



Revisiting the association between childhood trauma and psychosis in bipolar disorder: A quasi-dimensional path-analysis



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ABSTRACT

Background: Childhood trauma has been associated with a more severe clinical expression of bipolar disorder (BD). However, the results that specifically associated traumatic events and psychotic features in BD have been inconsistent, possibly due to the low resolution of the phenotypes being used.

Methods: 270 normothymic patients with BD completed the Childhood Trauma Questionnaire (CTQ) and the Peters Delusion Inventory (PDI) that assessed 21 delusional beliefs. Patients were characterized for the lifetime presence of psychotic features during episodes and cannabis misuse in accordance with DSM-IV. We performed a series of path analyses to investigate the links from three types of childhood abuse (physical, sexual and emotional) directly to delusional beliefs and psychotic features, and indirectly through cannabis misuse.

Results: A first path analysis showed no link between any of the childhood abuse types and psychotic features when only a categorical definition of psychosis was used. When incorporating the quasi-dimensional measure of delusional beliefs in a second path analysis, we found that emotional and physical abuse and cannabis misuse were each directly associated with PDI score. PDI score and psychotic features were strongly correlated. Childhood abuse did not operate through cannabis misuse to increase delusional beliefs. Including type of BD in the model did not alter the results.

Conclusion: Emotional and physical abuse, but also cannabis misuse, increased delusional beliefs in patients with BD. Using a quasi-dimensional measure of psychotic symptoms in BD provided higher resolution of the psychosis phenotype and helped reconcile ambiguous findings from previous studies.

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1. Introduction

Among environmental risk factors that contribute to the pathophysiology of bipolar disorder (BD) (Lichtenstein et al., 2009), childhood traumatic events are considered to be one of the major determinants (Etain et al., 2008). Indeed, reviews of case-control studies have demonstrated that childhood trauma is reported as

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more frequent and severe in patients with BD as compared to unaffected individuals (Aas et al., 2016; Daruy-Filho et al., 2011; Etain et al., 2008, 2010; Fisher and Hosang, 2010; Maniglio, 2013). A study from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) also found an increased risk for BD in those individuals exposed to childhood physical abuse (Sugaya et al., 2012), BD thus being ranked fourth in the top associated psychiatric disorders (after PTSD, ADHD, and suicide attempt). Furthermore, childhood trauma is not only a risk factor for BD but also for a more severe clinical expression of the disorder (Aas et al., 2016; Agnew-Blais and Danese, 2016; Etain et al., 2013), including earlier age at onset, rapid cycling, high levels of psychiatric comorbidities and suicide attempt among other clinical characteristics.

Findings regarding associations between childhood trauma and psychotic features in BD have been relatively inconsistent due to heterogeneity in sample sizes, the type of assessment for childhood trauma employed, and the definitions used for psychotic features (mainly presence of lifetime delusions or hallucinations) (see online Supplementary Table S1). The majority of studies published before 2013 reported no associations between childhood trauma and psychotic features in BD, with the exception of two (Hammersley et al., 2003; Romero et al., 2009). All these studies have been included in a recently published meta-analysis (Agnew-Blais and Danese, 2016) that concluded in favour of an association between childhood trauma and greater psychosis severity in BD. However, this conclusion deserves some comment. First, removing the study that contributed the most to the effect size estimates (Romero et al., 2009) resulted in a non-significant estimate for the meta-analysis of the association between childhood maltreatment and psychosis severity. This study has some particularities compared to the other included studies, such as being performed in a large sample of youths (age range 7–17) and including a large proportion of BD-NOS (Bipolar Disorder Not Otherwise Specified) patients (Romero et al., 2009). Second, another positive study found an association between spontaneous self-report of trauma and auditory hallucinations and might be viewed as questionable because of the method used to assess childhood trauma and the extraction of this sample from a clinical trial of cognitive-behavioural therapy in BD (Hammersley et al., 2003). One previous study published in 2007 has not been included in the meta-analysis (Kauer-Sant'Anna et al., 2007) and showed no association between childhood trauma and psychotic features. More recently, Cakir et al. found an association between childhood trauma and psychotic features (Cakir et al., 2015), while the largest published sample to date found no association with delusions, but with hallucinations, in a sample of 2019 patients with BD (Upthegrove et al., 2015). Therefore, whether there is an association between early adversity and delusions and/or hallucinations in BD remains unclear.

Using a more dimensional approach (quantitative symptom measure) and combining it with the traditional categorical approach (presence/absence of psychotic features) might help reconcile these conflicting results. Indeed, Allardyce et al. (2007) found that incorporating continuous symptom measures and categorical diagnoses improved aetiological understanding of psychosis (Allardyce et al., 2007). It also seems crucial to consider the impact of different subtypes of trauma (e.g., emotional, physical and sexual abuse, and neglect) as their associations with psychotic symptoms may not be uniform (Ajnakina et al., 2016; Fisher et al., 2010), as well as taking into account the correlation between them as different trauma types often co-occur (Finkelhor et al., 2007). Finally, incorporating other environmental factors (such as cannabis misuse) into the analyses may also be of potential interest since they could moderate or mediate the impact of childhood

trauma on psychosis (Aas et al., 2016; Sideli et al., 2015). Therefore, we sought to explore the associations between several types of childhood trauma and psychotic symptoms in a sample of stabilized BD patients, taking into account the overlap between trauma types and including both a continuous measure of delusional experiences and a dichotomous measure of psychotic symptoms. We focussed on delusions because of their greater frequency (as compared to hallucinations) in patients with BD. Indeed, lifetime presence of psychotic features is high in patients with BD (more than two-thirds of patients with subtype I) (Etain et al., 2012), with delusions being around twice as frequent as hallucinations (Black and Nasrallah, 1989; Dunayevich and Keck, 2000; Keck et al., 2003).

2. Material and methods

2.1. Samples

Patients fulfilled DSM-IV criteria (American Psychiatric Association, 1994) for bipolar disorder (BD) type I or II and were recruited during their follow-up appointments at three university-affiliated psychiatric departments in France (Paris/Créteil, Bordeaux, Nancy). Patients were interviewed by trained psychiatrists or psychologists, using the French version (Preisig et al., 1999) of the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994). The following inclusion criteria were used: older than 18 years and currently normothymic (i.e., to have a Montgomery-Asberg Depression Rating Scale score and a Mania Rating Scale score below 5) (Bech et al., 1978; Montgomery and Asberg, 1979). All included individuals were of Caucasian origin. This research protocol received appropriate Ethical Committee and Institutional Review Board approvals. We obtained written informed consent from all study participants before inclusion. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

2.2. Clinical variables related to BD

Patients were interviewed using the French version of the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994), providing lifetime DSM-IV Axis I diagnoses (American Psychiatric Association, 1994). A set of variables was extracted from the DIGS to characterize the clinical expression of BD. The age at onset (AAO) of BD was determined retrospectively and was defined as the age at which a patient first met DSM-IV criteria for a major depressive or (hypo)manic episode according to information collected with the DIGS. Suicide attempt and rapid cycling were recorded as present if they occurred at any point during the course of BD (lifetime presence). Substance misuse (for alcohol or cannabis) was coded as present if the patient fulfilled the DSM-IV criteria for abuse or dependence to these substances at any point during the course of their BD (lifetime presence). Lifetime psychosis was considered present if any episode (whatever polarity) could be considered as severe with psychotic features (delusions or hallucinations) according to DSM-IV criteria and the data collected using the DIGS.

2.3. Assessment of childhood trauma and delusional beliefs

Childhood traumatic events were recorded using the French validated version (Paquette et al., 2004) of the Childhood Trauma Questionnaire (CTQ), a 28-item self-report questionnaire (Bernstein and Fink, 1998). The CTQ yields a total score and five subscale scores with 5 items each for Emotional and Physical

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