diagnosis, n (%)			
Non affective psychosis	139 (75.5%)	207 (79.6%)	0.35
Affective psychosis	45 (24.5%)	53 (20.4%)	

Variance with Bonferroni post-hoc comparisons; the same differences in educational level, marital status, working status, nationality and diagnosis were estimated by Chi-square tests. PANSS (total, dimensions and items) and CAN (total and dimensions) mean levels at baseline were compared between males and females by *t*-test for independent groups. Differences among the 4 sub-groups (physical abuse and no physical abuse, males and females; sexual abuse and no sexual abuse, males and females, respectively) in PANSS mean scores (total and dimensions), CAN mean scores (total and dimensions) and age of onset were assessed by Analysis of Variance with Bonferroni post-hoc comparisons. No comparison was adjusted for demographic variables (marital status, education and employment) because they could act both as direct and as reverse causal factors. All tests were bilateral at $p < 0.05$. Analyses were performed by SPSS 22.0 for Windows.

3. Results

3.1. Composition of the sample

Overall, 626 FEP patients (364 experimental; 262 TAU) were eligible for the study in the recruitment phase in the GET UP catchment area. Fifty-two (11.7%) patients dropped out: 33 (12.1%) and 19 (11.0%) in the experimental and TAU groups, respectively (not significant). There were no significant differences in demographic variables between completers and noncompleters. A total of 444 FEP patients were assessed at baseline, 260 males and 184 females. The groups did not differ in socio-demographic characteristics, except marital and working status (males were more frequently unmarried and unemployed than females) (Table 1).

3.2. Childhood traumatic experiences

Childhood physical abuse was reported by 30.6% (N = 103) of patients, with similar rates for males and females [29.0% (N = 40) of females and 31.7% (N = 63) of males]. Sexual abuse was reported by 16.2% (N = 53) of patients, 22.6% (N = 31) in women, 11.6% (N = 22) in men (OR = 0.45) (Fisher test, $p < 0.01$).

Socio-demographic characteristics of CECA-Q completers and CECA-Q non-completers are presented in Table 2. There was no difference between female completers and non-completers, whereas male completers were less likely to be married, widowed/separated/divorced and more likely to be Italian than male non-completers.

3.3. Psychopathology

There were some gender differences in PANSS subscales. For positive symptoms, female patients showed higher levels of excitement compared to males, whereas male patients showed higher levels of grandiosity compared to females. Male patients showed higher levels of negative symptoms than females in the PANSS negative subscale total and in the items of blunted affect, emotional withdrawal, passive/apathetic social withdrawal, difficulty in abstract thinking and lack of spontaneity. General psychopathology scale revealed higher levels of guilt

Table 2
Gender differences in socio-demographic characteristics by CECA-Q completers.

	CECA-Q completers		CECA-Q non-completers		p-Value Chi-square or ANOVA	Bonferroni post-hoc
	Females (n = 150)	Males (n = 206)	Females (n = 34)	Males (n = 54)		
Age at onset, mean (SD)	32.72 (10.31)	27.65 (8.59)	36.24 (9.53)	28.88 (8.22)	<0.001	F comp > M comp F non-comp > M comp F non-comp > M non comp
Educational level, n (%)	(3 missing)	(6 missing)	(9 missing)	(4 missing)	0.55	
Low (prim-middle school)	57 (38.8%)	72 (36.0%)	12 (48.8%)	22 (44.0%)		–
High (sec school, college)	90 (61.2%)	128 (64.0%)	13 (52.0%)	28 (56.0%)		–
Marital status, n (%)	(5 missing)	(9 missing)	(6 missing)	(4 missing)	<0.001	
Unmarried	85 (58.6%)	172 (87.3%)	17 (60.7%)	39 (78.0%)		–
Married	46 (31.7%)	19 (9.6%)	8 (28.6%)	7 (14.0%)		M non-comp > M comp
Widow, separat, divorc	14 (9.7%)	6 (3.0%)	3 (10.7%)	4 (8.0%)		M non-comp > M comp
Working status, n (%)	(6 missing)	(3 missing)	(4 missing)	(2 missing)	0.52	
Employed	50 (34.7%)	80 (39.4%)	10 (33.3%)	19 (36.5%)		–
Unemployed	42 (29.2%)	71 (35.0%)	9 (30.0%)	22 (42.3%)		–
Housewife, stud, retir	52 (36.1%)	52 (25.6%)	11 (36.7%)	11 (21.2%)		–
Nationality, n (%)	(1 missing)	(3 missing)	–	(1 missing)	0.03	
Italy	133 (89.3%)	186 (91.6%)	30 (88.2%)	41 (77.4%)		M comp > M non-comp
Other	16 (10.7%)	17 (8.4%)	4 (11.8%)	12 (22.6%)		M non-comp > M comp
Diagnosis n (%)					0.36	
Non-affective psychosis	111 (74.0%)	161 (78.2%)	28 (82.4%)	46 (85.2%)		–
Affective psychosis	39 (26.0%)	45 (21.8%)	6 (17.6%)	8 (14.8%)		–

feelings in females compared to males and higher levels of poor impulse control in male patients than females (Table 3).

The impact of gender and childhood traumatic experiences on psychopathology is presented in Table 4. There were no gender differences in positive symptoms for patients (male or female) with or without a history of physical abuse; however, for negative symptoms, physical abuse was associated with higher levels of symptoms in both men and women. Similarly, while there were no differences for positive symptoms for CSA by gender, CSA was associated with higher levels of negative symptoms for both men and women.

Table 3
Gender differences in psychopathology, mean PANSS scores (SD) (*t*-test).

	Females (n = 184)	Males (n = 260)	p-Value
Total	2.29 (0.65) 1 missing	2.40 (0.69)	0.07
Positive sub-scale	2.27 (0.86) 2 missing	2.27 (0.89)	0.98
Delusions	3.39 (1.92) 2 missing	3.37 (1.85) 2 missing	0.90
Conceptual disorganization	2.00 (1.22) 3 missing	1.96 (1.35) 3 missing	0.73
Hallucinatory behaviour	2.12 (1.65) 3 missing	2.07 (1.64) 2 missing	0.79
Excitement	1.78 (1.24) 3 missing	1.53 (1.01) 3 missing	0.02*
Grandiosity	1.50 (1.03) 4 missing	1.76 (1.38) 5 missing	0.02*
Suspiciousness/persecution	3.40 (1.79) 2 missing	3.29 (1.76)	0.51
Hostility	1.64 (1.02) 3 missing	1.85 (1.33) 3 missing	0.07
Negative sub-scale	2.28 (1.01) 2 missing	2.70 (1.18) 1 missing	<0.001*
Blunted affect	2.39 (1.48) 3 missing	3.04 (1.59) 4 missing	<0.001*
Emotional withdrawal	2.62 (1.56) 2 missing	3.12 (1.69) 3 missing	0.001*
Poor rapport	1.76 (1.18) 2 missing	1.86 (1.38) 2 missing	0.40
Passive/apathetic social withdrawal	2.82 (1.73) 6 missing	3.37 (1.78) 1 missing	0.001*
Difficulty in abstract thinking	2.13 (1.34) 8 missing	2.47 (1.42) 13 missing	0.01*
Lack of spontaneity	1.99 (1.43) 3 missing	2.54 (1.68) 2 missing	<0.001*
Stereotyped thinking	2.20 (1.42) 3 missing	2.40 (1.48) 6 missing	0.17
General psychopathology sub-scale	2.29 (0.66) 1 missing	2.34 (0.56)	0.44
Somatic concern	2.39 (2.68) 4 missing	2.07 (1.59) 5 missing	0.12
Anxiety	3.58 (1.38) 1 missing	3.55 (1.61) 4 missing	0.82
Guilt feelings*	2.44 (1.50) 3 missing	2.07 (1.35) 1 missing	0.01*
Tension	2.12 (1.25) 2 missing	2.34 (1.39) 2 missing	0.09
Mannerisms and posturing	1.26 (0.80) 6 missing	1.25 (0.81) 3 missing	0.87
Depression	3.17 (1.50) 2 missing	3.20 (1.55) 1 missing	0.82
Motor retardation	1.80 (1.17) 3 missing	2.00 (1.26) 3 missing	0.09
Uncooperativeness	1.55 (1.00) 2 missing	1.58 (1.14) 3 missing	0.81
Unusual thought content	2.44 (1.55) 1 missing	2.50 (1.61) 2 missing	0.73
Disorientation	1.32 (0.76) 4 missing	1.44 (0.87) 5 missing	0.14
Poor attention	1.61 (0.99) 4 missing	1.67 (1.06) 3 missing	0.59
Lack of judgment and insight	3.52 (1.72) 3 missing	3.83 (1.66) 1 missing	0.06
Disturbance of volition	1.73 (1.08) 5 missing	1.86 (1.30) 5 missing	0.27
Poor impulse control*	1.65 (1.06)* 4 missing	1.88 (1.25)* 3 missing	0.049*
Preoccupation	2.68 (1.46) 5 missing	2.77 (1.44) 4 missing	0.52
Active social avoidance	3.12 (1.98) 4 missing	3.35 (1.90) 3 missing	0.21

3.4. Age of onset

Age at psychosis onset was 27.9 years for males and 33.4 for females (Table 1). Physical abuse and sexual abuse reduced the age of onset in women only (ANOVA, $p < 0.01$) (Table 5).

3.5. Needs for care

Females showed higher levels of total [mean = 4.73 (SD = 2.89) *vs.* mean = 2.44 (SD = 2.77)], met (mean = 2.38 (SD = 2.00) *vs.* mean = 2.27 (SD = 1.92)) and unmet [mean = 2.35 (SD = 2.29) *vs.* mean = 2.01 (SD = 2.08)] needs for care compared to males, though these differences were not statistically significant (Table 6). Abuse had little impact on needs for care other than unmet functioning and service, which showed higher levels in both men and women (Table 7).

4. Discussion

We found that gender and childhood abuse impacted on some outcome measures of interest. We detected high rates of childhood physical and sexual abuse, with sexual abuse more frequently endorsed by women than men. Both types of abuse were associated with differences in psychopathology, with physical abuse associated with higher levels of negative symptoms in both men and women, and sexual abuse associated with higher levels of negative symptoms for both men and women (though men still had a higher level of negative symptoms). Physical abuse and sexual abuse were associated with a lower age of onset in women but not men and both types of abuse had little impact on increased needs for care in either men and women (though their needs for care around abuse were not measured), but female patients showed higher levels of total and unmet service needs than males (information, telephone use, transport, and benefits). Overall these findings suggest that childhood abuse is associated with a more "male" (lower age of onset, higher negative symptoms) presentation of FEP in women.

Our findings for FEP patients are largely consistent with research in more chronic patients though with some notable differences. Our first hypothesis was only partly confirmed as we did not find a stronger impact of childhood sexual abuse on positive symptoms for female patients compared to males unlike Misiak et al. (2016), who found that childhood sexual abuse predicted higher levels of auditory-verbal hallucinations in female patients. Nevertheless, in line with our hypothesis, we found that childhood sexual and physical abuse were associated with higher levels of negative symptoms in both males and females. The association between childhood sexual abuse and severity of negative symptoms in FEP patients has been previously noted (Burns et al., 2011), but gender effects have not been previously examined. In our sample, males and females with childhood abuse showed similar levels of negative symptoms thus the present study revealed that the tendency of male patients towards showing higher levels of negative symptoms compared to females at psychosis onset (Hui et al., 2014) disappears when the trauma variable is included in the analysis, as a result of the increase in negative symptoms reported by female patients with a history of both physical and sexual abuse during childhood.

Our findings have face validity as we report similar levels of childhood physical abuse as previous reports. A critical review of the literature on childhood abuse rates in people with psychosis (Morgan and Fisher, 2007) reported a prevalence of physical abuse at 35% for both sexes. However, our rates of childhood sexual abuse were lower than

Table 4
Gender differences in psychopathology by childhood abuse (PANSS).

Mean (SD)	Physical abuse		No physical abuse		p-Value ANOVA	Bonferroni post-hoc
	Females (n = 40)	Males (n = 63)	Females (n = 98)	Males (n = 136)		
PANSS positive	2.30 (0.84)	2.42 (0.82)	2.23 (0.83)	2.18 (0.68)	0.25	–
PANSS negative	2.40 (0.96)	2.66 (0.98)	2.16 (1.01)	2.59 (1.14)	<0.01	M PA > F no PA M no PA > F no PA
PANSS gen psychopatol	2.32 (0.65)	2.37 (0.52)	2.17 (0.63)	2.29 (0.61)	0.20	–
PANSS total	2.33 (0.63)	2.45 (0.51)	2.18 (0.63)	2.33 (0.64)	0.05	M PA > F no PA
Mean (SD)	Sexual abuse		No sexual abuse		p-Value ANOVA	Bonferroni post-hoc
	Females (n = 31)	Males (n = 22)	Females (n = 106)	Males (n = 168)		
PANSS positive	2.30 (0.79)	2.44 (0.78)	2.23 (0.84)	2.24 (0.83)	0.70	–
PANSS negative s	2.37 (0.84)	2.80 (1.08)	2.20 (1.03)	2.58 (1.10)	0.01	M no SA > F no SA
PANSS gen psychopatol	2.39 (0.64)	2.42 (0.77)	2.18 (0.63)	2.30 (0.56)	0.14	–
PANSS total	2.36 (0.58)	2.51 (0.70)	2.20 (0.64)	2.35 (0.60)	0.08	–

their reports of 42% for females and at 28% for males (compared with 22.6% for females *vs.* 11.6% for males in this study). The reliability of self-reports in adulthood of childhood traumatic events has often been questioned (Schaefer et al., 2012) because the shift from a concrete construct to a theoretical construct in reporting early experiences of abuse allows for the distortion that time, memory, emotions, denial, and other factors put on the events and their recall to remain part of the abstraction (Hulme, 2004). Nevertheless, Fisher et al. (2011) compared the similarity of abuse ratings obtained using different measures of childhood adversity (CECA-Q PBI scales and independent clinical case notes) found that reports of childhood abuse were similar when obtained by different assessment methods. It has also been noted that for research purposes the variable "childhood trauma" often requires a dichotomization (present/absent) and this makes it difficult to understand the real extent of trauma presence in their samples (Vergano et al., 2015).

Age at psychosis onset was higher for females compared to males (33.4 *vs.* 27.9), in line with other studies that indicate an average 1–5 years difference in age of psychosis onset between sexes (Eranti et al., 2013). Childhood physical and sexual abuse reduced the age of onset in female patients only. Moreover, gender difference in age of psychosis onset lost its significance as soon as trauma variables were included in the analysis. Our result confirms our first hypothesis and adds information to the work by Kocsis-Bogár et al. (2018), run on a sample of chronic psychotic patients, who found that childhood physical abuse, but not sexual abuse, acted as a predictor of earlier age of psychosis onset for females only. As a possible explanation, we can speculate that gender-specific protective factors in women, but not in men, such as better premorbid adjustment (Addington et al., 2003), higher levels of insight (Parellada et al., 2011) and shorter duration of untreated psychosis (Cascio et al., 2012), may be outweighed by the consequences of childhood abuse.

Service needs were higher in females compared to males, both total and unmet, consistently with other findings reporting women with psychosis as having more services needs than men (Ochoa et al., 2012). Our second hypothesis on the impact of gender and childhood abuse on needs for care was then confirmed but, given that the present paper is the first one investigating this aspect in FEP patients, we cannot make proper comparison with other studies. However, gender differences in needs for care in FEP patients have been reported, with female patients showing more service (Ochoa et al., 2012) and functioning (Bertani et al., 2012) unmet needs than males, and childhood abuse does not seem to add a significant impact on them. However, this result should be considered in the light of some sociocultural factors, as Latin families appear to be more likely to accept and cope with underperforming males (Bimbi, 2003) and to provide them greater support in everyday activities. The lack of a gender perspective in the Italian public mental health services may lead clinicians to be unaware of gender-specific issues and to replicate those behavioral patterns of FEP patients' families, thus hyper-investing in the rehabilitation programs of males and underestimating the needs of females with psychotic disorders.

4.1. Strengths and limitations

Strengths of the present study include the large sample size, the community-based study design, high levels of retention, and no significant differences in demographic variables between completers and non-completers (Ruggeri et al., 2015). Although the GET-UP study was not intended to address gender differences, its design ensures a good

Table 5
Gender differences in age of psychosis onset by childhood abuse.

Mean (SD)	Physical abuse		No physical abuse		p-Value ANOVA	Bonferroni post-hoc
	Females (n = 40)	Males (n = 63)	Females (n = 98)	Males (n = 136)		
Age at onset	31.4 (9.7)	27.5 (8.0)	33.5 (10.8)	27.5 (8.8)	<0.001	F PA > M PA F no PA > M no PA F no PA > M PA
Mean (SD)	Sexual abuse		No sexual abuse		p-Value ANOVA	Bonferroni post-hoc
	Females (n = 31)	Males (n = 22)	Females (n = 106)	Males (n = 168)		
Age at onset	30.9 (9.5)	29.7 (9.1)	33.0 (10.5)	27.2 (8.5)	<0.001	F no SA > M no SA

Table 6
Gender differences in needs for care, mean CAN scores (SD) (*t*-test).

Mean (SD)	Females (n = 184)	Males (n = 260)	p-Values *t*-Test
CAN total	4.73 (2.89)	2.44 (2.77)	0.10
	21 missing	35 missing	
• Health	1.78 (1.05)	1.82 (1.12)	0.70
	25 missing	44 missing	
• Basic	0.68 (0.83)	0.66 (0.86)	0.83
	23 missing	41 missing	
• Social	1.10 (1.08)	0.98 (1.04)	0.31
	26 missing	44 missing	
• Services	0.64 (0.65)	0.47 (0.57)	0.01*
	25 missing	43 missing	
• Functioning	0.55 (0.89)	0.41 (0.75)	0.12
	29 missing	55 missing	
CAN met	2.38 (2.00)	2.27 (1.92)	0.60
	32 missing	57 missing	
• Health	0.92 (0.91)	0.93 (0.97)	0.94
	25 missing	44 missing	
• Basic	0.40 (0.66)	0.36 (0.62)	0.53
	23 missing	41 missing	
• Social	0.37 (0.69)	0.39 (0.67)	0.76
	26 missing	44 missing	
• Services	0.31 (0.53)	0.27 (0.46)	0.43
	25 missing	43 missing	
• Functioning	0.39 (0.76)	0.30 (0.63)	0.25
	29 missing	55 missing	
CAN unmet	2.35 (2.29)	2.01 (2.08)	0.15
	32 missing	57 missing	
• Health	0.86 (1.01)	0.90 (0.99)	0.73
	25 missing	44 missing	
• Basic	0.28 (0.58)	0.30 (0.58)	0.72
	23 missing	41 missing	
• Social	0.73 (0.99)	0.59 (0.93)	0.18
	26 missing	44 missing	
• Services	0.33 (0.53)	0.20 (0.44)	0.01*
	25 missing	43 missing	
• Functioning	0.16 (0.43)	0.11 (0.36)	0.24
	29 missing	55 missing	

representativeness of all patients in its area and overcomes the problem of gender differences in help-seeking behaviours (Walker and Lewine, 1993). Community-based study designs are considered the gold standard for describing true gender differences (Riecher-Rössler et al., 2018).

The possibility of selection and misclassification bias in the GET UP trial has been discussed in detail elsewhere (Ruggeri et al., 2015; Amaddeo et al., 2001). For selection bias, however, to test our hypotheses the age limit set in the GET-UP study (18–54) is potentially problematic. Women display a second peak in the incidence of psychosis in the perimenopausal period (Jackson et al., 2013), and studies with the upper age limit at 60 years show the same cumulative rates of psychosis for both gender (Riecher-Rössler et al., 2009), in contrast with studies in which the upper age limit is lower that showed a higher incidence of psychosis in men compared to women (Riecher-Rössler, 2017). It is therefore possible that a proportion of late-onset psychotic women may have been missed by the GET-UP study.

We decided to focus only on the impact of gender and childhood abuse on PANSS subscales rather than on PANSS single items in order to avoid multiple testing. However, distinguishing depressive and negative symptoms is particularly challenging, thus if the increase is related only to items involving avolition, including anhedonia and asociality (Blanchard and Cohen, 2006), this might be suggestive of a depressive component. We cannot rule out that the increase in negative symptoms in female patients exposed to childhood abuse may be due to an increase in the depression levels.

Needs for care have been assessed using the standard version of the CAN, which is not gender-sensitive (Ramsay and Youard, 2001). We were not able to examine the number of mothers or pregnant women in our sample (pregnancy was not an exclusion criteria in the GET-UP study protocol), but it is known that over 60% of women with severe mental illnesses are mothers (Howard et al., 2001) and they have specific, complex needs, including needs around CSA and domestic violence and abuse, contraception and different domains of childcare that are not detected adequately by generic assessment tools (Howard and Hunt, 2008). Therefore, it is extremely likely that actual needs for care in female patients in our sample are higher and more diversified than those detected. Future studies could use a validated and more specific assessment tool such as the CAN-M which provides a more comprehensive picture of needs for care of women with severe mental illnesses who are pregnant or mothers (Howard and Hunt, 2008). (NICE) guidelines (2015) recommend discussing contraception and optimisation of physical and mental health in potential future pregnancies at all stages of care, thus an adequate assessment of needs for care in this area appears crucial. Other gendered needs include comorbid substance abuse (Riecher-Rössler et al., 2018) - men show high rates of cannabis (Crocker and Tibbo, 2018), alcohol, cocaine and hallucinogens (Ochoa et al., 2012) abuse compared to women. Unfortunately, we were not able to control for cannabis abuse, which has been found to decrease the age of psychosis onset in both sexes (Di Forti et al., 2014).

Finally, patients in the GET-UP trial have been assessed after clinical stabilization (defined as a condition allowing the patient to collaborate

Table 7
Gender differences in needs of care by childhood abuse (CAN).

Mean (SD)	Physical abuse		No physical abuse		p-Value ANOVA	Bonferroni post-hoc
	Females (n = 40)	Males (n = 63)	Females (n = 98)	Males (n = 136)		
CAN tot	5.21 (2.44)	4.59 (2.60)	4.53 (3.17)	4.27 (2.83)	0.35	–
CAN met	2.23 (1.73)	2.56 (1.83)	2.54 (2.09)	2.31 (2.00)	0.72	–
CAN unmet	2.77 (2.18)	1.96 (1.82)	2.00 (2.27)	2.00 (2.12)	0.24	–
CAN unmet services	0.35 (0.63)	0.17 (0.38)	0.27 (0.47)	0.18 (0.44)	0.14	–
CAN unmet functioning	0.26 (0.51)	0.18 (0.39)	0.07 (0.27)	0.07 (0.34)	0.02	F PA > M no PA
Mean (SD)	Sexual abuse		No sexual abuse		p-Value ANOVA	Bonferroni post-hoc
	Females (n = 31)	Males (n = 22)	Females (n = 106)	Males (n = 168)		
CAN tot	5.37 (2.33)	4.14 (2.80)	4.64 (3.07)	4.38 (2.78)	0.30	–
CAN met	2.50 (2.05)	2.20 (2.19)	2.48 (2.01)	2.48 (1.94)	0.95	–
CAN unmet	2.86 (2.49)	2.00 (1.75)	2.11 (2.17)	1.89 (2.02)	0.17	–
CAN unmet services	0.47 (0.63)	0.33 (0.48)	0.23 (0.47)	0.16 (0.41)	0.005	F SA > M no SA
CAN unmet functioning	0.24 (0.51)	0.10 (0.30)	0.10 (0.31)	0.11 (0.37)	0.29	–

at least in a brief examination) and this may have different implications for males and females with FEP. Women with FEP, compared to men, show higher levels of insight into illness (Karow et al., 2008), have greater risk of self-harm (Haro et al., 2008) and express more depressive symptoms (Carpenter, 2007) and for these reasons tend to seek effective treatment more often and earlier than men.

5. Conclusions

The investigation of gender differences in people with psychosis is important because it is likely to increase the understanding of the etiological pathway leading to the development of psychosis. Personalization of treatment for people with psychosis is an important goal and taking gender into account is likely to make a big difference, as it is for other fields of medicine. Our results seem to suggest that childhood sexual abuse in female FEP patients may be linked to a form of psychosis whose presentation is characterized by earlier age of onset and higher levels negative symptoms, but additional research is needed to conform this However, the impact of gender and childhood abuse on psychopathology, age of onset and needs for care appears to be small and further research, is needed to disentangle whether these small differences are due to the lack of gender-sensitive assessment tools or simply reflect a lack of gender difference in itself.

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Competing interests

The authors declare that they have no competing interests.

Contributors

Author MR and AL designed the study and wrote the protocol. Author CC managed the literature searches and analyses. Authors CB and DC undertook the statistical analysis. Authors CC and LH wrote the first draft of the manuscript. Authors RLP, KF, ES, AP, LM, GN, GDG were involved in patient recruitment. Authors MR and KDS coordinated data management and supervised patient recruitment. Authors EM and ST prepared the tables. All authors contributed to and have approved the final manuscript.

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