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Original article

Clinical correlates of trauma spectrum and bipolar disorder

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SUMMARY

Objectives

To evaluate the relationships between trauma and clinical correlates, quality of life and global functioning in a sample of individuals with bipolar disorder (BD).

Methods

65 subjects with BD type I or II, aged between 18 and 75 years, were assessed with the Clinical Global Impression - Severity (CGI-S), Trauma and Loss Spectrum Self Report (TALS-SR), Quality of life index (QL-index), and Global Assessment of Functioning (GAF) scales. Data analysis were performed using SPSS version 20.0. Basic statistics were used to describe the demographic, clinical and traumatic spectrum characteristics of the participants. Pearson's correlation analysis was performed to analyse the correlations between psychometric scores and clinical data. The independent t-test was used to compare the two groups (BD I and BD II).

Results

Statistically significant correlations were observed between BD severity, as measured by CGI-S, and TALS-SR mean scores in Domains pertaining to III ($p < 0.01$), IV ($p < 0.05$), VII ($p < 0.01$), VIII ($p < 0.05$) and IX ($p < 0.05$). No significant correlations were found between the score in the TAL-SR 'history of trauma' domain and number of hospitalisations, history of suicide attempts, quality of life and global functioning indexes. However, a statistically significant correlation emerged between Domain VII score and history of suicide attempts ($p < 0.01$). The majority of subjects (92.3%) believed that traumatic experiences had an impact on their BD symptoms.

Conclusions

Our data confirms a relationship between trauma spectrum and certain BD characteristics. The absence of a relationship between trauma history and number of hospitalisations, suicide attempts, quality of life and global functioning may be due to lack of statistical power. The significant relationship between suicide attempts and Domain VII -TALS-SR score is worth being better explored in longitudinal and prospective studies.

Key words: trauma spectrum, bipolar disorder, functioning

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Conflict of interest
A. Fagiolini declares conflict of interest

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Introduction

Bipolar disorder is a chronic and recurrent mood disease, whose prevalence in general population rises above 1%, representing the fourth disability global cause in adolescents and young adults [1].

It is well known that bipolar disorder has a strong genetic etiology, however there are evidence that it could be influenced also by environmental events, such as childhood trauma [2,3]. Childhood trauma include physical, emotional and sexual abuse, physical and emotional neglect [4,5].

Several studies showed that young people with genetic vulnerability are more susceptible to developing bipolar disorder when exposed to trauma [6], as confirmed by some recent reviews that showed that adversities

during childhood are associated to bipolar disorder, representing a risk factor for its development [7,8].
Some studies [9] hypothesized that vulnerability to the development of bipolar disorder could manifest itself not only through genetic risk factors, but also through exposure to traumatic environmental factors related to the pathology of one or more family members. In this sense, familiarity for bipolar disorder could be mediated in part by traumatic events.
Between 30 and 50% of individuals with bipolar disorder suffered from childhood trauma [10], resulting often in a comorbid diagnosis of Post Traumatic Stress Disorder [11].
These traumatic experiences often lead to a worse clinical outcome: individuals with bipolar disorder who suffered from trauma are more likely to develop rapid cycling, suicide attempts, substance use or abuse, cognitive impairment, early and lifetime functional impairment, poor adherence to treatment [6,12-14].
Trauma in these patients can be expressed in different forms depending on the gender: it has been observed, in fact, how in females it is most manifested in negative thoughts and suicidal behaviors, while in males in aggression and heterodirect anger [15]; moreover, it seems that females with bipolar disorder with a history of traumatic events show more clinical characteristics of rapid cycling, an early onset of disease, an increased suicidal risk and a greater frequency of depressive episodes [1].
Traumatic events influence the severity of the disease not only during childhood, but also during adolescence and adulthood; it has been observed that the presence of stressful events in adult life correlates with a more severe symptomatology and with a greater recurrence of depressive symptoms [16].
Although several studies have highlighted the relationship between bipolar disorder and traumatic events, the frequency of the different types of traumatic experience in bipolar disorder is less studied. However, emotional trauma appears to be the most associated with DB [17,18].
Some authors specifically investigated the frequency of sexual abuse in bipolar patients, finding a significantly higher prevalence compared to the general population [10].
Traumatic events also seem to play a role in determining cognitive alterations: in fact, it has been observed that, in bipolar patients with a history of trauma, there is a compromise of all cognitive domains, including memory, attention, executive functions, IQ.
Underlying these deficits, several neurobiological mechanisms may be involved, inherent in neuroplasticity, inflammation, HPA axis and regulation of the circadian system. it appears that trauma may induce a dysregulated state of glucocorticoid release, which could alter normal neurogenesis and physiological brain development. In fact, imaging studies have shown, in bipolar patients with a history of childhood trauma, alterations of the prefrontal cortex, amygdala, corpus callosum, hippocampus, hypothalamus and pituitary. Another possible mechanism could concern BDNF-mediated neuroplasticity, whose serum levels are reduced in this population [19]. In addition, in these patients high levels of cytokines and inflammatory mediators are often observed; this could play a role in biological changes induced by trauma [20].
Literature points out that there is an important correlation between traumatic events and the onset and development of bipolar disorder and its characteristics, still the impact that these events have on the functioning of patients is less studied. Indeed, despite clinical evidence of global functional impairment in patients with bipolar disorder who experienced childhood trauma, only few studies [21] have been investigated the correlation between these two features.
Therefore, our study aims to analyze the prevalence of traumatic events in DB patients, with particular attention to the impact that trauma has on clinical manifestations, prognosis and overall functioning in these patients.

Aim of the study

Our aim is to outline the impact of the spectrum of trauma and loss on bipolar disorder, analyzing the frequency and showing the effects on the clinical features of the desease, over the quality of life and on the global functioning of the patient.

Materials and methods

Partecipants

The study sample included 65 adult out- and inpatients, recruited over a 3-month period, with a diagnosis of Bipolar Disorder (BD), seeking treatment at the Department of Psychiatry of the University of Siena. Inclusion criteria for patients were: diagnosis of BD type I or II according to DSM-5 and age between 18 and 75 years. Exclusion criteria were: diagnosis of post-traumatic stress disorder, severe systemic or neurological illnesses, inability to give consent or to perform Self-Report for Trauma and Loss Spectrum (TALS-SR).

Measure

Instruments and assessments

We collected patients' sociodemographic and clinical data through a structured interview. Patient's clinical condition was assessed via Clinical Global Impression - severity of illness (CGI-S), a scale that assesses the severity of the disease at the time of the interview, with a score ranging from 0 (normal) to 7 (extremely ill) [22].

An overall assessment of patients' quality of life was obtained through the Quality of Life Index - QL-Index, which is a simple and short tool of hetero-evaluation that has been created for the evaluation of patients suffering from oncological diseases, but it is often used in other pathological conditions. It consists of 5 item that explore activity, daily life, health, support and mood of patients and provides an overall judgment by the clinician about the accuracy of his assessment. The rating scale consists of 3 points (0-2) and the higher scores correspond to the positive responses. The index derives from the sum of the individual scores, so higher index scores express a better quality of life [23].

The overall functioning of patients was assessed via the Global Functional Assessment (GAF), a scale that considers the psychosocial and working functioning of the subject by placing it in a hypothetical continuum ranging from mental health (100) to very serious mental illness with risk of death (1), regardless of the nature of the psychiatric disorder: it has been included in the DSM- III-R and in DSM-IV as Axis V of the multiaxial classification [24].

TALS-SR

TALS-SR is a questionnaire consisting of 116 items that explores lifetime potentially traumatic or loss events and the set of symptoms, behaviors and personality characteristics that can predispose or detect a stress response syndrome.

The TALS-SR is divided into 9 domains: Domain I (loss events) describes loss events of different severity; Domain II (grief reaction) explores symptoms related to persistent grief in response to loss; Domain III (potentially traumatic events) includes potentially traumatic events that can occur lifetime; Domain IV (reactions to losses or upsetting events) investigates acute reactions to loss or traumatic events; Domains V, VI, VIII describe the symptoms related to re-experiencing, avoidance/numbing and hyperarousal respectively; Domain VII (maladaptive coping) searches for maladaptive behaviors; Domain IX (personal characteristics/risk factors) explores the personality characteristics that can represent a risk factor for the development of a symptomatology in relation to trauma and/or loss.

Items' response consist of yes or no and the domain score is obtained by adding the positive answers [25].

Statistical analysis

Data analysis were performed using SPSS (Statistical Package for the Social Sciences for Windows, IBM) version 20.0. Basic statistics were used to describe the demographic, clinical and traumatic spectrum characteristics of the participants.

Pearson's correlation analysis was performed to analyze the correlations between TALS-SR, CGI-S, QoL-I, GAF and clinical data (hospitalizations and suicide attempts). The independent *t-test* was used to compare the two groups (BD I and BD II) with respect to continuous quantitative variables, i.e. the average scores obtained in the TALS-SR domains.

Results

Demographic and clinical characteristics

Thirty-two of the 65 patients were women and the mean age was 50.2.

The sample was divided into 36 patients with bipolar disorder I and 29 patients with bipolar disorder II, among these 22 patients had psychiatric comorbidity: 12 (18.6%) with borderline personality disorder, 4 (6.2%) with narcissistic personality disorder, 3 (4.6%) with obsessive compulsive disorder, 1 (1.5%) patient with binge eating disorder, 1 (1.5%) with dependent personality disorder and 1 (1.5%) with attention deficit hyperactivity disorder.

Table I describes the CGI-S scores of the total sample (n = 65).

Analyzing the sample in terms of lifelong hospitalizations and suicide attempts, it emerges that 64.6% were hospitalized at least once in their lives and 21.5% made at least ≥ 1 suicide attempt. In particular 4.6% of the sample had ≥ 10 hospitalizations, 13.8% made one suicide attempt, 6.2% made two attempts, 1.5% made three attempts.

In our sample the average BMI was 27.46 (*sd* ± 5.81).

The average scores obtained regarding quality of life and overall functioning were 7.63 (*sd* ± 2.25) (QoL-I) and 70.60 (*sd* ± 16.01) (GAF) respectively.

Table II shows the mean TALS-SR domain scores obtained in our sample, in 30 patients with PTSD [25] and 30 healthy controls [25].

Furthermore, we assessed in the opinion of subjects, what impact the traumatic or loss event have had on the bipolar disorder: 36.9% rated a serious impact, 46.2% average, 9.2% mild impact and 7.7% no impact.

Correlations

We have linked the domains that mainly indicate the loss and trauma events with the patient's clinical condition, in particular by correlating TALS-SR Domain I (loss events) and Domain III (potentially traumatic events) respectively with the CGI-S: in the first case we didn't find any correlation, in the second one we obtained a statistically significant correlation ($p < 0.01$), indicating that the increase in potentially traumatic lived events corresponds to a worse disease severity.

By relating the CGI-S to the other TALS-SR domains, we obtained a statistically significant correlation in the case of Domain IV (reactions to losses or upsetting events)

TABLE I. *CGI-S scores of the total sample (n = 65).*

CGI-S	1	2	3	4	5	6	7
Sample n = 65	3 (4.6%)	21 (32.3%)	22 (33.8%)	10 (15.4%)	8 (12.3%)	1 (1.5%)	0

CGI-S: Clinical Global Impression - Severity. Frequency and percentage are reported.

p < 0.05, Domain VII (maladaptive coping) p < 0.01, Domain VIII (arousal) p < 0.05, Domain IX (personal characteristics/risk factors) p < 0.05.
By studying the correlation of domains I and III with hospitalizations (n°), suicide attempts (n°), QoL (score) and GAF (% score), there does not seem to be a statistically significant correlation in our study between the traumatic events and loss and the number of hospitalizations, suicide attempts, quality of life and general patient functioning.
However, an important statistically significant correlation emerges between Domain VII (maladaptive coping) and suicide attempts (p < 0.01), which explains the relationship between maladaptive behaviors following a traumatic experience and the greater risk of suicidal thoughts or acts.

Comparison between groups

We have compared, via independent t-test, the difference in the mean scores of Domain I and Domain III between patients with BD I disorder and II.
The results did not show a significant difference in the case of Domain I (loss events), while we found a significant difference (p < 0.05) between the two groups in Domain III (potentially traumatic events): average score was 5.64 (*sd* ± 4.18) in the BD I group, 3.66 (*sd* ± 2.62) in BD II group. This may point out that patients with BD I have more traumatic events in their lives than patients with BD II.
Furthermore, statistically significant differences between BD I and II emerged in Domain IV (p < 0.05), Domain V (p < 0.05), Domain IX (p < 0.07), indicating greater reactions to losses or upsetting events, re-experiencing and personal characteristics / risk factors in the BD I group.
These results are fully described in Table III.
Finally, we made a gender comparison by comparing the difference in the mean scores of the TALS-SR domains in males and females. In this comparison, no statistically significant differences emerged except for Domain VIII (arousal) in which the comparison of the averages between males (1.94 *sd* ± 1.66) and females (2.97 *sd* ± 1.67) was significant (p < 0.05).

Discussion

The results of our study show that, in the examined sample, there is a statistically significant positive relationship between the reported incidence of potentially traumatic events (domain III of TALS-SR) and severity of Bipolar Disorder (defined by CGI-S scores). Our results seem to be in accordance with available scientific literature data: a recent comprehensive review emphasized the high prevalence of traumatic events observed in the lifespan of BD patients, showing the importance that trauma might have in the development and natural course of disease [17].
To this end, a meta-analysis that collected data from 30 different studies found a positive association between the occurring of childhood traumatic events, and the severity of manic, depressive and psychotic symptoms experienced by the patients [26,27].
In order to assess the impact of trauma on the course of BD, a 2017 study by Aldinger and colleagues

TABLE II. *Mean TALS-SR domain scores obtained in our sample (n = 65), in patients with PTSD (n = 30) [25] and healthy controls (n = 30) [25].*

	Domain I	Domain II	Domain III	Domain IV	Domain V	Domain VI	Domain VII	Domain VIII	Domain IX
BD (n = 65)	4.85 (± 1.90)	12.98 (± 5.25)	4.75 (± 3.68)	8.18 (± 4.17)	4.05 (± 2.42)	4.71 (± 3.09)	2.02 (± 1.99)	2.45 (± 1.74)	2.66 (± 1.61)
PTSD (n = 30)	4.20 (± 2.19)	12.27 (± 6.84)	5.00 (± 2.79)	10.60 (± 3.19)	5.03 (± 1.47)	6.17 (± 2.86)	2.03 (± 1.47)	3.47 (± 1.28)	1.97 (± 1.38)
Controls (n = 30)	2.90 (± 1.51)	7.83 (± 4.62)	2.63 (± 2.19)	4.20 (± 3.34)	1.37 (± 1.45)	1.23 (± 1.77)	0.33 (± 0.84)	0.93 (± 1.17)	1.27 (± 1.28)

BD: Bipolar Disorder; PTSD: Post Traumatic Stress Disorder.

TABLE III. *Comparison of the mean scores of TALS-SR domains between Bipolar I disorder and Bipolar II disorder*

TALS-SR	BD	Mean ± SD	p
Domain I	I	5.14 (± 1.79)	0.168
	II	4,48 (± 1.99)	
Domain II	I	13,78 (± 5.05)	0.177
	II	12,00 (± 5.41)	
Domain III	I	**5,64 (± 4.18)**	**0.030**
	II	**3,66 (± 2.62)**	
Domain IV	I	**9,36 (± 4.13)**	**0.010**
	II	**6,72 (± 3.80)**	
Domain V	I	**4,58 (± 2.14)**	**0.045**
	II	**3,38 (± 2.61)**	
Domain VI	I	4,97 (± 2.86)	0.446
	II	4,38 (± 3.37)	
Domain VII	I	2,14 (± 2.11)	0.581
	II	1,86 (± 1.85)	
Domain VIII	I	2,64 (± 1.68)	0.324
	II	2,21 (± 1.82)	
Domain IX	I	**3,14 (± 1.71)**	**0.007**
	II	**2,07 (± 1.28)**	

TALS-SR: Trauma and Loss Spectrum Self Report, BD: Bipolar Disorder, SD: Standard Deviation.

analyzed the clinical features of bipolar patients who reported potentially traumatic life events in their medical history: they found early onset, greater tendency to rapid cycling, higher incidence of psychotic symptoms and higher risk of suicidal ideation and suicide attempts [28].

Several studies also agree that the presence of traumatic events in patients with BD correlates with greater comorbidity with substance use disorder. This correlation appears extremely important if we consider the negative impact that substance abuse can have on the course and prognosis of BD [17,28,29].

Furthermore, we analyzed the relationship between single patients CGI-S measures and TALS-SR remaining domains, finding a statistically significant positive correlation between disease severity and cumulative scores in Domain IV (reaction to losses or upsetting events), Domain VII (maladaptive coping), Domain VIII (arousal) and Domain IX (personal characteristics/risk factor). In particular, Domain VII (maladaptive coping) aims to identify the maladaptive behaviors that patients might develop following a traumatic experience, by investigating symptoms that are often associated with stressful events, impulsive conducts, self destructive behavior, somatic complaints, feelings of hopelessness and permanent damage.

As aforementioned, it seems that a positive correlation exists between the presence of past traumatic events in the life of bipolar patients, and a high risk of suicidal acts or thoughts: hence, suicidal behavior may represent the epiphenomenon of a maladaptive strategy, and Domain VII aims to investigate the presence of impulsive behavior or other maladaptive responses which may subtend suicidal thoughts and acts. In our study, we observed an important statistically significant correlation between domain VII (maladaptive coping) and suicide attempts ($p < 0.01$), confirming the relationship between maladaptive behaviors following a traumatic experience and the greater risk of suicidal thoughts or acts [17].

Scores obtained in Domain IX (personal characteristics/risk factors) also show a positive correlation with CGI-S score, and therefore with disease severity. Domain IX is aimed at identifying any personological changes induced by the traumatic event and, at the same time, investigates the presence of stable and pervasive personality traits that may predispose to the development/worsening of bipolar symptoms. To this end, Domain IX questions aim to investigate the presence of impulsiveness and marked reactivity to stressful events.

Comparing the results obtained by patients with BDI and BDII we found that the scores obtained in Domain III of TALS-SR (potentially traumatic events) are higher in the former group of patients (BDI). In line with our result, Dualibe and colleagues have found that there is a higher incidence of physical, emotional and sexual abuse in patients with BDI, rather than with BDII [17].

Analyzing the remaining TALS-SR domains, we also observed that the BDI group obtained higher scores in Domain IV (reaction to losses or upsetting events), Domain V (re-experiencing) and Domain IX (personal characteristic / risk factors), suggesting that patients with BDI may develop peculiar post-traumatic symptoms, and might show more frequently personological traits of vulnerability.

Comparing the scores obtained in the TALS-SR domains after clustering the sample by gender, no significant differences were found except in Domain VIII (arousal), where female patients obtained higher average scores. Some authors have hypothesized that among BD patients with a history of abuse, females are more susceptible to developing suicidal thoughts and behaviors, whereas males show an increase in irritability and aggression, thus larger studies may be useful to further explore sex differences in the response towards abusive experiences [30].

In addition, Etain and colleagues in a 2013 study hypothesized that the female gender could strengthen

the correlation between trauma and clinical characteristics of BD, mediating an additive effect. It seems that trauma in female subjects correlates more frequently with rapid cycling, age of early onset, suicidal behaviors, higher frequency of depressive episodes if compared to trauma in male patients [31].

Finally, we asked to patients their opinion on the impact of traumatic events on the course of their bipolar disorder: the majority of patients (92.3%) believe that traumatic experiences had some impact on psychiatric symptoms, whether of severe (36.9%), moderate (46.2%) or mild grade (9.2%).

Taking into account the subjective opinion of our sample, we furthermore emphasised the importance of accurately identifying trauma or potentially traumatic events in the life course of patients with BD.

Conclusions

Our data confirms previous findings pointing to a relationship between lifetime trauma exposure and BD characteristics. That we did not find a relationship between trauma and number of hospitalisations, suicide attempts, quality of life and global functioning is likely due to a lack of statistical power. The significant relationship between suicide attempts and Domain VII - TALS-SR score is worth being better explored in longitudinal and prospective studies. Of interest, over 90% of our study subjects felt that traumatic events negatively impacted the course of their disease. Larger, controlled, prospective studies are needed to explore more in depth issues such as the direction of causality and the possibility that an early treatment of BD may prevent trauma and trauma-consequences, and vice versa.

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