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Alcohol use disorders are associated with increased affective lability in bipolar disorder

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ABSTRACT

Background: Affective dysregulation is a core feature of bipolar disorder (BD), and inter-episodic affect lability is associated with more severe outcomes including comorbidity. Rates of daily tobacco smoking and substance use disorders in BD are high. Knowledge regarding relationships between affective lability and abuse of the most commonly used substances such as tobacco, alcohol and cannabis in BD is limited.

Methods: We investigated whether dimensions of inter-episodic affective lability as measured with the Affective Lability Scale – short form (ALS-SF) were associated with lifetime daily tobacco use or alcohol (AUD) or cannabis use disorders (CUD) in a sample of 372 French and Norwegian patients with BD I and II.

Results: ALS-SF total score and all sub-dimensions (anxiety-depression, depression-elation and anger) were significantly associated with AUD, while only the depression-elation sub-dimension was associated with CUD, after controlling for possible confounders such as gender, age at interview, age at illness onset, BD subtype, duration of illness and other substance use disorders. Daily tobacco smoking was not significantly associated with affective lability.

Limitations: Data for recent substance use or psychiatric comorbidities such as personality or hyperkinetic disorders were not available, and could have mediated the relationships.

Conclusion: AUD is associated with several dimensions of inter-episodic affective lability in BD, while CUD is associated with increased oscillations between depression and elation only. Increased affective lability may partly explain the increased illness severity of patients with BD and AUD or CUD. Affective lability should be treated in order to prevent these comorbidities.

1. Introduction

Bipolar disorder (BD) is a severe mental disorder estimated to affect approximately 1% of the population (Merikangas et al., 2011) characterized by recurrent manic, hypomanic, or depressive episodes. Importantly, burdensome sub-syndromal symptoms also persist between episodes (Judd et al., 2003). Affect disturbances are seen as core features of the disorder, and psychopathological studies have focused on deficits in emotion perception, -processing and -regulation (Aminoff et al., 2012; Rocca et al., 2009; Townsend and Altshuler, 2012; Wessa and Linke, 2009).

An important aspect of emotion dysregulation is affective instability

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or – lability, defined as "Rapid oscillations of intense affect, with a difficulty in regulating these oscillations or their behavioral consequences" (Marwaha et al., 2014). There is an increasing awareness that affective lability is relevant to the psychopathology of BD, based on studies showing increased levels in BD patients compared to healthy controls (Aas et al., 2014b; Richard-Lepouriel et al., 2016). Studies show increased affective lability both in manic/mixed episodes (Henry et al., 2003) in addition to persistent affective lability in euthymic periods (Aminoff et al., 2012; Henry et al., 2008; M'Bailara et al., 2009; Perugi and Akiskal, 2002). This inter-episodic affective lability may have clinical and prognostic implications, with indications that affective lability during euthymic periods is a marker of a more severe clinical outcome in BD with earlier illness onset and increased rates of psychiatric comorbidity (Henry et al., 2008).

One of the most common comorbidities in BD is substance use disorders (Grant et al., 2005). Rates of tobacco smoking are also substantially elevated in BD compared to the general population (Jackson et al., 2015), with severe physical health implications. Emotional dysregulation has been proposed as a risk factor for problematic substance use independently from psychiatric diagnoses (Gross, 2013), and associations have been found between emotional dysregulation and subsequent tobacco smoking (Lyvers et al., 2014), problem drinking (Berking et al., 2011; Dvorak et al., 2014; Kuvaas et al., 2014; Sher and Grekin, 2007) and excessive cannabis use (Dvorak and Day, 2014) in individuals without psychiatric disorders. Furthermore, substance use disorders (SUD) are also prevalent in psychiatric disorders where affective dysregulation is prominent, such as borderline personality disorders (Trull et al., 2000), PTSD (Ruglass et al., 2014), eating disorders (Harrop and Marlatt, 2010) and ADHD (Richard-Lepouriel et al., 2016; Yoshimasu et al., 2012). Taken together, these findings indicate that affective lability would be associated with SUD also in BD. The relationship could be based in affective lability being a risk factor for SUD as suggested previously. However, as substances of abuse including alcohol affect dopamine transmission (Charlet et al., 2013), long term use may potentially cause enduring alterations in brain systems involved in emotion regulation (Cadet et al., 2014) and SUDs could in this way be a risk factor for affective lability.

To our knowledge, only one previous study has investigated the relationship between affective lability and SUDs in adults with BD; reporting that increased affective lability was associated with increased rates of SUDs also in euthymic patients (Henry et al., 2008). The sample size however allowed only for investigations of the relationship between affective lability and all SUDs combined, and not the study of specific substances including the most used i.e. alcohol, cannabis and tobacco (Grant et al., 2005; Jackson et al., 2015; Regier et al., 1990). This question is of interest, since affective lability may be more strongly associated with use of specific substances due to their different neurochemical profiles, putatively affecting brain systems, including regulatory functions, differently. They might thus be associated with different levels- or aspects of affective lability. Alcohol use appears to elicit aggressive impulses to a greater extent than cannabis (Hoaken and Stewart, 2003). It is on the other hand possible that individuals with high affective lability prefer some substances, as reasons for alcohol use appear to vary across different mood states (Meyer et al., 2012). While alcohol and tobacco are commonly used by the general population, aspects of severe mental disorders, including affective lability, may lower the threshold for using illicit drugs per se. A previous study on adolescents with BD and their siblings, investigating the relationship between affective dysregulation and cigarette smoking and alcohol and drug use disorders separately, found that all types of substance abuse were significantly increased in subjects with affective dysregulation as measured with specific items from the Child Behavior Checklist (Wilens et al., 2013). It has also been hypothesized that the reason for the frequent cannabis use in BD is due to its effects on the endocannabinoid system, which is involved in affect regulation (Ashton and Moore, 2011; Leweke and Koethe, 2008). Whether this is the case also in adults with BD or whether it is specific to the adolescent population has to our knowledge not yet been investigated.

Affective lability is a multidimensional construct that comprises several sub-phenomena that can be differentiated (Harvey et al., 1989). One of the most used instruments, the Affect Lability Scale 18 items version (ALS short form - ALS-SF), has been shown to differentiate between several dimensions of affective lability, including oscillations between depression and anxiety, between depression and elation and between normal mood and anger (Aas et al., 2014b; Oliver and Simons, 2004). This instrument may thus be well suited to investigate the relationship between different substances of abuse and dimensions of affective lability.

The current study adds new cases, including an independent Norwegian sample, to the previous Henry et al. (2008) study thus doubling the sample size. This allows for investigations of specific substances of abuse, with the hypothesis, that both tobacco, alcohol and cannabis use is associated with higher levels of affective lability. We thus investigated a) Whether there were relationships between affective lability (as measured by the ALS total score) and lifetime daily tobacco smoking, lifetime alcohol use disorders and lifetime cannabis use disorders and b) Whether the putative misuse of these substance were associated with different dimensions of affective lability (as measured by the ALS subscales); in both cases controlling for differences in relevant demographic and clinical characteristics that might confound their relationships.

2. Methods

2.1. Participants

Three-hundred and seventy-two patients with BD (BD I=293 (79%), BD II=79 (21%)) participated in the study. Out of these, 329 patients were recruited from three French university-affiliated psychiatry departments (Créteil, Nancy, Bordeaux) from 2000 to 2009 and 43 patients were recruited from the major hospitals in the Oslo area for the Thematically Organized Psychosis (TOP) Study (Norway) from 2003 to 2013. The French subsample included 25 patients from the previous study by Henry et al. (2008). Inclusion criteria in France were: age 18+ years, meeting DSM-IV criteria for a diagnosis of bipolar I or II disorder, being euthymic at inclusion, and having at least three grandparents born in France based on the initial purpose of the study (genetic analyses). Inclusion criteria in Norway were: Age 18–65 years, a diagnosis of DSM-IV bipolar I or II disorder, and ability to give informed consent. Exclusion criteria in Norway were a history of severe head trauma, developmental delay and lack of knowledge of Scandinavian language. Written informed consent was obtained from all participating subjects in both countries. In France, The Research Ethics Board of Pitié-Salpêtrière Hospital reviewed and approved this study. In Norway, the project was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

2.2. Clinical assessments

In each country, clinical assessment was carried out by trained psychiatrists, MDs or clinical psychologists. In France diagnoses were established using the French version of the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994), which provides lifetime DSM-IV axis I diagnoses for psychiatric disorders, including lifetime SUDs. A similar approach was used in the Norwegian subsample where diagnoses were established using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) (First et al., 1995) and information from medical charts. French patients were euthymic at inclusion, i.e., having Young Mania Rating Scale (YMRS) (Young et al., 1978) and Montgomery-Asberg Depression Rating Scale (Montgomery and Asberg, 1979) scores of no more than 5. In the