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Highlights

- Comorbid anxiety disorders are frequent in patients with borderline personality disorder (BPD), with half of our BPD population suffering from two or more anxiety disorders.
- Social phobia, panic disorder and post-traumatic stress disorder (PTSD) were the most common anxious comorbidity in our population.
- History of childhood maltreatment was associated with an increased number of anxiety disorders.
- Both anxiety disorders and childhood abuse impacted severity of BPD.
- Anxiety disorders were significantly associated with increased number of DSM BPD criteria, suicide attempts, psychotic symptoms, level of depression and hopelessness.
- Childhood maltreatment impacted severity of illness, impulsivity and anger trait.

Childhood maltreatment, anxiety disorders and outcome in Borderline Personality Disorder.

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Abstract

Introduction: Anxiety disorders are a frequent in borderline personality disorder (BPD) and are associated with more severe symptomatology and poorer functional outcomes. Their presence in BPD is also believed to be the consequence of early life adversities. The aim of our study was to examine the relationship between comorbid anxiety disorders, childhood maltreatment and severity of BPD. ***Methods:*** 388 BPD outpatients were assessed for lifetime anxiety disorders and history of childhood maltreatment. Severity of BPD was measured by the number of DSM-IV BPD criteria, history of suicide attempts, hospitalizations, psychotic symptoms, comorbid substance use disorder, other comorbid disorders, level of depression, hopelessness, impulsivity and trait anger. We used logistic regressions to test the association between childhood maltreatment and anxiety disorders and the effect of those factors on severity indicators. ***Results:*** More than half of the participants suffered from two or more anxiety disorders. The most common comorbidity was social phobia. Childhood maltreatment was associated with an increased number of anxiety disorders. Both anxiety disorders and childhood maltreatment had, independently from one another, an effect on severity indicators. Anxiety disorders were significantly associated with the number of DSM-IV BPD criteria, suicide attempts and psychotic symptoms. Anxiety disorders had an impact on the level of depression and hopelessness, whereas childhood maltreatment impacted impulsivity and anger trait. ***Conclusion:*** Our results show the importance of comorbid anxiety disorders in BPD, as well as their impact on severity. Anxiety disorders and childhood maltreatment should be considered by healthcare professionals to ensure optimal care. Furthermore, interventions targeting those issues need to be developed.

Key Words

Borderline personality disorder

Childhood trauma

Anxiety disorders

Suicidality

Abbreviation

BPD = Borderline personality disorder; OCD = obsessive compulsive disorder; GAD = Generalized anxiety disorder; PTSD = post-traumatic stress disorder; SCID = Structured Clinical Interview for DSM-IV Axis I; CTQ = Childhood Trauma Questionnaire; BDI-II = Beck Depression Inventory; STAXI = State-Trait Anger Expression Inventory; BIS = Barratt Impulsiveness Scale Version 10; BHS = Beck Hopelessness

Introduction

Borderline Personality Disorder (BPD) is a fairly common psychiatric disorder. About 2 % of the general population is diagnosed with BPD. In clinical populations, BPD is the most common personality disorder, with a prevalence of 10% of psychiatric outpatients and 20% of psychiatric inpatients (Korzekwa et al., 2008; Leichsenring et al., 2011; Skodol et al., 2002a; Tomko et al., 2014). BPD is a serious mental disorder associated with severe behavioural and emotional dysregulation, severe functional impairment, a high rate of comorbid mental disorders, a high rate of suicide, and substantial costs to society (Leichsenring et al., 2011; Lieb et al., 2004; Oldham, 2006; Skodol et al., 2002; Winsper et al., 2016).

The literature indicates a high rate of comorbid mental disorders in BPD, with increased odds of major depressive disorders, anxiety disorders, post-traumatic stress disorders, substance use disorders and eating disorders (Skodol et al., 2002b; Winsper et al., 2016; Zimmerman and Mattia, 1999). Anxiety disorders are estimated to be three times more frequent in BPD than in the general population (Silverman et al., 2012), with an estimated lifetime prevalence of 48% for panic disorder, 12% for agoraphobia, 46% for social phobia, 32% for simple phobia, 14% for generalized anxiety disorder (GAD), 16% for obsessive-compulsive disorder (OCD) and 56% for post-traumatic stress disorder (PTSD) (Harned and Valenstein, 2013; Zanarini et al., 1998).

Longitudinal studies show that the prevalence of anxiety disorders in BPD declines with time. Remission is frequent, but recurrence is also common, which suggests that anxiety disorders often follow an intermittent course in subjects with BPD (Silverman et al., 2012; Zanarini et al., 2014). Ansell and colleagues (2011), over the course of a seven-year study, suggested that

individuals with BPD are at higher risk of new onset anxiety disorder episodes, specifically panic disorder and GAD, and have an increased risk for OCD relapse (Ansell et al., 2011). The course of BPD has been shown to influence anxiety disorders, with an improvement of BPD symptoms associated with remission of GAD and PTSD, and a worsening of BPD predicting a relapse of social phobia (Keuroghlian et al., 2015). Moreover, numerous studies have revealed that anxiety disorders negatively impact BPD, with lower remission and a higher risk of suicidal and self-damaging behaviours (Harned and Valenstein, 2013; Nepon et al., 2010),

Severity of anxiety also seems to be higher in BPD. In their study, Zanarini and al. found that BPD sufferers reported twice as many severe anxiety symptoms than the comparison group. They identified two predictors for severe anxiety: non-sexual childhood abuse and neuroticism traits (Zanarini et al., 2014). Gibb and colleagues have also demonstrated a high association between social phobia and PTSD and childhood emotional abuse (Gibb et al., 2007).

Anxiety disorders and childhood maltreatment are both named as factors influencing symptomatology and prognosis in BPD. Literature about the relation between these two factors is also beginning to see the day. Negative experiences in childhood are conducive to vulnerability to psychopathology and many studies have shown an association between childhood maltreatment and mental health illness in adulthood, such as depression, anxiety disorders and PTSD (Gibb et al., 2007; Stein et al., 1996). In BPD particularly, many studies have focused on the association between the disorder and childhood maltreatment (Battle et al., 2004; Herman et al., 1989; Johnson et al., 2001, 1999; Nickel et al., 2004; Weaver and Clum, 1993; Winsper et al., 2016; (Ibrahim et al., 2018; Widom et al., 2009) and show that all types of maltreatment (sexual, physical and emotional abuse) increase the risk of BPD and its severity,

including suicidal behaviours (Ibrahim et al., 2018; Kuo et al., 2015; Lobbestael et al., 2010). In the general population as well as in clinical populations, both childhood maltreatment and anxiety disorders have been associated with suicide ideation and attempts (Bentley et al., 2016). Pavlova and al. studied childhood maltreatment, anxiety disorders and severity of the disorder in bipolar disorder, finding a positive correlation between these factors (Pavlova et al., 2018). Personality disorders, childhood maltreatment and suicide have also been studied in panic disorder by Ozkan and al. These studies show increased severity of panic disorder and suicide attempts when comorbid personality disorder was present. Sexual abuse was associated with BPD and early onset panic disorder (Ozkan and Altindag, 2005).

Despite these observations, only a few studies have investigated anxiety disorders and their link with childhood maltreatment and severity of disorder in patients suffering from BPD (Nepon et al., 2010; Perroud et al., 2007). The aim of our study was therefore to examine the relationship between childhood maltreatment, comorbid anxiety disorders and severity of BPD, including, among other severity indexes, history of suicide attempts. To our knowledge, this is the first study evaluating the association between these factors in BPD. We hypothesized that exposure to maltreatment in childhood would be associated with increased comorbid anxiety disorders among patients with BPD and a higher severity of the disorder.

Methods

Sample

Three hundred and eighty-eight participants were recruited within a specialized unit providing healthcare to outpatients suffering from BPD at the Geneva University Hospital (HUG). The BPD diagnosis was established both by an anamnestic interview conducted by a psychiatrist and by a trained psychologist using the Structured Interview for Axis II Disorder-BPD part (SCID-II) (Maffei et al., 1997). Subjects meeting at least five criteria from DSM-IV-TR (Association, 2000) for BPD were enrolled into the programme and are therefore included in this study.

All subjects gave their informed written consent and the study was approved by the ethics committee of the Republic and Canton of Geneva, Switzerland.

Measurements

Childhood maltreatment

The history of childhood maltreatment was assessed using the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003). CTQ is a validated retrospective self-report questionnaire; it contains 28 items, including five items for each of the five domains of childhood maltreatment: emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect, as well as three items regarding social desirability. Each item is rated on a five-point ordinal scale (never true, rarely true, sometimes true, often true, very often true). The total score is obtained by summation of the 25 items corresponding to the five maltreatment domains (the three remaining items are not scored). Each domain is scored between five and 25, for a total score ranging from 25 to 125. In our analyses, we used the total score (for each of

the five domain subscales, and their sum as continuous variables) as a way to assess the cumulative severity of childhood maltreatment. The use of the CTQ total score as a measure of the severity of childhood maltreatment is supported in the existing literature (Scher et al., 2001; Spinhoven et al., 2014). The internal consistency of the five subscales of the CTQ, French version, is good with Cronbach's alpha ranging from 0.79 to 0.94 (Paquette et al., 2004). We used the CTQ total score as a measure of childhood maltreatment in primary analyses and we used the five subscales in secondary analyses in order to test effects of specific types of maltreatment.

Anxiety disorders and suicide attempt

Anxiety disorders, including panic disorder (PD), agoraphobia, social phobia (SP), generalized anxiety disorders (GAD), obsessive-compulsive disorders (OCD) and post-traumatic stress disorder (PTSD), were assessed using the French version of the Diagnostic Interview for Genetic Studies (DIGS) (Preisig et al., 1999) for DSM-IV-TR disorders. As we used the DSM-IV-TR, we included OCD and PTSD among the anxiety disorders. To better assess the impact of having multiple anxiety disorders on BPD outcomes, we created a three-point ordinal scale with 0: no anxiety disorder, 1: one anxiety disorder and 2: two and more anxiety disorders.

Severity

To assess the severity of BPD, we chose the following variables: the Score on the Screening Interview for Axis II disorders (SCID-II) BPD section (Maffei et al., 1997) (treated as an ordinal scale), History of one or more suicide attempts (Yes or No), Prior hospitalization for psychiatric reasons (0 = no hospitalization, 1= one hosp., 2 = two hosp.), History of psychotic symptoms (Yes or No), Comorbid substance use disorders (Yes or No), Other comorbid disorders (major

depressive disorder or bipolar disorder), the Score at the Beck Depression Inventory-II (BDI-II) (Beck AT., 1996), the Total score of the Barratt Impulsiveness Scale Version 10 (BIS-10) (Barratt, 1985), the subscale Trait Anger of the State-Trait Anger Expression Inventory (STAXI) (Spielberger, 1988) and the Beck Hopelessness Scale (BHS) (Beck et al., 1974).

Statistical analysis

In the primary hypothesis test, we used ordinal logistic regression to test the effect of childhood maltreatment (total CTQ score) on the sum of anxiety disorders. We then used, as an exploratory analysis, logistic regression to test the effect of childhood maltreatment (total CTQ score) on each individual anxiety disorder. We controlled for age and gender as covariates. In secondary analyses, we tested the effect of each type of childhood maltreatment (CTQ emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect score). Since only a single test was carried out to test the primary hypothesis and the purpose of the secondary tests was primarily descriptive, we consider tests with a *p* value smaller than 0.05 as statically significant. Analyses were conducted with STATA 13.0 software (StataCorp, 2013).

We then performed ordinal logistic regressions to test the effect of number of lifetime anxiety disorders on the SCID-II BPD part score and prior hospitalization, logistic regression on history of suicide attempt, psychotic symptoms, substance use disorders and other diagnoses, and linear regression for BDI-II, BIS-10, STAXI trait anger and BHS scores. We adjusted our model on age and gender. For this second part, as we conducted several tests (one for each severity index n= 10) for the same predictor (number of lifetime anxiety disorders), statistical significance was accepted for p values < 0.05/10 = 0.005. The same model was used to test the effect of childhood maltreatment (CTQ total score) on severity indicators.

Results

Sample characteristics

Clinical and demographic characteristics of the sample are described in Table 1. Only 74 participants (19.1 %) were free of any anxiety disorder, 97 (25.0 %) suffered from only one comorbid anxiety disorder, and a striking 55.9 % had two or more anxiety disorders.

Social phobia was the most common anxiety disorder (42.01%), followed by panic disorder (39.1%) and PTSD (33%). GAD (28 %), agoraphobia (15.2%) and OCD (14.4%) were less frequent.

Table 1: Clinical and demographic characteristics

		N	%
Gender (female)		358	92.27
Number of criteria on SCID-II BPD part	**5**	102	26.29
	6	71	18.3
	7	70	18.04
	8	86	22.16
	9	59	15.21
Number of anxiety disorders	**0**	74	19.07
	1	97	25
	2	217	55.93
Panic disorder		151	39.12
Agoraphobia		59	15.21
Social phobia		163	42.01
GAD		109	28.09
OCD		56	14.43
PTSD		128	32.99
Previous hospitalisation	**No (0)**	109	28.91
	1	91	24.14

	≥ 2	177	46.95
History of suicide attempts		226	58.25
Psychotic symptoms		76	21.35
Substance use disorders		235	60.57
Other diagnoses (MDD and BD)		152	40
		Mean	**SD**
Age		31.71	9.54
CTQ	**Total**	56.75	18.89
	Emo. Abuse	15.04	5.87
	Phys. Abuse	8.75	4.74
	Sex. Abuse	9.05	5.87
	Emo. Negl.	15.07	5.18
	Phys. Negl.	9.03	3.92
BDI-II		33.98	11.86
STAXI trait anger		23.84	8.37
BIS-10 total score		71.8	18.34
BHS		11.71	5.08

Abbreviations: CTQ = Childhood Trauma Questionnaire; SCID = Structured Clinical Interview for DSM-IV Axis I; GAD Generalized Anxiety Disorder; OCD = Obsessive-Compulsive Disorder; PTSD = Post-Traumatic Stress Disorder; MDD = Major Depressive Disorder; BD = Bipolar Disorder; BDI-II = Beck Depression Inventory; STAXI = State-Trait Anger Expression Inventory; BIS = Barratt Impulsiveness Scale Version 10; BHS = Beck Hopelessness Scale; 95 % CI = 95% confidence interval

The mean CTQ total score was of 56.8 (SD = 18.9), with emotional neglect being the most frequent form of maltreatment.

Effect of childhood trauma on anxiety disorders

As reported in Table 2, a higher CTQ total score was associated with more frequent lifetime anxiety disorders (OR = 1.02; 95% CI = 1.01 to 1.04; p<0.001). All types of maltreatment increased the risk of suffering from anxiety disorders, with emotional abuse being the most significant form of maltreatment (OR = 1.08; 95% CI = 1.04 to 1.11; p<0.001).

Table 2: effect of childhood maltreatment on the sum of anxiety disorders. Note: all analyses controlled for age and gender.

	Odds ratio	p	95% CI Lower	95 % CI Upper
CTQtot	1.02	<0.001	1.01	1.04
Emo abuse	1.08	<0.001	1.04	1.11
Phy. abuse	1.05	0.032	1.00	1.10
Sex. abuse	1.05	0.007	1.01	1.10
Emo neglect	1.06	0.001	1.01	1.12
Phy. Neglect	1.06	0.023	1.01	1.12

Abbreviations: CTQ = Childhood Trauma Questionnaire; 95 % CI = 95% confidence interval.

Among individual anxiety disorders, agoraphobia (OR = 1.02; p = 0.019; 95% CI 1.00 to 1.03), social phobia (OR = 1.02; p<0.001; 95% CI 1.01 to 1.04), GAD (OR = 1.02; p = 0.007; 95% CI 1.00 to 1.03) and PTSD (OR = 1.04; p<0.001; 95% CI 1.02 to 1.05) were all associated with the CTQ total score (Supplementary Table S1). Panic disorder (OR = 1.01; p = 0.078; 95% CI 1.00 to 1.02) and OCD (OR = 1.00; p = 0.592; 95% CI 0.98 to 1.01) were not.

Effect of anxiety disorders and childhood maltreatment on severity indicators

When we examined the association between anxiety disorders and severity indicators, we found that for every incremental increase in the number of anxiety disorders, an increase of 1.77 in the odds of being at a higher level of SCID-II was expected, when all of the other variables in the model were held constant. Severity indicators were also associated with the number of anxiety disorders. Anxiety disorders increased the risk of history of suicide attempts (OR = 1.74; 95%CI 1.31 to 2.27), of having been hospitalized (OR= 1.45; 95%CI 1.13 to 1.85) and of psychotic symptoms (OR = 2.11; 95% 1.39 to 3.2). These associations were still significant (p<0.005) when we controlled for the CTQ total score, except for hospitalization. The BDI-II (b =

3.51; 95%CI 2 to 5.01) and the BHS (b = 1.99; 95%CI 1.33 to 2.66) total scores were also significantly associated with anxiety disorders. This association was still present when we controlled for the CTQ total score (Table 3). The effect of individual anxiety disorders on severity indicators is displayed in the Supplementary Table S2. Significant associations (p<0.005) were found for panic disorder and history of suicide attempts (p<0.001; OR = 1.97; 95%CI 1.28 to 3.02), psychotic symptoms (OR = 4.49; p<0.001; 95%CI 2.58 to 7.82), other comorbid disorders (OR = 2.00; p<0.001; 95%CI 1.31 to 3.07); SCID-II BPD part (OR = 1.93; p<0.001; 95%CI 1.30 to 2.86), depression severity and hopelessness (p<0.001 for both variables), agoraphobia and hopelessness (p<0.001), social phobia and history of suicide attempts (OR = 1.99; p<0.001; 95% CI 1.31 to 3.04), other comorbid disorders (OR = 1.97; p<0.001; 95%CI 1.30 to 3.00) and hopelessness (p<0.001), GAD and depression severity (p<0.001), STAXI trait anger (p<0.001) and hopelessness (p<0.001), PTSD and (OR = 1.92; p<0.001; 95%CI 1.22 to 3.01), depression (p<0.001) and hopelessness (p<0.001). OCD did not yield any significant association.

Table 3: Effect of anxiety disorders on severity indicators

	Controlled for Age and Gender				**Controlled for Age, Gender and CTQ total score**			
	OR	**p**	**95% CI lower**	**95% CI upper**	**OR**	**p**	**95% CI lower**	**95% CI upper**
History of suicide attempt	1.74	<0.001	1.34	2.27	1.56	0.001	1.19	2.06
Hospitalization (0-2)	1.45	0.003	1.13	1.85	1.36	0.017	1.05	1.76
Psychotic symptoms	2.11	<0.001	1.39	3.2	1.97	0.002	1.28	3.01
Substance use disorders	1.35	0.023	1.04	1.77	1.39	0.018	1.06	1.82
Other diagnoses	1.36	0.026	1.04	1.79	1.22	0.165	0.92	1.63

SCID-II BPD part	1.77	<0.001	1.35	2.31	1.62	0.001	1.23	2.13
	b	**p**	**95% CI lower**	**95% CI upper**	**b**	**p**	**95% CI lower**	**95% CI upper**
BDI-II	3.51	<0.001	2	5.01	2.81	<0.001	1.29	4.33
STAXI trait anger	0.69	0.128	-0.19	1.58	0.49	0.282	-0.41	1.41
BIS total score	2.36	0.11	-0.53	5.26	1.28	0.387	-1.62	4.17
BHS	1.99	<0.001	1.33	2.66	1.82	<0.001	1.13	2.51

Abbreviations: CTQ = Childhood Trauma Questionnaire; SCID = Structured Clinical Interview for DSM-IV Axis I; BDI-II = Beck Depression Inventory; BIS= Barratt Impulsiveness Scale Version 10; STAXI = State-Trait Anger Expression Inventory; BHS = Beck Hopelessness Scale.
Nominal level of significance: *p*-value < 0.005.

Concerning the effect of childhood maltreatment on severity indicators, we found that history of suicide attempt (OR = 1.02; 95%CI 1.01 to 1.04) and SCID-II BPD part (OR = 1.03; 95%CI 1.01 to 1.03) were positively associated with childhood maltreatment. These associations were still significant when we controlled for the number of anxiety disorders. The BDI-II total score (p<0.001), STAXI trait anger (p<0.001)), the BIS-10 total score (p=0.002) and the BHS (p=0.001) were all significantly associated with the history of childhood maltreatment. Except for BHS, these associations were still significant after controlling for anxiety disorders.

Table 4: Effect of childhood maltreatment on severity indicators

	Controlled for Age and Gender				**Controlled for Age, Gender and Anxiety Disorders**			
	OR	**p**	**95% CI lower**	**95% CI upper**	**OR**	**p**	**95% CI lower**	**95% CI upper**
History of suicide attempt	1.02	<0.001	1.01	1.04	1.01	0.001	1.01	1.03
Hospitalisation (0-2)	1.01	0.01	1.01	1.02	1.01	0.041	1.01	1.02
Psychotic symptoms	1.02	0.023	1.01	1.03	1.01	0.14	0.99	1.02
Substance use disorders	1	0.408	0.99	1.01	1	0.75	0.99	1.01
Other diagnoses	1.03	<0.001	1.01	1.04	1.02	<0.001	1.01	1.04
SCID-II BPD part	1.03	<0.001	1.01	1.03	1.02	0.001	1.01	1.03

	b	p	95% CI lower	95% CI upper	b	p	95% CI lower	95% CI upper
BDI-II	0.16	<0.001	0.09	0.22	0.14	<0.001	0.07	0.21
STAXI trait anger	0.09	<0.001	0.04	0.13	0.07	0.001	0.03	0.12
BIS total score	0.18	0.002	0.07	0.3	0.18	0.004	0.06	0.29
BHS	0.05	0.001	0.02	0.08	0.03	0.028	0.01	0.06

Abbreviations: CTQ = Childhood Trauma Questionnaire; SCID = Structured Clinical Interview for DSM-IV Axis I; BDI-II = Beck Depression Inventory; BIS= Barratt Impulsiveness Scale Version 10; STAXI = State-Trait Anger Expression Inventory; BHS = Beck Hopelessness Scale.
Nominal level of significance: *p*-value < 0.005.

Discussion

Firstly, we found that anxiety disorders were quite prevalent in BPD, with more than half of participants diagnosed with two or more comorbid anxiety disorders. The most common anxious comorbidity was social phobia (42%), followed by panic disorder (39%), PTSD (33%), GAD (28 %), agoraphobia (15%) and OCD (14%). These results are supported by the literature, which not only shows that anxiety disorders are common comorbidities in BPD, but also that panic disorder, social phobia, simple phobia and PTSD are the most common anxiety disorders found among patients with BPD, with rates between 19.4% and 46.9% depending on diagnosis (McGlashan et al., 2000); Zanarini et al., 1998; Zimmerman and Mattia, 1999).

Secondly, we found that a history of childhood maltreatment was associated with more frequent lifetime anxiety disorders among patients suffering from BPD. All types of childhood maltreatment were associated with an increased risk of having an anxiety disorder, although emotional abuse had the strongest effect. This confirms the results of studies conducted among the general population that suggest there is a relationship between a history of childhood emotional abuse and anxiety disorders, especially social phobia (Harkness and Wildes, 2002;

McCabe et al., 2003). Pavlova and al. found that, in bipolar disorder, the CTQ total score and particularly emotional and physical abuse were also significantly linked to lifetime anxiety disorders (Pavlova et al., 2016). However, the association between the type of trauma and specific anxiety disorders was different in bipolar disorder than the association we found in BPD, suggesting different patterns of vulnerability across disorders. PTSD was also significantly linked to a history of childhood maltreatment, with the strongest association found with sexual abuse as described in previous studies (Dvir et al., 2014; Teicher et al., 2003); (Molnar et al., 2001). We did not find an association between OCD and any of the CTQ subscales among patients with BPD. This result contradicts most of the findings in the general population showing that childhood trauma is associated with obsessive symptoms and an increased rate of suicide in patients diagnosed with OCD (Ay and Erbay, 2018). However, some studies suggest that this link is not direct and that childhood adversities are associated with OCD comorbidity, such as depression (Ivarsson et al., 2016; Visser et al., 2014) or difficulties in emotional processing (Carpenter and Chung, 2011), which are the factors associated with suicide. OCD is now classified as a separate category in DSM-V, as it appears to be related to a different psychobiology than other anxiety disorders, which might explain why risk factors differ.

Thirdly we found that both anxiety disorders and severity of childhood maltreatment had, independently from one another, an effect on several severity indicators of BPD, such as the SCID-II BPD part score and suicide attempts. Although the impact of child maltreatment on the severity of psychiatric disorders, including BPD, is well known (Taillieu et al., 2016), the impact of anxiety disorders has been less investigated, especially in relation to the severity of BPD, although risk of suicidality is known to be increased among patients suffering from BPD who

have a comorbid anxiety disorder (Harned and Valenstein, 2013; Nepon et al., 2010). Apart from the severity of the disorder per se (SCID-II BPD part), anxiety disorders had an effect, regardless of childhood maltreatment, on two other severity indicators: history of suicide attempt and psychotic symptoms. The number of anxiety disorders was indeed significantly linked to the history of suicide attempt: the greater the number of anxious comorbidities present, the higher the likelihood of patients having attempted suicide at least once in their lives. Panic disorder, social phobia and PTSD showed the strongest association. This is supported by the literature, which shows that anxiety disorders are often diagnosed among suicide attempters (Lopez-Castroman et al., 2011). This association has also been found in studies on bipolar disorder, where social phobia has been found to be a risk factor for suicide attempt (Perroud et al., 2007). Our results also show an association between anxiety disorders and psychotic symptoms in BPD. This increased risk was mainly due to panic disorder. Some studies have reported that individuals with an anxious disorder were more prone to experience psychotic symptoms (Wigman et al., 2012) (Hanssen et al., 2003). In addition, PTSD and childhood trauma have been reported to increase vulnerability to psychosis (Janssen et al., 2004). Anxiety disorders mainly had an effect on state-dependant psychological measurements, such as depression and hopelessness, whereas childhood maltreatment impacted more trait dependant measurements such as impulsivity and trait of anger. These results suggest that anxiety disorders and childhood maltreatment have different repercussions on BPD symptomatology, anxiety disorders temporarily increasing the severity of the disorder, whereas childhood maltreatment has a stronger long-term impact on personality dimensions. In this perspective, anxiety disorders have been identified in the general population as a risk factor for

depression (Meier et al., 2015; Stein et al., 2001). Hopelessness is known to be a risk factor for suicide (Beck et al., 1990) and some studies found a propensity to negative perspective of future among patients suffering from anxiety disorders (Iliceto et al., 2011).

Our study has several limitations. Firstly, we did not have any information regarding the medication taken by the patients. Some subjects were receiving pharmacological treatment and others were not. We decided not to include the data on medication, due to lack of information on the indications for treatment initiation, dosage and response to treatment. The presence of medication may have influenced our results by concealing the symptoms of anxiety disorder (Bandelow et al., 2017, 2015). In this context, we can presume that anxiety could have been even higher than our results in a population not following a pharmacological treatment. Secondly, our sample was recruited in a specialized tertiary centre, which can limit the generalization of results, as the patients referred to our clinic suffer from severe forms of BPD with more comorbidities. A further limitation would be the retrospective assessment of childhood maltreatment. Widom and al. showed that a significant proportion of childhood maltreatment, even court-proven, may be forgotten and not reported later in life (Widom, 2019). Therefore, the accuracy and completeness of childhood maltreatment might have been reduced by the use of self-report measurements. On the other hand, Scott and al. (Scott et al., 2012) reported that studies comparing retrospective and prospective measurements of maltreatment found similar associations with psychopathology. While it seems likely that childhood maltreatment predicts the development of anxiety disorders in individuals with BPD, the retrospective assessment means that a temporal association cannot be established from current dataset, and therefore reversed causality remains a possibility.

The categorical nature of the DSM limits the generalisation of our results, as we did not evaluate anxiety at the dimensional level. Level of anxiety, independently of a specific anxiety disorder, should thus be considered in future studies as it has been suggested that anxiety disorders and emotional disorders probably reflect morphological variations related to a transdiagnostic factor (Norton and Paulus, 2017). In this perspective, a general factor (g-factor) has been identified among personality disorders and BPD criteria load almost entirely on it. This suggests that BPD does not represent a distinct type of personality disorder but a general impairment in personality (Sharp 2015). The exact nature of this g-factor, which may be linked to an overall susceptibility to psychopathology, is still unknown but might be linked to severity of psychopathology or self/interpersonal functioning. In that sense, increased severity of BPD in the context of comorbid anxiety disorders may only be linked to this g-factor. On the other side, our study and others have shown that specific anxiety disorders may still be interesting to consider as they differently, one from each other, influence the severity and course of other psychiatric disorders (Pavlova and al., 2016, Harned and Valenstein, 2013). This has also been shown for other BPD comorbidities such as ADHD that has been found to negatively influence response to treatment in BPD (Prada et al., 2015). We thus believe that investigating specific anxiety disorders as well as other psychiatric comorbidities in BPD is still of clinical relevance.

In conclusion, BPD was associated with a high prevalence of all anxiety disorders. The presence of comorbid anxious disorders was associated with a higher severity of illness, showing more DSM BPD criteria, higher suicidality, psychotic and depressive symptoms as well as despair. Considering these results, the development of efficient treatments to address comorbid anxiety disorders in BPD seems to be necessary. It would be interesting to see how anxious disorders

evolve among patients receiving psychotherapies designed for BPD (e.g. Dialectical-Behavioural Therapy), and whether specific interventions should be added for patients suffering from BPD with comorbid anxiety disorders. Adherence to treatment can be limited by anxiety disorders, with high dropout rates reported in literature (Santana and Fontenelle, 2011). Attendance to group and behavioural sessions, as well as the emotional exposition proposed in therapeutic programmes for BPD might be difficult for anxious patients and need to be carefully considered by healthcare professionals. Anxious disorders were also associated with childhood maltreatment, emotional abuse being associated with all anxious disorders except OCD among patients suffering from BPD. The importance of emotional forms of childhood maltreatment in this population should therefore be considered (Gunderson and Chu, 1993), with prevention and early interventions among at-risk populations to be developed to limit adulthood psychopathology.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

Ansell, E.B., Pinto, A., Edelen, M.O., Markowitz, J.C., Sanislow, C.A., Yen, S., Zanarini, M., Skodol, A.E., Shea, M.T., Morey, L.C., Gunderson, J.G., McGlashan, T.H., Grilo, C.M., 2011. The association of personality disorders with the prospective 7-year course of anxiety disorders. Psychol Med 41(5), 1019-1028.

Association, A.P., 2000. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR).

Ay, R., Erbay, L.G., 2018. Relationship between childhood trauma and suicide probability in obsessive-compulsive disorder. Psychiatry Res 261, 132-136.

Barratt, E., 1985. Impulsiveness subtraits: arousal and information processing. Spence JT, Izard CE (eds) Motivation, emotion, and personality. , In Spence JT, Izard CE (eds). Motivation, emotion, and personalityMotivation, emotion, and personality. Elsevier Science Publishers, North Holland, pp. pp 137–146.

Beck, A.T., Brown, G., Berchick, R.J., Stewart, B.L., Steer, R.A., 1990. Relationship between hopelessness and ultimate suicide: a replication with psychiatric outpatients. Am J Psychiatry 147(2), 190-195.

Beck, A.T., Weissman, A., Lester, D., Trexler, L., 1974. The measurement of pessimism: the hopelessness scale. J Consult Clin Psychol 42(6), 861-865.

Beck AT., S.R., Brown GK., 1996. BDI-II: Beck Depression Inventory Manual. 2nd ed., San Antonio: Psychological Corporation.

Bentley, K.H., Franklin, J.C., Ribeiro, J.D., Kleiman, E.M., Fox, K.R., Nock, M.K., 2016. Anxiety and its disorders as risk factors for suicidal thoughts and behaviors: A meta-analytic review. Clin Psychol Rev 43, 30-46.

Bernstein, D.P., Stein, J.A., Newcomb, M.D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D., Zule, W., 2003. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl 27(2), 169-190.

Dvir, Y., Ford, J.D., Hill, M., Frazier, J.A., 2014. Childhood maltreatment, emotional dysregulation, and psychiatric comorbidities. Harv Rev Psychiatry 22(3), 149-161.

Gibb, B.E., Chelminski, I., Zimmerman, M., 2007. Childhood emotional, physical, and sexual abuse, and diagnoses of depressive and anxiety disorders in adult psychiatric outpatients. Depress Anxiety 24(4), 256-263.

Gunderson, J.G., Chu, J.A., 1993. Treatment implications of past trauma in borderline personality disorder. Harv Rev Psychiatry 1(2), 75-81.

Hanssen, M., Peeters, F., Krabbendam, L., Radstake, S., Verdoux, H., van Os, J., 2003. How psychotic are individuals with non-psychotic disorders? Soc Psychiatry Psychiatr Epidemiol 38(3), 149-154.

Harned, M.S., Valenstein, H.R., 2013. Treatment of borderline personality disorder and co-occurring anxiety disorders. F1000Prime Rep 5, 15.

Ibrahim, J., Cosgrave, N., Woolgar, M., 2018. Childhood maltreatment and its link to borderline personality disorder features in children: A systematic review approach. Clin Child Psychol Psychiatry 23(1), 57-76.

Iliceto, P., Pompili, M., Lester, D., Gonda, X., Niolu, C., Girardi, N., Rihmer, Z., Candilera, G., Girardi, P., 2011. Relationship between Temperament, Depression, Anxiety, and Hopelessness in Adolescents: A Structural Equation Model. Depress Res Treat 2011, 160175.

Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollebergh, W., de Graaf, R., van Os, J., 2004. Childhood abuse as a risk factor for psychotic experiences. Acta Psychiatr Scand 109(1), 38-45.

Keuroghlian, A.S., Gunderson, J.G., Pagano, M.E., Markowitz, J.C., Ansell, E.B., Shea, M.T., Morey, L.C., Sanislow, C., Grilo, C.M., Stout, R.L., Zanarini, M.C., McGlashan, T.H., Skodol, A.E., 2015. Interactions of borderline personality disorder and anxiety disorders over 10 years. J Clin Psychiatry 76(11), 1529-1534.

Kuo, J.R., Khoury, J.E., Metcalfe, R., Fitzpatrick, S., Goodwill, A., 2015. An examination of the relationship between childhood emotional abuse and borderline personality disorder features: the role of difficulties with emotion regulation. Child Abuse Negl 39, 147-155.
Lobbestael, J., Arntz, A., Bernstein, D.P., 2010. Disentangling the relationship between different types of childhood maltreatment and personality disorders. J Pers Disord 24(3), 285-295.
Lopez-Castroman, J., Perez-Rodriguez, M.D., Jaussent, I., Alegria, A.A., Artes-Rodriguez, A., Freed, P., Guillaume, S., Jollant, F., Leiva-Murillo, J.M., Malafosse, A., Oquendo, M.A., de Prado-Cumplido, M., Saiz-Ruiz, J., Baca-Garcia, E., Courtet, P., Suicide, E.R.C., 2011. Distinguishing the relevant features of frequent suicide attempters. J Psychiatr Res 45(5), 619-625.
Maffei, C., Fossati, A., Agostoni, I., Barraco, A., Bagnato, M., Deborah, D., Namia, C., Novella, L., Petrachi, M., 1997. Interrater reliability and internal consistency of the structured clinical interview for DSM-IV axis II personality disorders (SCID-II), version 2.0. J Pers Disord 11(3), 279-284.
McGlashan, T.H., Grilo, C.M., Skodol, A.E., Gunderson, J.G., Shea, M.T., Morey, L.C., Zanarini, M.C., Stout, R.L., 2000. The Collaborative Longitudinal Personality Disorders Study: baseline Axis I/II and II/II diagnostic co-occurrence. Acta Psychiatr Scand 102(4), 256-264.
Meier, S.M., Petersen, L., Mattheisen, M., Mors, O., Mortensen, P.B., Laursen, T.M., 2015. Secondary depression in severe anxiety disorders: a population-based cohort study in Denmark. Lancet Psychiatry 2(6), 515-523.
Molnar, B.E., Berkman, L.F., Buka, S.L., 2001. Psychopathology, childhood sexual abuse and other childhood adversities: relative links to subsequent suicidal behaviour in the US. Psychol Med 31(6), 965-977.
Nepon, J., Belik, S.L., Bolton, J., Sareen, J., 2010. The Relationship between Anxiety Disorders and Suicide Attempts: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions. Depress Anxiety 27(9), 791-798.
Norton, P.J., Paulus, D.J., 2017. Transdiagnostic models of anxiety disorder: Theoretical and empirical underpinnings. Clinical psychology review 56, 122-137.
Ozkan, M., Altindag, A., 2005. Comorbid personality disorders in subjects with panic disorder: do personality disorders increase clinical severity? Compr Psychiatry 46(1), 20-26.
Paquette, D., Laporte, L., Bigras, M., Zoccolillo, M., 2004. [Validation of the French version of the CTQ and prevalence of the history of maltreatment]. Sante Ment Que 29(1), 201-220.
Pavlova, B., Perroud, N., Cordera, P., Uher, R., Alda, M., Dayer, A., Aubry, J.M., 2018. Anxiety disorders and childhood maltreatment as predictors of outcome in bipolar disorder. J Affect Disord 225, 337-341.
Pavlova, B., Perroud, N., Cordera, P., Uher, R., Dayer, A., Aubry, J.M., 2016. Childhood maltreatment and comorbid anxiety in people with bipolar disorder. J Affect Disord 192, 22-27.
Perroud, N., Baud, P., Preisig, M., Etain, B., Bellivier, F., Favre, S., Reber, N., Ferrero, F., Leboyer, M., Malafosse, A., 2007. Social phobia is associated with suicide attempt history in bipolar inpatients. Bipolar Disord 9(7), 713-721.
Prada, P., Nicastro, R., Zimmermann, J., Hasler, R., Aubry, J.M., Perroud, N., 2015. Addition of methylphenidate to intensive dialectical behaviour therapy for patients suffering from comorbid borderline personality disorder and ADHD: a naturalistic study. Atten Defic Hyperact Disord 7(3), 199-209.
Preisig, M., Fenton, B.T., Matthey, M.L., Berney, A., Ferrero, F., 1999. Diagnostic interview for genetic studies (DIGS): inter-rater and test-retest reliability of the French version. Eur Arch Psychiatry Clin Neurosci 249(4), 174-179.
Santana, L., Fontenelle, L.F., 2011. A review of studies concerning treatment adherence of patients with anxiety disorders. Patient Prefer Adherence 5, 427-439.

Scher, C.D., Stein, M.B., Asmundson, G.J., McCreary, D.R., Forde, D.R., 2001. The childhood trauma questionnaire in a community sample: psychometric properties and normative data. J Trauma Stress 14(4), 843-857.
Silverman, M.H., Frankenburg, F.R., Reich, D.B., Fitzmaurice, G., Zanarini, M.C., 2012. The course of anxiety disorders other than PTSD in patients with borderline personality disorder and Axis II comparison subjects: a 10-year follow-up study. J Pers Disord 26(5), 804-814.
Spielberger, C., 1988. Manual for the State-Trait Anger Expression Inventory (STAXI). Odessa, FL: Psychological Assessment Resources.
Spinhoven, P., Penninx, B.W., Hickendorff, M., van Hemert, A.M., Bernstein, D.P., Elzinga, B.M., 2014. Childhood Trauma Questionnaire: factor structure, measurement invariance, and validity across emotional disorders. Psychol Assess 26(3), 717-729.
StataCorp, 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP.
Stein, M.B., Fuetsch, M., Muller, N., Hofler, M., Lieb, R., Wittchen, H.U., 2001. Social anxiety disorder and the risk of depression: a prospective community study of adolescents and young adults. Arch Gen Psychiatry 58(3), 251-256.
Stein, M.B., Walker, J.R., Anderson, G., Hazen, A.L., Ross, C.A., Eldridge, G., Forde, D.R., 1996. Childhood physical and sexual abuse in patients with anxiety disorders and in a community sample. Am J Psychiatry 153(2), 275-277.
Taillieu, T.L., Brownridge, D.A., Sareen, J., Afifi, T.O., 2016. Childhood emotional maltreatment and mental disorders: Results from a nationally representative adult sample from the United States. Child Abuse Negl 59, 1-12.
Teicher, M.H., Andersen, S.L., Polcari, A., Anderson, C.M., Navalta, C.P., Kim, D.M., 2003. The neurobiological consequences of early stress and childhood maltreatment. Neurosci Biobehav Rev 27(1-2), 33-44.
Widom, C.S., 2019. Are Retrospective Self-reports Accurate Representations or Existential Recollections? JAMA Psychiatry.
Widom, C.S., Czaja, S.J., Paris, J., 2009. A prospective investigation of borderline personality disorder in abused and neglected children followed up into adulthood. J Pers Disord 23(5), 433-446.
Wigman, J.T., van Nierop, M., Vollebergh, W.A., Lieb, R., Beesdo-Baum, K., Wittchen, H.U., van Os, J., 2012. Evidence that psychotic symptoms are prevalent in disorders of anxiety and depression, impacting on illness onset, risk, and severity--implications for diagnosis and ultra-high risk research. Schizophr Bull 38(2), 247-257.
Zanarini, M.C., Frankenburg, F.R., Dubo, E.D., Sickel, A.E., Trikha, A., Levin, A., Reynolds, V., 1998. Axis I comorbidity of borderline personality disorder. Am J Psychiatry 155(12), 1733-1739.
Zanarini, M.C., Frankenburg, F.R., Fitzmaurice, G.M., 2014. Severity of anxiety symptoms reported by borderline patients and Axis II comparison subjects: description and prediction over 16 years of prospective follow-up. J Pers Disord 28(6), 767-777.