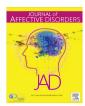
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Research paper

Childhood maltreatment and comorbid anxiety in people with bipolar disorder



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ABSTRACT

Background: Comorbid anxiety disorders and a history of childhood maltreatment are important determinants of outcome in bipolar disorder, but the relationship between these two factors is unclear. Methods: In 174 outpatients with bipolar disorder, we assessed history of childhood maltreatment with the Childhood Trauma Questionnaire (CTQ) and lifetime diagnosis of anxiety disorders with the M.I.N.I. International Neuropsychiatric Interview. We used ordinary logistic regressions to test associations between childhood maltreatment and the number of comorbid anxiety disorders, controlling for age, sex and the type of bipolar disorder.

Results: Ninety (51.7%) participants had no anxiety disorder, 50 (28.7%) had one anxiety disorder and 34 (19.5%) had two or more anxiety disorders. Childhood maltreatment, indexed by a higher CTQ total score, was associated with more lifetime anxiety disorders (OR=1.5; 95% CI=1.01 to 2.14; p=0.04). Of the CTQ subscales, emotional abuse (OR=1.68; 95% CI=1.13 to 2.49; p=0.01) and physical abuse (OR=1.43; 95% CI=1.02 to 2.01; p=0.04) were associated with anxiety disorders. Of the anxiety disorders, panic disorder was most strongly associated with childhood maltreatment (OR=2.27; 95% CI=1.28 to 4.02; p=0.01).

Limitations: The study is limited by a moderate sample size and the retrospective assessment of child-hood maltreatment.

Conclusions: Exposure to maltreatment in childhood is associated with comorbid anxiety disorders among individuals living with bipolar disorder. Bipolar disorder with comorbid anxiety may constitute a separate aetiological type with a greater contribution of early environment.

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1. Introduction

Bipolar disorder is characterised by episodes of depression and mania, with intervening periods of either complete remission or residual symptoms (Fava, 1999). Family, twin and molecular genetic studies suggest a strong contribution of genetic factors to the causation of bipolar disorder (Gershon et al., 1982; Lichtenstein et al., 2009; McGuffin et al., 2003; Sklar et al., 2011). Nonetheless, environmental factors are also important in the development of bipolar disorder. Exposure to maltreatment in childhood in particular has been associated with increased risk of bipolar disorder (Garno et al., 2005; Watson et al., 2013). It has been estimated that

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approximately 50% of people with bipolar disorder have been exposed to various forms of maltreatment in childhood (Garno et al., 2005; Leverich et al., 2002; Spinhoven et al., 2014). Moreover, history of childhood maltreatment has been associated with unfavourable course and outcomes among individuals with bipolar disorder, including earlier age of onset of bipolar disorder (Etain et al., 2008; Leverich et al., 2002), more frequent relapses (Erten et al., 2014; Etain et al., 2013) and increased risk of suicide attempts (Daruy-Filho et al., 2011; Etain et al., 2013; Perich et al., 2014).

Comorbid anxiety is emerging as another important feature in bipolar disorder. Individuals with bipolar disorder are more than three times more likely to have an anxiety disorder than general population controls (Pavlova et al., 2015); nearly one in two individuals with bipolar disorder has a comorbid anxiety disorder (Pavlova et al., 2015). The rates of anxiety disorders are also increased in unaffected biological relatives of people with bipolar

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disorder (Rasic et al., 2014) and their onset typically precedes and predicts the onset of bipolar disorder (Duffy et al., 2010). Hence, anxiety disorders have been described as an early expression of genetic risk to bipolar disorder (Duffy et al., 2013). Among individuals with bipolar disorder, comorbid anxiety disorders predict unfavourable outcomes, including more frequent mood episodes (Perroud et al., 2007; Simon et al., 2004), and increased risk of suicide attempts (Perroud et al., 2007; Simon et al., 2004; Thibodeau et al., 2013). Multiple comorbid anxiety disorders may be associated with particularly unfavourable outcomes (Deckersbach et al., 2014; Simon et al., 2004).

While both history of childhood maltreatment and comorbid anxiety are emerging as important prognostic features of bipolar disorder, the relationship between the two is unclear. On the one hand, anxiety has been conceptualized as a manifestation of genetic vulnerability to bipolar disorder (Duffy et al., 2013). On the other hand, environmental risk factors including childhood maltreatment have been associated with anxiety in the general population (Gibb et al., 2007; Stein et al., 1996). The relationship between childhood maltreatment and comorbid anxiety may help explain the aetiological and prognostic heterogeneity of bipolar disorder (Manchia et al., 2013). Yet, it has received little attention to date. While several reports suggest that history of childhood trauma may increase the likelihood of anxiety comorbidity in those with bipolar disorder (Leverich et al., 2002; Post et al., 2015; Sala et al., 2014), no previous study used a valid and reliable measure of childhood maltreatment. Moreover, a preponderance of females between those who experienced childhood trauma as well as among people with anxiety disorders (Kim et al., 2014; Sala et al., 2014; Saunders et al., 2012) may confound the apparent relationship between childhood trauma and anxiety disorders.

In the present study we aim to establish the relationship between childhood maltreatment and comorbid anxiety in bipolar disorder, using a valid and reliable measure of childhood maltreatment and controlling for potential confounders. We hypothesised that increasing severity of maltreatment exposure in childhood would be associated with comorbid anxiety disorders in individuals with bipolar disorder.

2. Methods

2.1. Sample

One-hundred and seventy four adult patients with a diagnosis of bipolar disorder type I or bipolar disorder type II were recruited as consecutive referrals to the specialized Mood Disorders Unit at the Geneva University Hospitals between January 2010 and December 2012. Patients were referred by general practitioners and psychiatrists in private practice or by other services within the hospital for diagnosis and treatment advice. Diagnosis of bipolar disorder type I or type II according to the Diagnostic and Statistical Manual-fourth edition-text revision (DSM-IV-TR; American Psychiatric Association, 2000) was established with the M.I.N.I. International Neuropsychiatric Interview (Sheehan et al., 1998) and confirmed in a consensus with an experienced psychiatrist specialized in mood disorders (J.M.A.). The study was approved by the ethics committee of the Republic and Canton of Geneva.

2.2. Measures

2.2.1. Childhood maltreatment

We assessed the history of maltreatment in childhood using the Childhood Trauma Questionnaire (CTQ), a validated retrospective self-report measure (Bernstein et al., 1994). CTQ is a 28item questionnaire, which contains five items for each of the five domains of childhood maltreatment: emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect. Each item is scored on a five-point ordinal scale (never true, rarely true, sometimes true, often true, very often true). Seven items are reversed scored. The total score is obtained as sum of the 25 items pertaining to the five domains of maltreatment (the remaining three items are not scored) and can range from 25 to 125. Higher CTQ score reflects more severe childhood maltreatment. Extensive literature and normative data support the reliability and validity of CTQ as a retrospective measure of childhood maltreatment (Scher et al., 2001; Spinhoven et al., 2014). The total CTQ score provides an overall measure of the cumulative severity of childhood maltreatment. We use the total CTQ score as a measure of childhood maltreatment in primary analyses. We use the five domain subscores in secondary analyses to test effects of specific types of maltreatment.

2.2.2. Anxiety disorders

We assessed the lifetime diagnoses of panic disorder, agoraphobia, social anxiety disorder, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), and obsessive compulsive disorder (OCD) according to DSM-IV-TR criteria, using the M.I.N.I. International Neuropsychiatric Interview (Sheehan et al., 1998). In agreement with previous literature on this topic (Deckersbach et al., 2014; Simon et al., 2009), we followed the DSM-IV-TR convention of including OCD and PTSD among anxiety disorders. To reflect the previously established role of multiple comorbid anxiety disorders in bipolar disorder, we quantified comorbid anxiety on a three-level ordinal scale as no anxiety disorder, one anxiety disorder, and two or more anxiety disorders (Deckersbach et al., 2014; Simon et al., 2009). In secondary analyses, we explored each of the six anxiety disorders separately.

2.3. Statistical analysis

In primary hypothesis test, we used ordinal logistic regression to test the effect of childhood maltreatment (total CTQ score) on anxiety disorders (0=no anxiety disorder diagnosis, 1=one anxiety disorder, 2=two or more anxiety disorders). We controlled for age, sex and type of bipolar disorder (I or II) 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 scores) and we used logistic regression to test the effects of childhood maltreatment on each anxiety disorder separately. Since only a single test was carried out to test the primary hypothesis and the purpose of secondary tests was primarily descriptive, we consider tests with a p value smaller than 0.05 as statistically significant. Analyses were conducted in Stata 12.1.

3. Results

3.1. Sample characteristics

Eighty-one (46.6%) participants were diagnosed with bipolar disorder type I, 98 (56.3%) were female and the mean age was of 41.79 (SD=12.71). Anxiety disorder comorbidity was common; 50 (28.7%) participants had one anxiety disorder and 34 (19.5%) participants had two or more anxiety disorders. Ninety (51.7%) participants had no anxiety disorder. The most prevalent anxiety disorder was GAD (28%), followed by agoraphobia (16%), panic disorder (15%), social anxiety disorder (14%), PTSD (5%) and OCD (4%). The mean CTQ total score was 46.2 (SD=16.5, range 25–111).

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