Research paper

Anxiety disorders and childhood maltreatment as predictors of outcome in bipolar disorder

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A B S T R A C T

Background: Comorbid anxiety disorders and childhood maltreatment have each been linked with unfavourable outcomes in people with bipolar disorder. Because childhood maltreatment is associated with anxiety disorders in this population, their respective predictive value remains to be determined.
Methods: In 174 adults with bipolar disorder, we assessed childhood maltreatment using the Childhood Trauma Questionnaire and lifetime anxiety disorders with the MINI International Neuropsychiatric Interview. We constructed an overall index of severity of bipolar disorder as a sum of six indicators (unemployment, psychotic symptoms, more than five manic episodes, more than five depressive episodes, suicide attempt, and hospital admission). We tested the relationship between childhood maltreatment, the number of anxiety disorders and the overall severity index using ordered logistic regression.
Results: The number of lifetime anxiety disorders was associated with the overall severity index (OR = 1.43, 95%CI = 1.01–2.04, p = 0.047). This relationship was only slightly attenuated when controlled for childhood maltreatment (OR = 1.39, 95%CI = 0.97–2.00, p = 0.069). The relationship between childhood maltreatment and the overall severity index was not statistically significant (OR = 1.26, 95%CI = 0.92–1.74, p = 0.151). Secondary analyses revealed that childhood maltreatment was associated with suicide attempts (OR = 1.70, 95%CI = 1.15–2.51, p = 0.008) and obsessive compulsive disorder was associated with the overall severity index (OR = 9.56, 95%CI = 2.20–41.47, p = 0.003).
Limitations: This was a cross-sectional study with a moderate-sized sample recruited from a specialist program.
Conclusions: While comorbid anxiety disorders are associated with the overall severity of bipolar disorder, childhood maltreatment is specifically associated with suicide attempts. Clinicians should systematically assess both factors. Interventions to improve outcomes of people with bipolar disorder with comorbid anxiety disorders and history of childhood maltreatment are needed.

1. Introduction

Bipolar disorder is a heterogeneous illness with variable symptomatic and functional outcomes (Treuer and Tohen, 2010). Despite available treatments (Yatham et al., 2013), thirty to sixty percent of people with bipolar disorder do not return to their original levels of functioning (MacQueen et al., 2001) and nine to twenty percent die of suicide (Gonda et al., 2012; Medici et al., 2015).

Identifying those most at risk for adverse outcomes has become a focus of numerous studies. Comorbid anxiety disorders and history of childhood maltreatment have each been associated with negative outcomes and are very common in this population. Almost a half have a lifetime anxiety disorder (Pavlova et al., 2015) and a similar proportion have experienced childhood maltreatment (Garno et al., 2005). Compared to people with bipolar disorder who do not have comorbid anxiety disorders, those with anxiety disorders experience more frequent relapses and mania with more psychotic symptoms (Azorin et al., 2009). They are admitted to hospital more often (Goldstein and Levitt, 2008), their psychosocial functioning is more impaired (Hawke et al., 2013; Simon et al., 2004) and they are more likely to engage in suicidal behaviour (Azorin et al., 2009; Perroud et al., 2007; Simon et al., 2004). Bipolar disorder also starts earlier in individuals with anxiety disorders

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(Perlis et al., 2004). Additionally, those with two and more anxiety disorders have worse prognosis than those with one (Deckersbach et al., 2014; Simon et al., 2004). History of childhood maltreatment has a very similar impact on outcomes of bipolar disorder; it is associated with an earlier age of onset (Aas et al., 2016; Agnew-Blais and Danese, 2016), greater number of mood episodes (Agnew-Blais and Danese, 2016), suicide attempts (Aas et al., 2016; Agnew-Blais and Danese, 2016), more severe psychotic symptoms (Agnew-Blais and Danese, 2016), and impaired functioning (Sala et al., 2014).

However, none of the above-mentioned studies explored the relative contribution of comorbid anxiety disorders and childhood maltreatment to outcomes in bipolar disorder. Because comorbid anxiety disorders and history of childhood maltreatment in people with bipolar disorder are associated with each other (Agnew-Blais and Danese, 2016; Pavlova et al., 2016), their relative contribution to unfavourable outcomes is not clear. Disentangling this relationship would clarify whether both factors are equally important to assess in routine clinical practice and help appropriately target interventions to improve outcomes of people living with bipolar disorder. In the present study, we aim to answer the question whether we need to assess both factors to predict outcome of bipolar disorder.

2. Method

2.1. Sample

We used the same sample as in our previous study (Pavlova et al., 2016). The sample consisted of adults with bipolar I or bipolar II disorder who were recruited between January 2010 and December 2012 as consecutive referrals to the Mood Disorders Unit at the Geneva University Hospital. This is a tertiary specialist service which accepts referrals for diagnosis and treatment recommendations from various health professionals, including general practitioners and psychiatrists. The study was approved by the ethics committee of the Republic and Canton of Geneva.

2.2. Measures

2.2.1. Diagnoses

The diagnoses of bipolar I or bipolar II disorder were established according to the Diagnostic and Statistical Manual-fourth edition-text revision DSM-IV-TR (American Psychiatric Association, 2000) using the MINI International Neuropsychiatric Interview (Sheehan et al., 1998) and were confirmed in a consensus meeting with a psychiatrist with an expertise in mood disorders (JMA).

We also used the MINI International Neuropsychiatric Interview (Sheehan et al., 1998) to diagnose DSM-IV-TR lifetime anxiety disorders. The assessed anxiety disorders included panic disorder, agoraphobia, social anxiety disorder, specific phobia, obsessive compulsive disorder (OCD) and post-traumatic stress disorder. As we used the DSM-IV-TR, we included OCD and post-traumatic stress disorder among anxiety disorders. To capture the role of multiple anxiety disorders in bipolar disorder outcomes (Deckersbach et al., 2014; Simon et al., 2004), we classified the presence of anxiety disorders on a three-point ordinal scale as no anxiety disorder, one anxiety disorder and two and more anxiety disorders. In secondary analyses, we explored each anxiety disorder separately.

2.2.2. Childhood maltreatment

History of childhood maltreatment was established using the Childhood Trauma Questionnaire (Bernstein et al., 1994). This is a validated self-report questionnaire that retrospectively assesses frequency of physical abuse, emotional abuse, sexual abuse, emotional neglect and physical neglect. It consists of 28 items. Each item is scored on a five-point ordinal scale based on how frequently the person experienced each event in childhood (never true, rarely true, sometimes

true, often true, very often true). The questionnaire includes five questions for each maltreatment domain; the remaining three items form a denial score and are not included in the total score. We used the total score to capture the cumulative severity of childhood maltreatment in our analyses. The use of CTQ total score as an overall measure of childhood maltreatment has been supported by previous literature (Scher et al., 2001; Spinhoven et al., 2014). The total score can range between 25 and 125. Higher score reflects more severe maltreatment.

2.2.3. Severity

To assess the overall severity of bipolar disorder, we calculated the overall severity index by combining the following severity indicators that were established in an interview with a psychiatrist: age of onset before 21 years of age, more than five lifetime depressive episodes, more than five lifetime manic episodes, history of one or more suicide attempts, history of at least one hospital admission for bipolar disorder, history of psychotic symptoms and unemployment at the time of the interview. We rated each severity indicator on a binary scale (0 = indicator not present, 1 = indicator present). The overall severity index is a sum of all severity indicators and can range from 0 to 6. Higher ratings suggest greater severity. We used the overall severity index in the primary analyses and explored the individual severity indicators in the secondary analyses.

2.3. Statistical analysis

In the primary analyses, we used ordered logistic regression to test the effect of the number of lifetime anxiety disorders (0 = no anxiety disorder, 1 = one anxiety disorder, 2 = two and more anxiety disorders) and of history of childhood maltreatment (total CTQ score) on the overall severity index. We consider tests with a p-value smaller than 0.05 as statistically significant. In the secondary analyses we used logistic regression to explore the association of childhood maltreatment and the number of anxiety disorders with each severity indicator (i.e. unemployment, more than five lifetime depressive episodes, more than five lifetime manic episodes, history of psychotic symptoms, one or more hospital admission for bipolar disorder, and suicide attempts). Further secondary analyses explored the relationship between individual anxiety disorders and the overall severity index using ordered logistic regression. All analyses were controlled for age, sex and type of bipolar disorder (bipolar I or bipolar II disorder). We used Stata 12.1 to conduct all analyses.

2.4. Power calculation

We aimed to detect a moderate effect of predictors on the overall severity index, equivalent to odds ratio 1.4 in ordered logistic regression with five levels of the outcome variable. Power calculation by simulation in STATA suggested that a sample of 173 individuals is required to detect such effect with a power of 80% at an alpha level of 0.05. To achieve a similar power at alpha level 0.01, a sample of 260 individuals would be required. The available sample of 174 individuals with valid data was sufficient for a powered test at alpha 0.05 but not at alpha 0.01. Given these considerations and the available sample, we chose to carry out only one primary test per predictor and consider results with p < 0.05 as statistically significant.

3. Results

3.1. Sample description

We recruited 174 individuals. Ninety-eight (56.3%) were female and their mean age was 41.79 years (SD = 12.71). Eighty-one (46.6%) were diagnosed with bipolar I disorder. Fifty (28.7%) had one lifetime anxiety disorder and thirty-four (19.5%) had two or more lifetime anxiety disorders. Generalized anxiety disorder was the most commonly