



Gender differences in the relationship of childhood trauma and the course of illness in schizophrenia

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ABSTRACT

Introduction: Different types of childhood trauma have been repeatedly shown to contribute to psychotic symptoms. Gender differences in schizophrenia are well known. Some studies argue that trauma history means a significantly higher risk of psychosis for women than men. However, there is evidence of early adverse life events to be associated with higher stress-sensitivity in men. Little is known about the connection of specific type of trauma and specific psychotic symptoms as well as the course of illness with explicit regard to gender differences. **Methods:** 102 men and women with schizophrenia spectrum disorder were tested using Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Scale for Assessing Positive Symptoms, Early Trauma Inventory-SR. **Results:** Although, women had a later age at onset without regarding trauma history ($d = 0.74$), this difference became non-significant when introducing trauma variables. Patients reporting physical abuse had a significantly earlier age at onset, regardless of their sex ($V = 0.13, F = 3.11, p = 0.03$). Physical abuse predicted an earlier age at onset only in women ($R^2 = 0.23$). History of general trauma predicted more frequent hospitalizations only in men ($R^2 = 0.55$). **Conclusions:** Although women generally tend to have a more favorable course of illness including a later age at onset men, women with CPA seem to lose this “advantage”. It is necessary to investigate the contribution of gender interacting with adverse life events in contribution to the phenomenology and etiology of schizophrenia.

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1. Introduction

There is continuously growing evidence of cross-sectional [1,2] as well as longitudinal studies using large community samples [3–6] for childhood trauma being a risk factor for later psychotic symptoms [7]. Read’s traumagenic model [8,9] suggests that traumatic experiences play a significant causative role in the etiology of schizophrenia via biochemical and structural alteration of the brain. A bidirectional causal relationship between childhood physical abuse (CPA)/bullying and psychotic experiences has been demonstrated by Kelleher et al. [10].

Events with the intent to harm have been consistently found to have stronger connections to positive psychotic symptoms than events without such an intent, although general traumatic experiences (e. g. loss of one or both parents through death or separation) have also been shown to represent a greater risk for psychosis compared to the lack of these events [4,11]. Previous results suggest that early traumas were more linked to positive than to negative psychotic symptoms [8,12,13], however the exact nature of traumatic events and their connection to specific symptoms show a wide diversity. Evidence supporting the

connection of childhood physical (CPA), emotional (CEA) and sexual (CSA) abuse and psychotic state or different psychotic symptoms have been found [7,14] and CPA has been repeatedly shown to be the most persistent type of abuse to predict psychosis after adjusting for possible confounders [14]. A possible interpretation of the somewhat inconsistent results may be that childhood abuse possibly represents a non-specific risk factor for psychotic symptoms [7,15]. Some recent results of network analyses offer the explanation that childhood traumas are probably not directly connected to psychotic symptoms, but general psychopathology symptom seem to mediate these relationships [16]. It is also possible that different forms of childhood trauma increase risk of co-occurrence of hallucinations and delusions, rather than that of isolated symptom dimensions [11].

There is evidence that the course of illness is less favorable in schizophrenia patients with trauma history. A tendency of patients with a history of childhood abuse having an earlier age at onset [17] and more frequent contact with psychiatric services [3] or psychiatric admissions [18,19] has been repeatedly found, although there are some contradictory results regarding relapse hospital admissions [20]. These findings can be explained by various models of childhood trauma having a detrimental effect on the developing nervous system, such as the Mc Glashan and Hoffman’s [21] Developmental Reduced Synaptic Connectivity Model (claiming that disturbances of the synaptogenesis before birth

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or in the early childhood which may lead to schizophrenia) or Read's [9] traumagenic neurodevelopmental model (claiming that early traumas result a change in the HPA axis which in turn may lead to an overactivity of the dopamine system and consequently to psychotic symptoms).

Gender differences in schizophrenia (generally higher incidence, earlier age at onset, more negative symptoms, more cognitive deficits and consequently a more unfavorable course of illness in men [22,23, see 24 for a meta-analysis] are well known and have been connected to protective role of estrogen [25,26] and oxytocin [27] in women.

According to some studies systematically addressing gender differences regarding the connection of trauma history and symptom severity, childhood abuse has been shown to be stronger associated with the psychotic symptoms in women than men, although some other studies failed to find any gender differences [3,28]. In two large case-control studies female schizophrenia patients were twice as likely to have suffered either physical or sexual abuse compared to healthy women, whereas no such difference was found in men [29,30]. A further study [31] addressing positive, negative and depressive symptoms in schizophrenia patients reported a significant interaction of gender and CPA and argued that physically abused women tend to have significantly more severe psychotic symptoms than non-abused women or men with or without abuse history. As an interpretation of some of these findings, Fisher et al. [29] argued that abused girls tend to internalize their problems, therefore stand more chance to develop psychiatric symptoms, abused boys in turn tend to externalize, therefore more likely to commit aggressive or criminal actions. Contrary to this interpretation, there is evidence that childhood trauma may be associated with poorer physical health, more chronic pain and less insight in men, whereas no such association was found in women [32]. At the same time, there is evidence that excess testosterone in the developing brain may lead to a greater stress-vulnerability [33] and adult males with early loss of a parent may show greater adrenal sensitivity to stress hormone release than females [34] which may mean a greater vulnerability to psychosis according to the traumagenic model.

CEA was not addressed in the above cited studies of gender differences and the possible connections between different types of abuse and specific symptom dimensions were not explored in detail in a sex-stratified analysis. According to our knowledge, the study of Garcia et al. [35] is the only attempt to have done so and their results show significant connections between different forms of childhood trauma, especially emotional neglect and psychotic as well as depressive symptoms and low functionality in the group of women, but only the connection of physical abuse and the sum of positive and negative symptoms in men [35]. The reasons for CEA not to be involved in previous studies may be on the one hand that emotional abuse is usually present when other types of abuse are too. On the other hand, this type of abuse is considered to be less memorable and objective than other types of abuse [36]. Additionally, reports of CEA have been found biased in the way that it is regarded as less abusive by the victim than other types of abuse [37] and therefore may be less likely to be reported, but on the other hand women tend to report CEA more than men, whereas no such effect of gender has been found for the other types of abuse [38].

Although some other important aspects have been addressed in the above studies, there is no information about the gender differences in the course of illness (age at onset and number of psychiatric admissions) which may be an important issue for a gender-sensitive psychiatric care in schizophrenia. It is a vital etiological question, whether the assumed greater stress-sensitivity in women might outweigh the protective effect of estrogen and contribute to an earlier onset of schizophrenia. At the same time, it would be important to know, if childhood trauma is associated with an even earlier age of onset in men.

Bearing all this in mind, the primary aim of this study was to see, how gender differences, general childhood trauma as well as childhood physical and sexual abuse or the interaction of these contribute to

positive symptoms as well as the age at onset and the number of psychiatric admissions in schizophrenia patients. We hypothesized that patients with childhood trauma, physical or sexual abuse are more frequently hospitalized, have an earlier age at onset and suffer from more severe positive symptoms. At the same time, being aware of the general tendency of later age at onset in women (as described above) and less frequent utilization of mental health services in men [39], we hypothesized a possible interaction of gender and trauma as well as abuse history on these variables. Our additional aim was to systematically explore how general childhood trauma, childhood physical and sexual abuse are connected to adult psychotic symptom groups and to the age at onset or the number of psychiatric admissions in men and women separately, with the expectation of finding out if different traumatic and abuse experiences contribute to positive symptoms and course of illness differently in the two gender groups. Based on previous results, we expected the history of childhood physical and/or sexual abuse to be stronger predictors of positive symptoms, an earlier age at onset and more frequent hospitalizations than history of general childhood trauma, regardless of the effect of gender.

2. Materials and methods

2.1. Ethics

Ethical permission (151-4/2011) was obtained from the responsible scientific ethical commission. All participants provided an informed consent.

2.2. Study sample

102 patients (52% women, $M = 46.68$ years, $SD = 11.79$) with the diagnosis of schizophrenia (85%) and schizoaffective disorder (15%) were recruited in 7 different psychiatric institutions (4 inpatient and 3 outpatient units). Our final sample consisted of in-patients (63%) and out-patients (37%). Descriptive values are shown in Table 1.

Exclusion criteria were: acute psychotic state, history of regular alcohol or drug consume (based on information collected as part of the sociodemographic data), borderline personality disorder and trauma history (based on hospital documentation). Subgroups diagnosed with schizophrenia and schizoaffective disorders and subgroups of inpatients and outpatients were compared along all the measured variables and because no significant differences were found, they were all allocated into one common study sample.

Table 1

Socio-demographic and clinical characteristics of the sample. Abbreviations: SAPS: Scales for Assessing Positive Symptoms, ETI: Early Trauma Inventory, CPA: childhood physical abuse.

	Minimum	Maximum	M (SD)
Education	7 years	18 years	12.05 (2.83) years
Age	18 years	69 years	46.68 (11.79) years
Duration of illness	6 months	468 months ≈ 39 years	199.96 months ≈ 16.66 years (122.67 months ≈ 10 years)
Number of hospitalisations	0	30	8.54 (8.03)
PSYCHOTIC SYMPTOMS			
SAPS total mean	0.1	2.67	0.98 (0.51)
SAPS hallucinations mean	0	4.17	1.41 (1.12)
SAPS delusions mean	0	2.92	0.99 (0.63)
SAPS disorganized thought mean	0	2.88	0.71 (0.75)
TRAUMA			
ETI general trauma	0	23	4.09 (4.76)
ETI physical abuse (CPA)	0	6	1.47 (1.48)

2.3. Measures

2.3.1. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, SCID-I [40]

SCID-I. Clinical Interview is used to establish axis I. diagnoses according to DSM-IV [41]. Following modules were used in our study: A. Mood Episodes, B. Psychotic and Associated Symptoms and C. Psychotic Disorders.

2.3.2. Scale for Assessment of Positive Symptoms, SAPS [42]

The 30-item questionnaire (sample $\alpha = 0.74$) measures positive symptoms of schizophrenia and contains 4 subscales: hallucinations (sample $\alpha = 0.66$), delusions (sample $\alpha = 0.65$), bizarre behaviour or disorganized symptoms (sample $\alpha = 0.26$, excluded from further analyses, because according to the analysis of the α when item deleted internal consistency could not have been improved substantially even by removing any of the four items) and disorganized thought (sample $\alpha = 0.73$). Symptoms are scored on a 6-point Likert-type scale, 0 meaning not present at all and 5 meaning very severe. Mean values of the total score were calculated and used in further analysis.

2.3.3. Early Trauma Inventory – self report, ETI-SR [43]

It consists of 62 dichotomous items and is aimed at measuring the occurrence of the different traumatic experiences. Only the scales assessing the following childhood events were included in our analyses: 1. Non-intentional childhood traumas (for example: loss of a parent, serious injury; sample $\alpha = 0.58$) 2. childhood physical (sample $\alpha = 0.65$), and 3. sexual abuse. The subscale childhood sexual abuse (sample $\alpha = 0.50$) was excluded from further analyses because of low internal validity which could not have been improved substantially by removing any of the items and additionally because 25% of the sample did not have a sexual abuse score due to completely or partly missing values which would have meant further loss of power).

2.4. Procedure

Patients were reached through their psychiatrists in the in-patient and outpatient units. After obtaining a voluntary written informed consent, the SCID-I and SAPS interviews took place in a separate room and were led by the first author – a trained clinical psychologist. The interviews were followed by the administration of ETI-SR.

2.5. Statistics

Data analysis followed with the use of SPSS 20. Missing values were not substituted, because they were not missing at random and this meant a decrease of the sample size in most analyses. All variables were checked for normal distribution within the gender groups. A square root (sqrt) transformation was used to reduce skewness of the following variables which were not normally distributed: SAPS disorganized thought, age at onset and number of psychiatric admissions. Group comparisons on continuous variables were executed using *t*-test or when homogeneity of variance violated, using Welch's test, on categorical variables using Chi-squared test. In order to test the effect of gender, general trauma and childhood physical abuse as well as the possible interaction of these on psychotic symptoms and the course of illness, a 3×2 MANOVA was conducted, because of the relatively small sample size including only the total mean score of positive symptoms (SAPS total), the age at onset and the number of hospitalizations. The MANOVA was followed up by a discriminant analysis for the categorical variables that differentiated the groups significantly. Connections between the independent and dependent variables were tested by multiple linear regression analyses enter method, within the separate groups of men and women. Data gained from the Early Trauma Inventory were used in the analyses in two different ways. On the one

involved in regression analyses. On the other hand the fact of having been or not having been traumatized or abused physically has been included as a grouping variable in the analyses. Level of significance was set at $p < 0.05$.

3. Results

When comparing basic sociodemographic and clinical variables of men and women, the only difference was the earlier age at onset in men than women (Welch's test = 13.94, $p < 0.001$, $d = 0.74$) (Table 2). When comparing men and women, patients with and without general childhood trauma, as well as patients with and without history of childhood physical abuse along positive symptoms, age at onset and the number of hospitalizations, our MANOVA (Box's *M* test = 40.97, $p = 0.71$) showed a significant effect of both general childhood trauma ($V = 0.14$, $F = 3.51$, $p = 0.02$) and childhood physical abuse ($V = 0.13$, $F = 3.11$, $p = 0.03$). Gender differences did not have a significant effect on the tested variables ($V = 0.10$, $F = 2.35$, $p = 0.08$). The discriminant analysis for childhood trauma (Box's *M* test = 3.38, $p = 0.79$) revealed one discriminant function which explained 100% of the variance, canonical $R^2 = 0.11$. This discriminant function significantly differentiated the traumatized and non-traumatized groups $\Lambda = 0.89$, $\chi^2 = 8.73$, $p = 0.03$. The correlations between outcomes and the discriminant function revealed that positive symptoms ($r = -0.59$) and the number of hospitalizations ($r = 0.59$) loaded highly on this discriminant function, whereas age at onset showed a low value ($r = 0.14$). 80.2% of the cases were correctly classified by the model which was however very unreliable in classifying participants as traumatized and non-traumatized. It classified 96% of the traumatized, but 0% of the non-traumatized participants correctly. The discriminant analysis for childhood physical abuse (Box's *M* test = 10.60, $p = 0.12$) also revealed one discriminating factor which explained 100% of the variance, canonical $R^2 = 0.15$. This discriminant function significantly differentiated the abused and non-abused groups $\Lambda = 0.85$, $\chi^2 = 12.18$, $p = 0.007$. The correlations between outcomes and the discriminant function revealed that only age at onset loaded highly ($r = 0.95$) on this discriminant function, whereas both positive symptoms ($r = -0.05$) and the number of hospitalizations ($r = -0.04$) showed a low value. 73.4% of the cases were correctly classified by the model which was only moderately reliable in classifying 30% of the non-abused participants but 90% of the abused participants correctly.

In order to get a more detailed picture, gender-stratified regression analyses were conducted to see, if trauma and CPA predicts specific symptom groups, the total of positive symptoms, age at onset or the number of hospitalizations in men and women separately. Looking at the explorative analyses as presented in Table 3, general childhood trauma proved to be a significant predictor of the number of psychiatric admissions in men only, accounting for the 62% of the variance of this. CPA in turn was found to be a significant predictor of the earlier age at onset in women, accounting for 23% of the variance.

Although trauma history seemed to be a significant predictor of positive symptoms (SAPS total) in men ($\beta = 0.48$, $t = 2.58$, $p = 0.02$), the whole regression model was only significant at tendency level ($F(4, 22) = 2.70$, $p = 0.06$). Regression analyses yielded no significant results in men in case of age at onset ($F(4, 23) = 2.38$, $p = 0.10$). Regression analyses yielded no significant results in women in case of the sum of positive symptoms ($F(4, 31) = 0.65$, $p = 0.63$) and the number of psychiatric admissions ($F(4, 31) = 0.51$, $p = 0.73$).

4. Discussion

The most important finding of this study is that physical abuse seems to be an important factor for an earlier age at onset, especially in women. In line with the well-known tendency [24] women had a significantly later age at onset in our sample too, however, this difference has lost its significance as soon as trauma variables were included in

Table 2

Comparison of sociodemographic and clinical characteristics of men and women with schizophrenia. Abbreviations: SAPS: Scales for Assessing Positive Symptoms, ETI: Early Trauma Inventory, CPA: childhood physical abuse.

	Women n = 53 Mean (SD)	Men n = 49 Mean (SD)	Statistic	Gender difference p value	Cohen's d
Education	11.77 (2.98)	12.37 (2.64)	t = 0.949	0.345	
Age	48.32 (10.68)	44.92 (12.70)	t = 2.13	0.148	
Duration of illness	187.02 (120.55) months	214.89 (124.71) months	t = 1.13	0.26	
Psychiatric admissions	9.55 (9.18)	7.43 (8.46)	Welch test = 1.75	0.19	
Age at onset	32.74 (10.28)	26.09 (6.79)	Welch's test = 13.94	< 0.001	0.74
PSYCHOTIC SYMPTOMS					
SAPS total	0.96 (0.43)	1.07 (0.63)	Welch's Test = 0.99	0.32	
SAPS hallucinations	1.40 (1.10)	1.45 (1.14)	t = 0.25	0.80	
SAPS delusions	1.00 (0.59)	1.12 (0.83)	t = 0.89	0.38	
SAPS disorganized thought	0.61 (0.68)	0.82 (0.81)	t = 1.41	0.16	
TRAUMA					
ETI general trauma	4.11 (4.57)	6.12 (5.61)	t = 1.86	0.07	
ETI physical abuse (CPA)	1.51 (1.47)	1.91 (1.65)	t = 1.19	0.24	

Bold: significant after Bonferroni-Holm correction, p = 0.005.

the analyses. According to our results, patients with history of abuse had a significantly earlier age at onset, regardless of their sex. In the gender-stratified explorative analysis however, CPA has been found to be the only significant predictor of an earlier age at onset in women. These results may suggest that women with history of physical abuse have an earlier age at onset than those without, whereas this is not the case in men. Contrary to our hypotheses, no significant interactions between physical abuse and gender in our MANOVA have been found in support of this expectation. The implication of our findings may be however that gender-specific protective factors in women are possibly outweighed by the consequences of childhood abuse. This is in line with some previously cited findings showing that women with history of physical or sexual abuse had more chance to become schizophrenia patients than those without, whereas this was not the case in men [29,30].

An additional finding was that patients with and without general trauma also differed significantly from each other along the examined variables, but this group difference could not be explained in terms of either positive symptoms, age at onset or number of hospitalizations. Regarding the very low rate of explained variance and the inability of our model to correctly identify patients without general childhood trauma, it can be assumed that several other factors are at play which haven't been included in our analyses. However, looking at only male patients, general trauma was a strong predictor of the number of hospitalization, which is in line with previous results in not sex-stratified samples [28]. This connection is especially important, regarding that men tend to have a lower tendency to utilize mental health services than women [39] and it has relevance for the clinical praxis where childhood trauma may be an important factor to clear in the case of revolving-door male patients with schizophrenia and is in line with previous findings in non-psychotic psychiatric outpatients with trauma history [44]. According to the authors' interpretation [44], it is more acceptable to seek help at the hospital with clearly defined psychiatric symptoms than with

trauma consequences. The same might be applicable for male schizophrenia patients with trauma history.

Contrary to our hypothesis, no interaction of gender and general childhood trauma contributing to a more frequent hospitalization in males was found in our analysis of variance. This negative result is in line with previous findings too [29,30] and based on this it is difficult to understand psychological risk factors of psychosis specifically in men. Contrary to these negative results there are some findings that suggest a positive association between childhood adversities (especially emotional and physical neglect and physical abuse) and anxiety, depressive and somatic symptoms specifically in male psychiatric outpatients with mixed disorders, but no psychotic symptoms [44].

Our findings did not support the hypothesis that patients with abuse history or trauma have more severe positive symptoms than those without history of trauma or abuse. Similarly, we did not find evidence of childhood abuse predicting psychotic symptoms stronger than general trauma. The difference between groups with and without CPA was clearly based on the different age at onset, whereas the difference between groups with and without general trauma could not be explained just by one factor. This result may be due to general trauma being a multifaceted phenomenon, including such different events as serious accidents, injuries, death of a family member or a friend or being the victim of armed robbery, whereas CPA can be regarded as more or less unidimensional.

The first important limitation of our study was the small sample size which made it impossible to conduct a more detailed analysis of variance and control for further confounding variables in the regression analyses. An additional limitation is the relatively low internal validity of the ETI subscale measuring general trauma history. Further, traumatic life events were measured in a retrospective way and we had to rely on self-report data and previous documentation of the patients without the opportunity of a heteroanamnesis. A further limitation is that the exact reason for repeated hospital admissions (relapse, depressive symptoms,

Table 3

Possible predictors of symptom severity, age of onset and number of psychiatric admissions in men and women. Abbreviations: CPA: child physical abuse.

Model fit	Men			Women		
	β	t	p	β	t	p
	Number of psychiatric admissions			Age at onset		
	F(4, 23) = 9.05			F(3, 31) = 3.33		
	p < 0.001			p = 0.03		
	R ² = 0.62, adjusted R ² = 0.55			R ² = 0.23, adjusted R ² = 0.16		
Age	0.25	1.69	0.11	-	-	-
Years of education	-0.07	-0.48	0.64	0.25	1.57	0.13
General childhood trauma	0.83	5.89	<0.001	0.13	0.83	0.41
CPA	-0.08	-0.50	0.62	-0.40	-2.55	0.02

suicide attempts, change of medication etc.) was not assessed in detail. Additionally, several other factors such as self-esteem or support of significant others that are known to be important for the consequences of trauma as well as in psychosis [30] could not be included in the analysis. The findings of this study should however be regarded as important tendencies that may inform future research in larger samples.

The most important conclusions of our study are the importance of trauma history that may change known gender differences in both sexes. At the same time, it is of crucial importance to understand gender differences in the etiology of symptoms, in order to be able to provide gender-specific interventions [22].

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