

The mediation role of impulsivity between childhood trauma and dissociative symptomatology in bipolar disorder

RENATO DE FILIPPIS¹, ELVIRA ANNA CARBONE², MARTINA D'ANGELO¹, MARCO TULLIO LIUZZA³, PASQUALE DE FAZIO¹, LUCA STEARDO JR¹

¹Psychiatry Unit, Department of Health Sciences, University Magna Graecia of Catanzaro, Italy; ²Psychiatry Unit, Department of Medical and Surgical Sciences, University Magna Graecia of Catanzaro, Italy; ³Department of Medical and Surgery Sciences, University of Catanzaro, Italy.

Summary. Background. In bipolar disorder (BD) patients, trauma has been associated with emotional dysregulation, potentially leading to an increase in impulsivity and dissociative symptomatology. We aimed to investigate the relationship between childhood trauma, impulsivity, and dissociative symptomatology in BD with a special focus on the role of impulsivity as a mediator between childhood trauma and dissociative symptomatology. **Methods.** We administered the Childhood Trauma Questionnaire (CTQ), Barratt Impulsivity Scale (BIS-11), Dissociative Experience Scale (DES-II), and Alda scale. Spearman correlation analysis assessed the independent variables associated with CTQ and DES-II. We performed a mediation analysis using the bootstrapping technique to verify the hypothesis that impulsivity represented an intervening variable between childhood trauma and dissociation. **Results.** CTQ and DES-II scores in 100 BD patients were both significantly associated with the number of lifetime affective episodes, a clinical course of mania-depression-euthymia, suicidal ideation, a history of antidepressant-induced manic switch, poor response to mood stabilizers, mixed features, psychotic symptoms, aggressive behavior, and BIS-11 ($p < 0.01$). At the regression analysis, CTQ was associated with DES-II ($p < 0.001$), while DES-II was associated with the CTQ ($p < 0.001$) and BIS-11 ($p < 0.001$), as well as with aggression ($p = 0.002$). The mediation analysis showed that impulsivity significantly mediated the effect of childhood trauma on dissociative symptomatology ($z = 25.71$; $0.930-1.084$). **Conclusions.** Impulsivity might play a key role in onset and prognosis of BD patients. Our findings may help in increasing the knowledge about the possible association between impulsivity, childhood traumatic experiences and dissociative symptomatology. BD patients with dissociative symptoms might benefit from a tailored treatment which could include a training based on emotional and behavioral regulation.

Key words. Bipolar disorder, childhood trauma, clinical course, impulsivity, mediation analysis.

Il ruolo di mediazione che riveste l'impulsività fra il trauma infantile e la sintomatologia dissociativa nel disturbo bipolare.

Riassunto. Scopo. Nei pazienti con disturbo bipolare (DB) il trauma è stato associato a disregolazione emotiva, conducendo potenzialmente a un aumento dell'impulsività e della sintomatologia dissociativa. In questo lavoro abbiamo indagato la relazione fra trauma infantile, impulsività e sintomatologia dissociativa nel DB con particolare attenzione al ruolo dell'impulsività come mediatore fra trauma infantile e sintomatologia dissociativa. **Metodi.** Abbiamo somministrato il Childhood Trauma Questionnaire (CTQ), la Barratt Impulsivity Scale (BIS-11), la Dissociative Experience Scale (DES-II) e la scala Alda. L'analisi di correlazione di Spearman ha valutato le variabili indipendenti associate a CTQ e DES-II. Abbiamo eseguito un'analisi di mediazione attraverso la tecnica di bootstrapping per verificare l'ipotesi che l'impulsività rappresentasse una variabile interveniente tra trauma infantile e dissociazione. **Risultati.** I punteggi di CTQ e DES-II in 100 pazienti con DB erano entrambi significativamente associati a numero di episodi affettivi, decorso clinico di mania-depressione-eutimia, ideazione suicidaria, storia di switch maniaco indotto da antidepressivi, scarsa risposta agli stabilizzanti dell'umore, caratteristiche miste, sintomi psicotici, comportamento aggressivo e BIS-11 ($p < 0.01$). All'analisi di regressione, la CTQ era associata alla DES-II ($p < 0.001$), mentre la DES-II era associata alla CTQ ($p < 0.001$) e alla BIS-11 ($p < 0.001$), nonché all'aggressività ($p = 0.002$). L'analisi di mediazione ha dimostrato un effetto di mediazione dell'impulsività sulla sintomatologia dissociativa ($z = 25.71$; $0.930-1.084$). **Conclusioni.** L'impulsività potrebbe svolgere un ruolo chiave nell'insorgenza e nella prognosi del DB. I nostri risultati possono aiutare ad aumentare le conoscenze sulla possibile associazione tra impulsività, esperienze traumatiche infantili e sintomatologia dissociativa. I pazienti affetti da DB con sintomi dissociativi potrebbero beneficiare di un trattamento su misura che potrebbe includere una formazione basata sulla disregolazione emotiva e comportamentale.

Parole chiave. Analisi di mediazione, decorso clinico, disturbo bipolare, impulsività, trauma infantile.

Introduction

The mental health consequences of childhood trauma have been widely investigated recently¹⁻³. Previous research highlighted those stressful events during early life may represent a significant environmental risk factor in facilitating the development of severe mental illnesses, especially in vulnerable individuals⁴. Indeed, subjects who reported a history of trauma during childhood more likely display an increased risk of developing psychotic spectrum⁵ and mood disorders^{6,7}, compared to those who did not experience any trauma. Particularly, subjects suffering from bipolar disorder (BD) reported a three-fold higher rate of childhood adversities than healthy controls⁶. Recently, it has been reported that specific childhood adversities can predict BD⁸ in later life, and, among these, emotional neglect/abuse represents the kind of childhood adversity that better differentiates BD patients from healthy controls^{9,10}. Furthermore, childhood trauma can negatively impact the clinical course of BD¹¹, and specific early negative experiences are associated with different clinical features^{12,13}. Several studies demonstrated that physical, sexual, and emotional abuse are associated with early onset of the disorder, a higher number of lifetime mood episodes and hospitalizations, substance use disorder, rapid cycling, suicide attempts, psychotic symptoms, a less favorable response to treatment, and poorer social functioning both during acute episodes and remission phases^{11,14-17}. According to the trauma theory¹⁸, dissociative symptomatology represents a frequent sequela of adverse life experiences¹⁹. It may act as a defense mechanism (initially adaptive, but subsequently maladaptive) against overwhelming emotions triggered by negative life experiences²⁰. Previous research demonstrated that BD patients exposed to childhood adversities had a higher prevalence of dissociative symptoms than individuals who reported little or no trauma^{21,22}, thus reinforcing a trauma-induced psychopathological model of BD²¹. Indeed, in addition to the above-reported clinical and course features, childhood trauma in BD leads to emotional dysregulation with subsequent affective lability and affect intensity²³. Childhood trauma is associated with traits of aggression in BD²⁴, suggesting that also components of hostility or impulsivity may be influenced. In turn, such emotional, behavioral, and impulsive dysregulation is associated with BD clinical complexity/severity. Traumatic childhood experiences contribute to higher impulsivity in BD patients^{25,26}, even during the euthymic phase, thus influencing a poor prognosis²⁶. We hypothesized that affective lability and traumatic memory increase impulsivity, which lead to dissociative symptomatology worsening the outcome. Despite this evidence,

to date, there is a lack of research addressing interrelationships among dissociative symptoms and impulsivity in patients with BD who experienced early traumatic events. Particularly, to our best knowledge, the mediator role of impulsivity between childhood trauma and dissociative symptoms has not been previously investigated in BD.

Therefore, the present study aims at investigating: 1) the relationship between childhood trauma, impulsivity, and dissociative symptomatology in BD; 2) impulsivity as a mediator between childhood trauma and dissociative symptomatology in BD; 3) clinical and psychopathological correlates of childhood trauma and dissociative symptoms in BD.

Material and methods

PARTICIPANTS AND PROCEDURE

This is a cross-sectional study carried out in a naturalistic setting. Participants were recruited at the Mood Disorder Unit of the University Hospital Mater Domini in Catanzaro (Italy) from May 2019 to January 2020. All subjects who met the following criteria were included in the present study: a) age between 18 and 70 years; b) a diagnosis of type-I BD (BD-I) or type-II BD (BD-II) according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria²⁷, by using the Structured Clinical Interview for DSM-5 disorders, clinician version-SCID-5-CV²⁸; c) willingness to participate in the study, expressed by written informed consent provided after the complete description of the protocol. Exclusions criteria were: a) inability to give written consent to participate in the study; b) diagnosis of any neurologic disease; c) presence of a substance and/or alcohol use disorders; d) receiving any psychotherapeutic intervention at the time of the recruitment. The study has been carried out following the latest version of the Declaration of Helsinki²⁹. All patients gave their informed written consent and were enrolled in the study. The study was approved by the local ethical review board (Ethical Committee of University Hospital Mater Domini at Catanzaro n. 307).

MEASURES

- The SCID-5-CV²⁸ was administered to confirm the diagnosis and type of BD and to assess the presence of comorbid psychiatric disorders. Socio-demographic characteristics were recorded in ad-hoc Excel spreadsheet. Clinical features were also collected, particularly age at onset, number of episodes, clinical course of BD, mixed features, anxiety and psychotic symptoms, previous suicide attempts. The clinical course of BD was classified according to four clinical patterns: mania-de-

pression-euthymia; depression-mania-euthymia; mania-euthymia-depression and irregular pattern.

- The administration of the following scales was carried out for all recruited patients: Childhood Trauma Questionnaire (CTQ)³⁰; Dissociative Experience Scale (DES-II)³¹; Barratt Impulsivity Scale (BIS-11)³²; Alda scale³³.
- The CTQ was used to assess the history of childhood trauma³⁰. This scale evaluates five dimensions: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. A total score >36 reveals the presence of childhood trauma (ordinal Cronbach's $\alpha > 0.90$).
- The dissociative symptomatology was assessed through the DES-II. This scale is a self-assessment measure developed by Bernstein and Putnam³¹ and translated into Italian to screen dissociative psychopathologies. It consists of 28 items describing dissociative experiences (amnesia, absorption, depersonalization, and derealization). This is the most used questionnaire to assess dissociative symptomatology, and the Italian version has shown an excellent internal consistency (Cronbach's $\alpha = 0.94$)³⁴.
- Impulsivity was assessed by BIS-11 (Cronbach's $\alpha = 0.83$)³², which incorporates three behavioral components of impulsivity: motor, which refers to acting on the spur of the moment without thinking; non-planning, which refers to a lack of future orientation; and cognitive, that refer to issues with concentration and tendency to shift attention rapidly.
- The patient's response to mood stabilizers treatments was assessed using the retrospective criteria of long-term treatment response in BD (Alda Scale), which consist of two criteria: A) rating of the association between clinical improvement and treatment; B) rating of the degree of the causal relationship between clinical improvement and treatment. A score was obtained by subtracting the B score from the A score^{33,35}. Patients were scored on a 0-10 scale. A score of ≥ 7 indicated a good response, a score from 4 to 6 a moderate response, and a score of ≤ 3 a poor response. The Alda Scale is a valid measure with Interrater reliability of 0.54-0.75 in assessing long-term response to treatment (Cronbach's $\alpha 0.7$)^{33,35}.

STATISTICAL ANALYSIS

Descriptive statistics were performed to assess the distributional properties of socio-demographic and clinical variables in the sample. Data are described as means and standard deviations (SD) for continuous variables and as frequencies and percentages (%) for categorical ones. Considering the

variables non normal distribution, Spearman correlation analysis was performed to assess significant associations between CTQ and DES-II total score and the following variables: socio-demographic, clinical characteristics, and scores at each psychopathological assessment tool. Two linear regression analyses were run considering DES-II and CTQ total scores as dependent variables and variables concerning psychopathological features significant at the correlation analysis as independent variables. Tolerance values were > 0.1 for all the variables entered in the two models, meaning that the multicollinearity assumption was not violated. A $p < 0.05$ was considered significant. A bootstrapping approach by Preacher and Hayes³⁶ was performed to test the mediation role of impulsivity between childhood trauma and dissociation. Statistical Package for Social Sciences version 26 (SPSS, Chicago, IL, USA) was used to perform the statistical analyses.

Results

The sample consisted of 100 BD patients. Socio-demographic and clinical characteristics of recruit-

Table 1. Clinical and sociodemographic characteristics.

Variable	Sample n=100
Age, M (\pm SD)	46.50 (13.94)
Sex (female), %	50
Age of school, M (\pm SD)	13.3 (\pm 3.5)
Married, yes %	48
Diagnosis BD-I, yes %	55
Age at onset, M (\pm SD)	27.3 (\pm 9.85)
Number of episodes, M (\pm SD)	10.5 (\pm 9.60)
Antidepressant switch, yes %	29
Suicide, yes %	32
Mixed features, yes %	50.6
Anxious features, yes %	66.3
Aggressive behavior, yes %	57
Psychotic symptoms, yes %	46
CTQ tot, M (\pm SD)	59.18 (\pm 18.9)
DES-II, M (\pm SD)	31.7 (\pm 21.6)
BIS-11, M (\pm SD)	80.48 (\pm 10.85)
Alda tot	
Lack (0-3)	48
Moderate (4-6)	40
Good (7-10)	12

Legend: BD= bipolar disorder; BIS-11= Barratt impulsivity scale II; CTQ= Childhood trauma questionnaire; DES-II= dissociative experience scale II; M= mean; SD= standard deviation.

ed subjects are reported in table 1. The sample is composed of 50 males (50%) and 50 females (50%), with a mean age of 46.5 years (SD ± 13.9 range 22-75). No between-sex differences were detected for age ($p=0.441$). The most frequent diagnosis was BD-I (55%; M n=27, 49.1%, F n=28, 50.9%). More than half of the sample declared to be employed (60%), and 48% of the included subjects declared to be in a stable relationship. Around 68% of the sample had a positive history of psychiatric disorders, and 60% declared a comorbid medical condition. The mean age at onset of BD was 27.3 ± 9.8 (range 16-66, no between-sex differences $p=0.615$) with an illness duration of 19.0 ± 13.0 years. In the whole sample, thirty-two patients experienced suicidal ideation, and more than half of them presented aggressive behaviors (57%) and anxious symptoms (59%). The mean number of total episodes was 10.5 ± 9.6 (range 1-58). As for the response to mood stabilizer treatment, as measured by the Alda scale, 48% of all subjects manifested a scarce response, 40% a moderate response, and 12% a good response (without any between-sex differences in the Alda total score, $p=0.439$). The mean scores reported at psychopathological scales were: 31.7 ± 21.6 at DES-II; 59.1 ± 18.9 at CTQ; 80.4 ± 10.8 at BIS-11 total score.

Results of the Spearman correlation analysis are reported in table 2. The total scores at the CTQ and DES-II scales were both positively associated with the number of lifetime total episodes ($p<0.01$), a clinical course of mania-depression-euthymia ($p<0.01$), suicidal ideation ($p<0.01$), a history of antidepressant-induced manic switch ($p<0.01$), poor response to mood stabilizers ($p<0.01$), the presence of mixed features ($p<0.01$), psychotic symptoms ($p<0.01$), aggressive behavior ($p<0.01$), and BIS-11 ($p<0.01$) total score. Moreover, CTQ and DES-II total scores were positively associated one with each other ($p<0.01$).

The results of the linear regression analyses are reported in table 3. The models were run to assess the independent predictors associated with the CTQ total score and DES-II total score. The first model, performed with CTQ score as a dependent variable and DES-II and BIS-11 total scores, aggression, psychotic, anxiety, and mixed features as independent variables, reached statistical significance ($p<0.001$) and the included independent variables explained 94.3% of the variance of the dependent variable. The only independent variable that was significantly associated with CTQ total score was DES-II total score (Beta coefficient= 1.019, $p<0.001$). As for the second model ($p<0.001$), which was run with DES-II total score as dependent variable and CTQ and BIS-11 total scores, aggression, psychotic, anxiety, and mixed features as independent variables, the independent variables explained 95.9% of the variance. DES-II scores were significantly associated with CTQ total score (Beta

Table 2. Spearman Correlation analysis.

	CTQ total	Age at onset	Clinical course	Number of episodes	Antidepressant switch	Suicide	Psychotic features	Mixed features	Anxious features	DES-II total	Alda total	BIS-11 total
CTQ total	-											
Age at onset	-0.086	-										
Clinical course	-.398**	.249*	-									
Number of episodes	.492**	-0.149	-.381**	-								
Antidepressant switch	.507**	.219*	-.280**	.393**	-							
Suicide	.543**	-0.055	-.456**	.455**	.412**	-						
Psychotic features	.778**	-0.090	-.348**	.541**	.462**	.544**	-					
Mixed features	.660**	-0.085	-.279**	.577**	.441**	.410**	.597**	-				
Anxious features	.549**	-0.145	-.274**	.397**	.307**	.393**	.553**	.582**	-			
DES-II total	.956**	-0.063	-.417**	.533**	.497**	.551**	.759**	.674**	.603**	-		
Alda total	-.570**	0.089	.262**	-.536**	-.377**	-.339**	-.417**	-.496**	-.213*	-.588**	-	
BIS-11 total	.712**	-0.174	-.460**	.400**	.435**	.475**	.604**	.418**	.408**	.740**	-.429**	-

*Correlation is significant at level of 0.05 (two-tailed correlation); **Correlation is significant at level of 0.01 (two-tailed correlation).

Legend: BD= bipolar disorder; BIS-11= Barratt impulsivity scale II; CTQ= childhood trauma questionnaire; DES-II= dissociative experience scale II.

Table 3. Linear regression.

Dependent variable: CTQ Total					
	B	Standard error	Beta	t	p
Psychotic features	.732	1.551	.019	.472	.638
Aggressive behaviors	1.741	1.439	.046	1.210	.229
Mixed characteristic	.493	1.408	.013	.350	.727
Anxious characteristic	-1.425	1.294	-.036	-1.102	.273
DES-II Total	.892	.053	1.019	16.906	.000
BIS-11 Total	-.154	.093	-.088	-1.647	.103

Legend: BIS-11= Barratt impulsivity scale II; CTQ= childhood trauma questionnaire; DES-II= dissociative experience scale II.

Dependent variable: DES-II					
	B	Standard error	Beta	t	p
Psychotic features	2.637	1.488	.061	1.772	.080
Aggressive behaviors	-4.338	1.339	-.100	-3.238	.002
Mixed characteristic	2.480	1.349	.058	1.838	.069
Anxious characteristic	2.173	1.249	.049	1.739	.085
DES-II Total	.415	.082	.208	5.080	.000
BIS-11 Total	.848	.050	.742	16.906	.000

Legend: BIS-11= Barratt impulsivity scale II; DES-II= dissociative experience scale II.

coefficient= 0.742; $p < 0.001$), BIS-11 total score (Beta coefficient= 0.208, $p < 0.001$), and aggression (Beta coefficient= 0.100; $p = 0.002$). A bootstrapping approach, as suggested by Preacher and Hayes³⁶, was performed to test the mediation effect of impulsivity explaining the effect of childhood trauma on the development of dissociative symptomatology, which turned out to be statistically significant ($z = 25.71$; 0.930-1.084), as displayed in table 4.

Discussion

The present study highlights the association between childhood trauma and clinical features that cause an overall worse clinical picture in BD. Nonetheless, a history of traumatic experiences in BD may underpin a high psychopathological burden, as emerged by the association with BIS-11 and DES-II

Table 4. Mediation analyses with bootstrapped 95% confidence intervals.

Path Estimates									
						95% Confidence Interval			
			Label	Estimate	SE	Lower	Upper	Z	p
CTQ Total	*	BIS Total	a	0.408	0.0354	0.337	0.480	11.54	<.001
BIS Total	*	DES-II Total	b	0.252	0.0530	0.142	0.352	4.75	<.001
CTQ Total	*	DES-II Total	c	1.005	0.0391	0.930	1.084	25.71	<.001

Mediation Estimates								
				95% Confidence Interval				
Effect	Label	Estimate	SE	Lower	Upper	Z	p	% Mediation
Indirect	a × b	0.103	0.0245	0.0559	0.152	4.20	<.001	9.29
Direct	c	1.005	0.0391	0.9301	1.084	25.71	<.001	90.71
Total	c + a × b	1.108	0.0303	1.0494	1.172	36.60	<.001	100.00

Legend: BIS-11= Barratt impulsivity scale 11; CTQ= Childhood trauma questionnaire; DES-II= dissociative experience scale II.

total score. Moreover, the main findings of the present study underlined a mediational effect of impulsivity in BD patients with a childhood trauma history to develop dissociative symptomatology. To date, this is the first clinical study analyzing impulsivity as a possible mediator of the effect that childhood trauma displays on dissociative symptoms in BD. To note, a history of childhood trauma, as measured by the CTQ, was associated with a high psychopathological load, higher suicide risk, and poor response to mood stabilizers in our sample. Previous literature has widely demonstrated this issue, and our study is in line with such findings^{13,14,37}. Childhood trauma and impulsivity seem to be significant predictors of developing a specific trajectory towards several clinical features. The correlation between childhood abuse and anxiety disorders, lifetime number episodes, and irregular cycling could indeed be mediated by impulsivity. The direct correlation between childhood trauma, aggressive behavior, and the high number of total episodes independently by the type of polarity underpins that trauma may be contingent on developing affective instability and impulsivity in subjects with a history of childhood abuse. Furthermore, mood symptoms mediate traumatic events and the new onset of psychotic symptoms in the general population³⁸. An interesting finding that our analysis showed is an association between childhood trauma and psychotic symptoms in people with BD. There is a predominant hypothesis that psychotic features in BD subjects may indicate a more severe form of the illness^{39,40}. Moreover, our previous study demonstrates that a high level of dissociation is strongly associated with psychotic symptomatology in BD subjects, and the results raised from the present study confirm our last findings⁴¹. The poor treatment response in BD patients with a high CTQ score may depend on the fact that early traumatic experiences predispose to the development of clinical features predictive of refractory response, such as mixed symptoms, impulsiveness, and psychotic characteristics^{16,25,42}. Furthermore, several studies highlighted a strong correlation between a higher suicide rate and impulsivity in subjects with childhood trauma⁴³.

The association between impulsivity and suicide risk is a topic of interest in psychiatry⁴⁴. Indeed, impulsivity correlates with all clinical features that worsened outcomes in BD. This finding is in line with several studies. BD patients with a history of child or adolescent trauma had a history of an earlier onset of bipolar illness, an increased number of comorbid psychiatric disorders, including drug and alcohol abuse, faster cycling frequencies, a higher rate of suicide attempts, and more psychosocial stressors occurring before the first and most recent affective episode and a worse response to treatment^{†26,45,46}.

Our results can be explained in the light that a higher load of impulsivity and aggressive behavior in association with dissociative symptomatology can lead to poor cognitive control of negative beliefs and emotions and lead the patient to commit self-injurious gestures or suicide^{24,47,48}. Indeed, childhood trauma doubles the risk of suicide in patients with BD⁴⁹.

The present results are in line with those of previous studies showing that BD patients with a childhood trauma are more impulsive and exhibit a greater suicidality rate than patients without a history of trauma. Indeed, childhood trauma in BD acts as an aggravating factor in the course of the illness, leading to more frequent hospitalizations and to a higher possibility of developing comorbid SUD due to increased impulsivity^{50,51}. This issue may lead the attention of clinicians to adopt tailored treatment strategies, such as psychotherapy focused on emotional dysregulation due to childhood trauma, to decrease the risk of suicide in at-risk subjects⁵²⁻⁵⁴. High scores at the CTQ scale have also been associated with dissociative symptoms and impulsivity, remarking the strict association between trauma and these two psychopathological variables. Children experiencing traumatic events in stressful situations may not show their stress in future events to prevent emotional arousal in themselves. This defense mechanism may be enduring and encourage dissociation in children to defend themselves from frightening or helpless experiences. However, such dysfunctional behavior throughout life may become chronic and lead to ineffective coping skills⁵⁵. These findings concerning the development of dissociation resulting from childhood trauma may have important clinical implications. This association had remained significant even when the mediating analysis was run, suggesting the potential role of impulsivity as the mediator between childhood trauma and dissociation. Few studies have focused on this issue until now⁵⁶⁻⁵⁸, and no one was conducted in a BD sample. The mediation effect of impulsivity between childhood trauma and dissociation has been investigated in a cohort of patients with substance abuse disorder, suggesting a key role of trauma on a higher psychopathological load in this population^{57,58}, but further studies are needed as literature on this topic is still scarce. Based on the present results, it is possible to hypothesize that childhood trauma destabilizes psychological regulatory functions, of which impulsivity is a behavioral expression^{26,59,60}. Individuals with impulsivity seem to be at greater risk for the development of dissociative psychopathology. However, in line with Briere's et al. findings⁶¹, our data imply that impulsivity could be a mediator between childhood trauma and dissociative psychopathology. To note, childhood traumatic experiences, impulsiveness, and aggression were significantly associated with the dissociative symptoms

at the regression analyses. Conversely, dissociative psychopathology was the variable most strongly associated with childhood trauma when this was analyzed as dependent variable. These findings have theoretical implications suggesting that the association between childhood trauma and dissociative psychopathology is complex and may also act following a bidirectional relationship. Childhood trauma is a known destabilizing factor of neuro-psychological regulatory functions, of which impulsivity is a behavioral manifestation. Our data shows that impulsiveness might have played a contributing role in the development of psychopathological dissociation among BD patients with a history of childhood trauma. We surmise that some dysregulated survivors could have down-regulated arousal with dissociative responses that later crystallize into dissociative psychopathology⁶². Clinically, this finding might imply that effective treatment of dissociative psychopathology should strive to identify and address potentially underlying dysregulating phenomena, such as impulsivity. Our findings may also explain the scarce response to mood stabilizers in the light of scarce treatment adherence, which might be due to affective instability and the difficulty to cope with the mood swing with a functional coping strategy⁶³. Conversely, a higher number of affective episodes and discontinuation of mood stabilizers therapy reduce the mood stabilizers' efficacy, especially lithium⁶⁴. Clinically, this finding also suggests that effective treatment of dissociative symptomatology should reduce dysregulating phenomena such as impulsivity.

Results from the present study present some limitations. Firstly, the hypothesis used to design the research protocol, namely that impulsivity could act as a mediator between childhood trauma and dissociative symptomatology in BD, is debated in the literature. Indeed, it could be hypothesized also that it is dissociation that could act as a mediator between impulsivity and childhood trauma in BD. Therefore, this dualism should be considered when interpreting the results presented in this work, since both models present might be reasonable, and will need to be better explored in the opposite direction as well. Secondly, the small sample size and the absence of a community sample might affect the ability to generalize our data. Moreover, cross-sectional nature of the study design, which do not allow to longitudinally evaluate whether trauma-focused based therapy could improve outcomes of BD patients with childhood trauma, the lack of clinician-administered clinical interview for assessing which traumatic experiences and the lack of a comparison if (any) differences are present between BDI vs BDII. Even though, this could represent a strength of the study to some extent, it would have been advantageous to integrate the assessment of impulsivity with observational data. Another limitation is

the lack of which subtype of impulsivity could mediate the presence of dissociative symptomatology, but we will investigate it further.

Conclusions

In conclusion, our study suggests that impulsivity is probably not a feature of BD itself but is associated with the presence of traumatic childhood experiences and has a mediator role in developing dissociative symptomatology. So, it seems essential to assess the presence of early trauma in BD subjects. Overall, early assessing and identifying the history of an early trauma in BD subjects and, hence, considering of this variable in planning tailored interventions, could potentially reduce impulsivity and improve BD course (i.e., less relapse into a hypomanic or manic mode, less suicide, for example).

Overall, findings from the present study underline the importance of investigating the processes that correlate the traumatic childhood event with the development of dissociative symptoms in BD. However, further studies are needed to clarify the role of emotional dysregulation and its clinical manifestations as possible mediators between trauma and dissociation in BD. Since psychological dysregulation and impulsivity might play a key role in the etiology and in worsening prognosis in BD patients, a possible clinical implication of our findings is that dissociative disordered individuals might benefit from a personalized treatment protocol that includes training in emotional and behavioral regulation and trauma-focused cognitive-behavioral therapy (TF-CBT).

Conflict of interest: no potential competing interest was reported by the authors.

Funding: no funding was received for this research.

Acknowledgements: the authors are grateful to all participants who accepted to contribute to this research.

References

1. Mall S, Mortier P, Taljaard L, Roos J, Stein DJ, Lochner C. The relationship between childhood adversity, recent stressors, and depression in college students attending a South African university. *BMC Psychiatry* 2018; 18: 63.
2. van Nierop M, Lataster T, Smeets F, et al. Psychopathological mechanisms linking childhood traumatic experiences to risk of psychotic symptoms: analysis of a large, representative population-based sample. *Schizophr Bull* 2014; 40 (Suppl_2): S123-30.
3. Wu NS, Schairer LC, Dellor E, Grella C. Childhood trauma and health outcomes in adults with comorbid substance abuse and mental health disorders. *Addict Behav* 2010; 35: 68-71.
4. Uher R. Gene-environment interactions in severe mental illness. *Front Psychiatry* 2014; 5: 48.
5. Fusar-Poli P, Tantardini M, De Simone S, et al. Decon-

- structuring vulnerability for psychosis: meta-analysis of environmental risk factors for psychosis in subjects at ultra high-risk. *Eur Psychiatry* 2017; 40: 65-75.
6. Palmier-Claus JE, Berry K, Bucci S, Mansell W, Varese F. Relationship between childhood adversity and bipolar affective disorder: systematic review and meta-analysis. *Br J Psychiatry* 2016; 209: 454-9.
 7. Tracy M, Salo M, Slopen N, Udo T, Appleton AA. Trajectories of childhood adversity and the risk of depression in young adulthood: results from the avon longitudinal study of parents and children. *Depress Anxiety* 2019; 36: 596-606.
 8. Bruni A, Carbone EA, Pugliese V, et al. Childhood adversities are different in Schizophrenic Spectrum Disorders, Bipolar Disorder and Major Depressive Disorder. *BMC Psychiatry* 2018; 18: 391.
 9. Menculini G, Balducci PM, Attademo L, Bernardini F, Moretti P, Tortorella A. Environmental risk factors for Bipolar Disorders and high-risk states in adolescence: a systematic review. *Medicina (B Aires)* 2020; 56: 689.
 10. Watson S, Porter RJ. Childhood adversity in bipolar disorder. *Aust New Zeal J Psychiatry* 2014; 48: 975-6.
 11. Garno JL, Goldberg JE, Ramirez PM, Ritzler BA. Impact of childhood abuse on the clinical course of bipolar disorder. *Br J Psychiatry* 2005; 186: 121-5.
 12. Daruy-Filho L, Brietzke E, Lafer B, Grassi-Oliveira R. Childhood maltreatment and clinical outcomes of bipolar disorder. *Acta Psychiatr Scand* 2011; 124: 427-34.
 13. Carbone EA, Pugliese V, Bruni A, et al. Adverse childhood experiences and clinical severity in bipolar disorder and schizophrenia: a transdiagnostic two-step cluster analysis. *J Affect Disord* 2019; 259: 104-11.
 14. Etain B, Aas M, Andreassen OA, et al. Childhood trauma is associated with severe clinical characteristics of Bipolar Disorders. *J Clin Psychiatry* 2013; 74: 991-8.
 15. Agnew-Blais J, Danese A. Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. *Lancet Psychiatry* 2016; 3: 342-9.
 16. Cakir S, Tasdelen Durak R, Ozyildirim I, Ince E, Sar V. Childhood trauma and treatment outcome in bipolar disorder. *J Trauma Dissociation* 2016; 17: 397-409.
 17. Hjelseng IV, Vaskinn A, Ueland T, et al. Childhood trauma is associated with poorer social functioning in severe mental disorders both during an active illness phase and in remission. *Schizophr Res* 2022; 243: 241-6.
 18. Guérin-Marion C, Sezlik S, Bureau J-F. Developmental and attachment-based perspectives on dissociation: beyond the effects of maltreatment. *Eur J Psychotraumatol* 2020; 11: 1802908.
 19. de Filippis R, Menculini G, D'Angelo M, et al. Internalized-stigma and dissociative experiences in bipolar disorder. *Front Psychiatry* 2022; 13: 953621.
 20. Şar V. Parallel-distinct structures of internal world and external reality: disavowing and re-claiming the self-identity in the aftermath of trauma-generated dissociation. *Front Psychol* 2017; 8: 216.
 21. Hariri AG, Gulec MY, Oregul FFC, Sumbul EA, Elbay RY, Gulec H. Dissociation in bipolar disorder: relationships between clinical variables and childhood trauma. *J Affect Disord* 2015; 184: 104-10.
 22. Kefeli MC, Turow RG, Yildirim A, Boysan M. Childhood maltreatment is associated with attachment insecurities, dissociation and alexithymia in bipolar disorder. *Psychiatry Res* 2018; 260: 391-9.
 23. Calabrò G, Musolino AF, Filippo AA, et al. Clinical impact of psychopathy on Bipolar Disorder. *Medicina (B Aires)* 2021; 57: 165.
 24. Garno JL, Gunawardane N, Goldberg JF. Predictors of trait aggression in bipolar disorder. *Bipolar Disord* 2008; 10: 285-92.
 25. Etain B, Lajnef M, Henry C, et al. Childhood trauma, dimensions of psychopathology and the clinical expression of bipolar disorders: a pathway analysis. *J Psychiatr Res* 2017; 95: 37-45.
 26. Richard-Lepouriel H, Kung A-L, Hasler R, et al. Impulsivity and its association with childhood trauma experiences across bipolar disorder, attention deficit hyperactivity disorder and borderline personality disorder. *J Affect Disord* 2019; 244: 33-41.
 27. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. fifth Ed. Washington: American Psychiatric Association, 2013.
 28. First M, Williams J, Karg R. *Structured Clinical Interview for DSM-5 Disorders, Clinician Version (SCID-5-CV)*. Washington: American Psychiatric Association, 2015.
 29. World Medical Association. *World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects*. *JAMA* 2013; 310: 2191.
 30. Bernstein DP, Stein JA, Newcomb MD, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl* 2003; 27: 169-90.
 31. Bernstein EM, Putnam FW. Development, reliability, and validity of a dissociation scale. *J Nerv Ment Dis* 1986; 174: 727-35.
 32. Patton JH, Stanford MS, Barratt ES. Factor structure of the barratt impulsiveness scale. *J Clin Psychol* 1995; 51: 768-74.
 33. Garnham J, Munro A, Slaney C, et al. Prophylactic treatment response in Bipolar Disorder: results of a naturalistic observation study. *J Affect Disord* 2007; 104: 185-90.
 34. Infurna MR, Reichl C, Parzer P, Schimmenti A, Bifulco A, Kaess M. Associations between depression and specific childhood experiences of abuse and neglect: a meta-analysis. *J Affect Disord* 2016; 190: 47-55.
 35. Manchia M, Adli M, Akula N, et al. Assessment of response to lithium maintenance treatment in Bipolar Disorder: a Consortium on Lithium Genetics (ConLiGen) report. *PLoS One* 2013; 8: e65636.
 36. Preacher KJ, Hayes AF. SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behav Res Methods Instrum Comput* 2004; 36: 717-31.
 37. Berk M, Post R, Ratheesh A, et al. Staging in Bipolar Disorder: from theoretical framework to clinical utility. *World Psychiatry* 2017; 16: 236-44.
 38. Catone G, Marwaha S, Kuipers E, et al. Bullying victimisation and risk of psychotic phenomena: analyses of British national survey data. *Lancet Psychiatry* 2015; 2: 618-24.
 39. Burton CZ, Ryan KA, Kamali M, et al. Psychosis in Bipolar Disorder: does it represent a more "severe" illness? *Bipolar Disord* 2018; 20: 18-26.
 40. Menculini G, Verdolini N, Murru A, et al. Depressive mood and circadian rhythms disturbances as outcomes of seasonal affective disorder treatment: a systematic review. *J Affect Disord* 2018; 241: 608-26.
 41. Steardo L, Carbone EA, Ventura E, et al. Dissociative symptoms in Bipolar Disorder: impact on clinical course and treatment response. *Front Psychiatry* 2021; 12: 732843.
 42. Etain B, Lajnef M, Brichant-Petitjean C, et al. Childhood trauma and mixed episodes are associated with poor response to lithium in bipolar disorders. *Acta Psychiatr Scand* 2017; 135: 319-27.
 43. McMahon K, Hoertel N, Olsson M, Wall M, Wang S, Blanco C. Childhood maltreatment and impulsivity as predictors of interpersonal violence, self-injury and suicide attempts: a national study. *Psychiatry Res* 2018; 269: 386-93.

44. Gvion Y, Levi-Belz Y, Hadlaczky G, Apter A. On the role of impulsivity and decision-making in suicidal behavior. *World J Psychiatry* 2015; 5: 255-9.
45. Belzeaux R, Boyer L, Mazzola-Pomietto P, et al. Adherence to medication is associated with non-planning impulsivity in euthymic bipolar disorder patients. *J Affect Disord* 2015; 184: 60-6.
46. Lewis M, Scott J, Frangou S. Impulsivity, personality and bipolar disorder. *Eur Psychiatry* 2009; 24: 464-9.
47. Cazala F, Bauer IE, Meyer TD, et al. Correlates of childhood trauma in children and adolescents with bipolar disorder spectrum: a preliminary study. *J Affect Disord* 2019; 247: 114-9.
48. Pompili M, Gonda X, Serafini G, et al. Epidemiology of suicide in bipolar disorders: a systematic review of the literature. *Bipolar Disord* 2013; 15: 457-90.
49. Mc Closkey MS, Look AE, Chen EY, Pajoumand G, Berman ME. Nonsuicidal self-injury: relationship to behavioral and self-rating measures of impulsivity and self-aggression. *Suicide Life-Threatening Behav* 2012; 42: 197-209.
50. Dualibe AL, Osório FL. Bipolar disorder and early emotional trauma: a critical literature review on indicators of prevalence rates and clinical outcomes. *Harv Rev Psychiatry* 2017; 25: 198-208.
51. Swann AC, Lijffijt M, Lane SD, Steinberg JL, Moeller FG. Increased trait-like impulsivity and course of illness in bipolar disorder. *Bipolar Disord* 2009; 11: 280-8.
52. Chen H, Li W, Cao X, et al. The association between suicide attempts, anxiety, and childhood maltreatment among adolescents and young adults with first depressive episodes. *Front Psychiatry* 2021; 12: 745470.
53. Xue S, Hodsoll J, Khoso AB, et al. Suicidality in patients with bipolar depression: findings from a lower middle-income country. *J Affect Disord* 2021; 289: 1-6.
54. Weintraub MJ, Schneck CD, Walshaw PD, et al. Longitudinal trajectories of mood symptoms and global functioning in youth at high risk for bipolar disorder. *J Affect Disord* 2020; 277: 394-401.
55. Feiring C. Emotional development, shame, and adaptation to child maltreatment. *Child Maltreat* 2005; 10: 307-10.
56. Somer E, Ginzburg K, Kramer L. The role of impulsivity in the association between childhood trauma and dissociative psychopathology: mediation versus moderation. *Psychiatry Res* 2012; 196: 133-7.
57. Evren C, Cinar O, Evren B, Ulku M, Karabulut V, Umut G. The mediator roles of trait anxiety, hostility, and impulsivity in the association between childhood trauma and dissociation in male substance-dependent inpatients. *Compr Psychiatry* 2013; 54: 158-66.
58. Zlotnick C, Shea MT, Recupero P, Bidadi K, Pearlstein T, Brown P. Trauma, dissociation, impulsivity, and self-mutilation among substance abuse patients. *Am J Orthopsychiatry* 1997; 67: 650-4.
59. Roy A. Childhood trauma and impulsivity. Possible relevance to suicidal behavior. *Arch Suicide Res* 2005; 9: 147-51.
60. Aas M, Henry C, Andreassen OA, Bellivier F, Melle I, Etain B. The role of childhood trauma in bipolar disorders. *Int J Bipolar Disord* 2016; 4: 2.
61. Briere J. Dissociative symptoms and trauma exposure. *J Nerv Ment Dis* 2006; 194: 78-82.
62. Barnow S, Limberg A, Stopsack M, et al. Dissociation and emotion regulation in borderline personality disorder. *Psychol Med* 2012; 42: 783-94.
63. Cavicchioli M, Scalabrini A, Northoff G, Mucci C, Ogliari A, Maffei C. Dissociation and emotion regulation strategies: a meta-analytic review. *J Psychiatr Res* 2021; 143: 370-87.
64. Simonetti A, Koukopoulos AE, Kotzalidis GD, et al. Stabilization beyond mood: stabilizing patients with bipolar disorder in the various phases of life. *Front Psychiatry* 2020; 11: 247.

Corresponding author:
Renato de Filippis, MD, PhD student
Psychiatry Unit
Department of Health Sciences
University Magna Graecia of Catanzaro
Viale Europa
88100 Catanzaro, Italy
E-mail: defilippisrenato@gmail.com