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Clinical outcomes and childhood trauma in bipolar disorder: A community sample of young adults

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ABSTRACT

Childhood trauma is a complex experience, much reported by subjects with bipolar disorder. There are still few studies that assess its consequences in a community sample of bipolar in early stage. The aim of the present study is to assess the association between childhood trauma and clinical outcomes, including the global functioning, in a community sample of young adults with bipolar disorder. This is a cross-sectional study with a community sample of subjects with bipolar disorder, from 23 to 30 years old, with and without childhood trauma. The trauma experiences during childhood were assessed by Childhood Trauma Questionnaire (CTQ). The functioning was assessed by Functioning Assessment Short Test (FAST). Ninety subjects with bipolar disorder were included in the study (30 with childhood trauma and 60 without childhood trauma). Young adults with bipolar disorder and childhood trauma showed higher prevalence of current suicide risk, higher severity of depressive symptoms, and higher functioning impairment as compared to subjects with bipolar disorder without childhood trauma. The childhood trauma experiences appear to be an environmental risk factor for worse clinical outcomes and higher functional impairment.

1. Introduction

The exposure to childhood trauma is associated with adverse outcomes in children and adolescents, including emotional (Bücker et al., 2012; Pears et al., 2008; Sesar et al., 2008), psychosocial (Pears et al., 2008; Sesar et al., 2008), cognitive (Bücker et al., 2012; De Bellis et al., 2013; Enlow et al., 2012; Mills et al., 2011; Pears et al., 2008), and functional impairments (Bücker et al., 2012). There is a growing interest in research about the consequences of childhood trauma during adulthood. Childhood trauma can affect brain development, causing long-term functional changes (Aas et al., 2012). It has been proposed that traumatic events during childhood are important contributors to the development or manifestation of psychiatric disorders (Bücker et al., 2013; Goldberg and Garno, 2009; Kuhlman et al., 2013; Nemeroff, 2004). There is evidence that young people who are genetically vulnerable are more susceptible to develop bipolar disorder when exposed to trauma (Garno et al., 2005; Goldberg and Garno, 2009; Leverich et al., 2002). In addition, a recent systematic review showed that childhood adversity is associated with bipolar disorder (Palmier-Claus et al., 2016), and a recent umbrella review of systematic reviews and meta-analyses showed that childhood adversity is a risk factor for bipolar disorder supported by highly suggestive evidence (Bortolato et al., 2017).

The occurrence of physical and sexual abuse has been associated with an increase in the number of mood episodes in people with bipolar disorder (Larsson et al., 2013). Sexual abuse is significantly higher in individuals with the diagnosis of bipolar disorder when compared to subjects with major depressive disorder (Hyun et al., 2000). When compared to healthy controls, young people with bipolar disorder show a higher prevalence of emotional abuse (Etain et al., 2010). Studies suggest that traumatic experiences can be associated with rapid cycling, substance use and abuse (Garno et al., 2005; Leverich et al., 2002; Post and Kalivas, 2013), suicide attempts (Garno et al., 2005; Leverich et al., 2002), cognitive impairment (Aas et al., 2012; Bücker et al., 2013), premorbid (Conus et al., 2010) and lifetime (Larsson et al., 2013) functioning impairment, and low adherence to treatment (Conus et al.,

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2010) of subjects with bipolar disorder. Moreover, these data were confirmed in a recent systematic review showing that childhood maltreatment predicts worse clinical features and course of illness in patients with bipolar disorder (Agnew-Blais and Danese, 2016).

Considering the potential consequences of the childhood trauma in individuals with bipolar disorder, community studies may contribute to understanding effects of trauma in early stages of bipolar disorder. The majority of the studies assessing the effect of childhood trauma in the course of bipolar disorder included outpatient samples. Community samples could add to the current literature, considering that subjects recruited in the community, especially in young adult age, are less affected by the burden of disease, as well as by the effect of multiple interventions, as compared to outpatient samples. Thus, the aim of the present study is to assess the association between childhood trauma and clinical outcomes, including the global functioning, in a community sample of young adults with bipolar disorder.

2. Methods

2.1. Subjects and procedures

This is a cross-sectional study corresponding to the second wave of a cohort study with a population sample. The full description of the first wave has been previously published (Jansen et al., 2011). Briefly, the first wave included 1560 participants from 18 to 24 years old living in urban Pelotas (Brazil), in the period from 2007 to 2009. The second wave happened from 2012 to 2014, a mean five years after the first phase, all young adults who participated in the first phase were invited to return for a follow-up assessment. The rate of reassessments at follow-up was 79.7% (n = 1244). Subjects were informed about the research objectives and signed an informed consent form. Respondents who had a psychiatric disorder were referred for the health services according to demand. This study was approved by the Research Ethics Committee of the *Universidade Católica de Pelotas* under protocol number 2008/118.

2.2. Measures

Young adults answered a questionnaire with socio-demographic and economic variables to assess gender, skin color, age, conjugal status, years of education, occupational status, and economic classification. The economic classification was evaluated and defined according to the criteria of the Brazilian Association of Research Companies (Associação Brasileira de Empresas de Pesquisa – ABEP, 2008). This instrument measures the economic classification through the accumulation of material goods and the householder's schooling, classified into five groups (A, B, C, D, and E), where A refers to the highest economic classification and E to the lowest. To data analysis, it was decided to categorize the economic classification in A/B (High), C (Intermediate), and D/E (Low).

Bipolar disorder was assessed using the Mini International Neuropsychiatric Interview - PLUS (MINI-PLUS; Amorim, 2000; Sheehan et al., 1998) by trained psychologists. In cases of doubt about bipolar disorder diagnosis, subjects were reassessed using the semi-structured clinical interview for DSM Structured Clinical Interview (SCID; Del-Ben et al., 2001; First et al., 1996) in order to confirm the diagnosis. In addition, the MINI-PLUS was used to assess clinical history, such as age of onset of bipolar disorder, rapid cycling, lifetime hospitalization, lifetime suicide attempts, current suicide risk, and anxiety disorders comorbidity. Young adults were also asked about lifetime psychopharmacological treatment.

Trauma experiences were assessed using the Brazilian version of the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003; Grassi-Oliveira et al., 2006). The CTQ is a 28-item retrospective self-report questionnaire that assesses the history of abuse and/or neglect during childhood. Measures five childhood trauma subtypes, including emotional, physical and sexual abuse, as well as emotional and physical neglect. Items are rated on a five points Likert scale from 1 = *never true* to 5 = *very often true*, according to the frequency with which each event occurred. The total score of the CTQ takes into consideration the frequency of the various forms of abuse and/or neglect (Grassi-Oliveira et al., 2006).

The Functioning Assessment Short Test (FAST; Cacilhas et al., 2009; Rosa et al., 2007) was performed to assess the global functioning. FAST is a 24-item scale and assesses difficulties in six functional domains: autonomy, occupational functioning, cognitive, financial issues, interpersonal relationships, and leisure time, according to the last fifteen days before evaluation. The sum of all items provides the total score, being that, higher scores indicate higher degrees of global functional impairment.

The severity of manic symptoms was assessed using the Young Mania Rating Scale (YMRS; Vilela et al., 2005; Young et al., 1978). To assess the severity of depressive symptoms was used the Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979). Substance abuse or dependence was assessed with the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), the cutoff for substance abuse/dependence was four (Henrique et al., 2004; WHO, 2002).

2.3. Statistical analysis

For statistical analysis young adults with bipolar disorder were stratified into two groups according to the frequency of traumatic experiences in childhood, for such, were included in bipolar disorder group with childhood trauma those who were located in the highest tercile of the CTQ and without childhood trauma when located in the two lowest terciles. We opted for this criterion of inclusion in the groups because there is no cut-off point of the CTQ validated for the Brazilian population. Socio-demographic, economic, and clinical characteristics of bipolar disorder groups with and without childhood trauma were analyzed using the t-test, Chi-square, and Mann-Whitney U test.

To evaluate the correlation between the frequencies of traumatic experiences in childhood and global functioning impairment was used the Pearson correlation. Posteriorly was performed a model of linear regression, adjusted for possible confounders. We considered as possible confounding factors all variables associated with scores of the FAST and CTQ with $p < 0.20$. For all statistical tests were considered significant associations when $p < 0.05$.

3. Results

The prevalence of bipolar disorder, in the second wave, was 7.2% (n = 91), being higher among women, subjects with fewer years of education, and lower economic classification. We verified a higher frequency of traumatic experiences in childhood in subjects with bipolar disorder (44.4 ± 16.5) as compared to community sample without bipolar disorder (34.3 ± 10.7; $p < 0.001$). We have one missing data in the CTQ scale, thus ninety young adults with bipolar disorder (30 with childhood trauma and 60 without childhood trauma) were included in this study. We did not verify significant differences regarding socio-demographic and economic characteristics between subjects with bipolar disorder with and without childhood trauma (Table 1).

The prevalence of current suicide risk was 43.3% in subjects with bipolar disorder presenting childhood trauma and 21.7% in subjects with bipolar disorder and without childhood trauma (p = 0.033). Young adults with bipolar disorder and childhood trauma also reported a higher severity of depressive symptoms when compared to subjects with bipolar disorder without childhood trauma (p = 0.011). In addition, young adults with bipolar disorder and childhood trauma showed higher global functioning impairment as compared to subjects with

Table 1
Socio-demographic and economic characteristics of the community sample of young adults with bipolar disorder with and without childhood trauma.

Characteristics	BD without trauma (n = 60)	BD with trauma (n = 30)	p-value
Gender[a]			0.448
Male	18 (30.0)	6 (20.0)	
Female	42 (70.0)	24 (80.0)	
Skin color[a]			0.938
White	38 (63.3)	20 (66.7)	
Non-white	22 (36.7)	10 (33.3)	
Age (years)[b]	25.73 (± 2.15)	25.87 (± 2.03)	0.779
Living with a partner[a]			0.813
No	21 (35.0)	9 (30.0)	
Yes	39 (65.0)	21 (70.0)	
Education (years)[b]	10.20 (± 3.00)	10.10 (± 3.28)	0.886
Economic classification[a,*]			0.209
High	25 (42.4)	10 (33.3)	
Intermediate	31 (52.5)	16 (53.3)	
Low	3 (5.1)	4 (13.3)	
Occupation (work or study)[a]			0.800
No	15 (25.0)	9 (30.0)	
Yes	45 (70.0)	21 (70.0)	

BD = Bipolar disorder.
[a] Absolute and relative (%) frequencies, p-value according to Chi-square test;
[b] Mean (standard deviation), p-value according to t-test;
[*] Missing (n = 1).

bipolar disorder without childhood trauma (p = 0.003; see Table 2).

According to data presented in Fig. 1, we found a moderate positive correlation between the scores of traumatic experiences in childhood (CTQ score) and the global functioning impairment (FAST score) of the community sample of young adults with bipolar disorder (r = 0.452; B = 0.385; 95% CI [0.224–0.547]; p < 0.001). The association between scores of traumatic experiences in childhood and global functioning impairment remained significant after adjusted for severity of depressive symptoms and current suicide risk (B = 0.197; 95% CI [0.057–0.337]; p = 0.005).

4. Discussion

This study showed that young adults with bipolar disorder and childhood trauma had higher severity of depressive symptoms, higher prevalence of current suicide risk, and higher global functioning impairment when compared to subjects with bipolar disorder without childhood trauma. Moreover, we verified that childhood trauma remained associated with functional impairment, independent of the current severity of the illness.

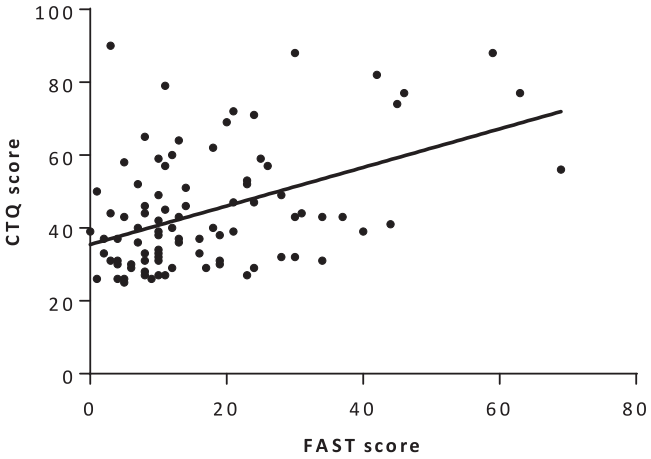

Fig. 1. Correlation between childhood trauma and global functioning impairment scores of the community sample of young adults with bipolar disorder (r = 0.452; p < 0.001).
CTQ score = Score of the Childhood Trauma Questionnaire; FAST score = Score of the Functioning Assessment Short Test.

Similarly, it has been shown that individuals with bipolar disorder who experienced trauma present significantly higher levels of inter-episode depressive symptoms than those without trauma history (Maguire et al., 2008). We did not find studies that evaluate the relationship between childhood trauma and the current suicide risk, especially, in subjects with bipolar disorder. However, studies suggest a powerful relation between the frequency of traumatic experiences in childhood and the number of lifetime suicide attempts (Dube et al., 2001; Leverich et al., 2002). It is noteworthy that the number of suicide attempts is a measure of course of the illness, and the current suicide risk reflects the severity of the current symptoms. In our study the prevalence of lifetime suicide attempts was low and we did not have information about the number of lifetime attempts, limiting such observation.

We also showed that the higher frequency of the traumatic experiences during childhood was associated with global functioning impairment in young adults with bipolar disorder. This result corroborates with the data reported in the literature (Bücker et al., 2013; Larsson et al., 2013). A recent systematic review showed that the childhood trauma presented a negative impact on cognitive performance during adulthood in patients with BD (Jiménez et al., 2017). Considering that the functioning assessments include a domain assessing cognition, the findings of that systematic review corroborate with our findings. In addition, a study with outpatients in first manic episode assessing the

Table 2
Clinical outcomes of the community sample of young adults with bipolar disorder with and without childhood trauma.

Characteristics	BD without trauma (n = 60)	BD with trauma (n = 30)	p-value
Age onset of BD[a]	17.50 (± 4.87)	18.46 (± 6.67)	0.799
Rapid cycling[b]	28 (46.7)	12 (40.0)	0.549
Lifetime hospitalization[b]	5 (8.3)	2 (6.7)	0.781
Lifetime suicide attempts[b]	13 (21.7)	10 (33.3)	0.347
Current suicide risk[b]	13 (21.7)	13 (43.3)	0.033
Lifetime pharmacological treatment[b,*]	34 (57.6)	15 (50.0)	0.494
Substance abuse or dependence[b]	13 (21.7)	5 (16.7)	0.576
Depressive symptoms (MADRS score)[c]	8 (2–17.5)	15 (7.5–22.5)	0.011
Manic symptoms (YMRS score)[c]	5 (3–11)	7 (4.5–9)	0.437
Comorbid anxiety disorders[b]	32 (53.3)	19 (63.3)	0.367
Global Functioning (FAST score)[c]	10 (6–18.75)	21 (10.75–28.5)	0.003

BD = Bipolar disorder; MADRS = Montgomery-Asberg Depression Rating Scale; YMRS = Young Mania Rating Scale; FAST = Functioning Assessment Short Test.
[a] Mean (standard deviation), p-value according to t-test;
[b] Absolute and relative (%) frequencies, p-value according to Chi-square test;
[c] Median (25th/75th quartiles), p-value according to Mann-Whitney U test;
[*] Missing (n = 1).

functioning through the Global Assessment of Functioning (GAF), verified that patients with trauma presented lower levels of functioning when compared to those who did not present trauma (Bücker et al., 2013). Another study verified that emotional abuse or neglect and physical abuse, assessed using CTQ, were associated with reduced level of functioning (GAF) in patients with bipolar disorder (Larsson et al., 2013). Similar results were also observed in young adults patients with bipolar disorder type I, in the first psychotic mania episode, who suffered physical and sexual abuse in childhood or adolescence, which showed premorbid functioning impairment (Conus et al., 2010), suggesting that the trauma may cause functioning impairment even before of the first manic episode with psychotic symptoms.

Furthermore, authors suggest that global functioning can be used as a measure of staging in bipolar disorder (Rosa et al., 2014). According to results of the present study, it is suggested that childhood trauma can influence the functional performance of young adults with bipolar disorder, independent of the current severity of the disorder, indicating that the childhood trauma can also accelerate the illness progression, such as highlighted in the literature (Larsson et al., 2013; Post, 2010). A potential mechanism involved in the association between childhood trauma and worse clinical outcomes in bipolar disorder includes the activity of the hypothalamic–pituitary–adrenal (HPA) axis. It is known that the degree of activity of the HPA axis is associated with childhood trauma in offspring of patients with BD (Schreuder et al., 2016). Since childhood maltreatment is a risk factor for the onset (Bortolato et al., 2017) and for unfavorable outcomes of BD (Agnew-Blais and Danese, 2016), HPA axis dysfunction might act as a mediator, on the basis of gene-environment interactions (Belvederi Murri et al., 2016).

The present study has some limitations that must be highlighted. First, the data about traumatic experiences during childhood were obtained retrospectively, as in the majority of studies that evaluated this problematic in adults, from a self-report measure. It is worth highlighting that it is a complex issue permeated of fears and prejudices becomes often difficult to trauma approach, seeing that account of these experiences suffers influence of the recall bias. Furthermore, the CTQ do not has a cut-off point validated for the Brazilian population. However, the CTQ is an instrument frequently used in studies validated for different populations. Second, we did not approach in this study the specific age in that the traumatic experience occurred and the effects of stressors events experienced in adulthood that might mediate the relationship between childhood trauma and a worse clinical manifestation of bipolar disorder. It is worth mentioning, according to neuroimaging studies, that traumatic experiences at specific time points during childhood have different effects, due to a sensitive period in different parts of the brain, according to age, such as the hippocampus and frontal cortex (Andersen et al., 2008). In addition, the literature shows the occurrence of long-term sensitization of the stress response after early stress in adults (Heim and Nemeroff, 2001; Post, 2010). Finally, the study has a cross-sectional design and therefore, cannot make causal inferences. Future longitudinal studies are needed in population samples of young adults with bipolar disorder, to thereby, confirm the present findings and provide more information about the phenomenological changes in the course of bipolar disorder in subjects with childhood trauma, evaluating this experience with genetic factors and genic expression.

Despite the above limitations, we showed a relationship between childhood trauma and clinical outcomes in a community sample of young adults with bipolar disorder. This is one of the few studies wherein the sample is coming from a community study and that assess young adults. Most studies show an outpatient design and convenience samples, including patients who have more severe symptoms and/or a longer course of the illness. It is worth highlighting, according to our search, that this is the first study that evaluates the childhood trauma and functional performance in subjects with bipolar disorder in a community sample.

The results of this study become relevant for mental health services, emphasizing the importance of identifying childhood trauma experiences as an environmental risk factor for a worse clinical manifestation of the illness and higher functional impairment independent of the severity of the symptoms. It becomes necessary the attention of professionals to some difficulties that permeate the treatment of individuals with childhood trauma experiences, such as: develop and maintaining a therapeutic alliance, because there are often significant problems related to confidence and, mainly, difficulty in maintaining therapeutic engagement and motivation (Lawson et al., 2013).

Thus, all professionals must be aware that these traumatic experiences may influence the course of treatment. Currently, there are a few studies assessing potential interventions for patients with bipolar disorder who suffered early childhood trauma. A Randomized Clinical Trial testing the effect of Cognitive Behavioral Therapy (CBT) as compared to treatment-as-usual (TAU) for patients with severe mental disorders and Posttraumatic Stress Disorder (PTSD), showed that the CBT was more effective than TAU in reducing PTSD symptoms and negative trauma-related cognitions, as well as in reducing depressive and anxious symptoms (Mueser et al., 2008). Despite this study had not included only patients with BD, the population included (severe mental disorders) involved some cases of patients with BD. A pilot study assessing the impact of Eye Movement Desensitization and Reprocessing (EMDR) therapy versus TAU in patients with BD with a history of traumatic events, showed that the EMDR therapy was more effective than TAU in the reduction of depressive and hypomanic symptoms, as well as in symptoms related to trauma (Novo et al., 2014). Also, the EMDR therapy will be tested in a large RCT, being the protocol already available (Moreno-Alcázar et al., 2017). Considering that there is few clinical trials testing the alternative treatments for patients who suffered childhood trauma, more studies are needed, especially when refers to bipolar disorder, aiming the identification of more target treatments, which may contribute to an improvement of the clinical course of subjects with bipolar disorder who were exposed to traumatic situations during childhood.

Conflict of interest

None.

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