



Research paper

Physical and mental health burden in cases of bipolar disorder classified as current, former, or non-tobacco smokers



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ABSTRACT

Background: Tobacco smoking increases the global burden of bipolar disorder (BD). We examined markers of physical and mental health that are associated with tobacco smoking, controlling for confounders that have not always been considered in previous studies of BD.

Methods: Over 600 individuals with BD I or II referred to the French Network for bipolar disorder (FACE-BD) who completed standardized assessments, and could be reliably classified as current (CS) or former smokers (FS), were compared with those who were never smokers (NS) on: BD symptom load and psychiatric comorbidities; prevalence of alcohol and substance use disorders (ASUD); medication usage; functioning and physical health parameters. The bivariate and multivariate analyses took into account age and gender.

Results: 300 cases (49%) were CS, 78 (13%) FS and 238 (39%) had never smoked. Rates were similar across genders regardless of BD subtype. Compared with NS, CS were more likely to have an ASUD (Odds Ratio (OR) 5.18), BD I (OR 2.09), and lower abdominal obesity (OR 0.97), and FS were more likely to have an ASUD (OR 6.32) and higher abdominal obesity (OR 1.03).

Limitations: The sample comprised of white Europeans; the FS subgroup was relatively small and we did not apply any statistical correction for the bivariate analyses.

Conclusions: The increased risk of physical and mental health burden in CS and FS compared to NS represents avoidable morbidity in BD. This study offers support to the argument that individuals with BD should be routinely offered support to prevent or stop tobacco smoking.

1. Introduction

In Europe, 28% of adults currently smoke tobacco (World Health Organization, 2014). Rates of smoking are increased two-to-four fold in individuals with severe mental disorders (Callaghan et al., 2014), with the prevalence in bipolar disorder (BD) ranging from about 45% to 70% (Lasser et al., 2000; McClave et al., 2010). It is reported that

individuals with BD are more likely to initiate smoking earlier in their adolescence, to be heavy smokers, and to become nicotine dependent compared to non-BD individuals who are lifetime smokers (Heffner et al., 2011). Despite evidence that individuals with BD have more difficulties in quitting smoking than other groups (Heffner et al., 2011) they are significantly less likely to be offered smoking cessation advice compared to individuals with less severe (so-called common) mental

Abbreviations: CS, current smoker; FS, former smoker; NS, individuals who were never smokers

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disorders (Mitchell et al., 2015), even when the person with BD expresses a desire to quit (Prochaska et al., 2011). These findings suggest that tobacco smoking is likely to amplify the health burden associated with BD; an idea reinforced by the fact that the standardized mortality ratio is about 1.5 for deaths from tobacco-related diseases in BD cases compared to age- and gender-matched general population controls (Callaghan et al., 2014).

It has been proposed that tobacco smoking contributes on several levels to the morbidity observed within the BD population. For example, independent studies have demonstrated an association between tobacco smoking and greater BD symptom load (Post and Kalivas, 2013; Saijad and El-Mallakh, 2012), higher prevalence of comorbid anxiety disorders (Ostacher et al., 2006), and increased risks of attempted suicide (Baek et al., 2013; Nunes et al., 2014; Ostacher et al., 2009). It is suggested that nicotine use increases the risk of developing alcohol (AUD), cannabis (CUD), or other substance use disorders (SUD) or combined co-morbidities (ASUD) because tobacco smoking can act as a ‘gateway’ phenomenon, inducing the increased use of alcohol and other substances via a range of psychosocial and physiological mechanisms (Heffner et al., 2008). Furthermore, some research indicates that the efficacy of guideline-recommended medications may be reduced because of changes in drug metabolism in tobacco smokers being prescribed mood stabilizers (Williams et al., 2012).

Medical comorbidities in BD also seem strongly related to tobacco smoking. For example, an analysis of baseline data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) project demonstrated that, although rates of tobacco smoking were relatively low (33%), smoking yielded the highest adjusted prevalence ratio for having a medical comorbidity than any other independent factor. Such findings become increasingly important when we consider the primary physical causes of increased morbidity and mortality in BD. For example, recent meta-analyses show that the increase in mortality is largely attributable to cardiovascular disease in BD (Walker et al., 2015), which in turn is associated with two risk factors that are highly prevalent in BD individuals: type 2 diabetes mellitus (Vancampfort et al., 2015a) and metabolic syndrome (Vancampfort et al., 2015b). These risks are increased in smokers as they are more likely to develop metabolic syndrome, accelerated vascular ageing or cardiovascular disease than non-smokers (Sodhi et al., 2012; Bortolasci et al., 2015; Walker et al., 2015). Furthermore, the weight gain associated with smoking cessation (Thorndike et al., 2016) may exacerbate the development of obesity and type 2 diabetes mellitus, meaning that risk factors for cardiovascular and metabolic problems are not necessarily reduced in individuals who quit smoking.

To date, the available publications report inconsistent associations between the above health-related phenomena, BD and tobacco smoking (Neves et al., 2009). The reasons for this variability in study findings is partly a function of different sampling strategies (size of the study population, recruitment process, and clinical representativeness); whether the hypotheses focused on demographic factors associated with risk of tobacco smoking, such as the STEP-BD publication (Waxmonsky et al., 2005); whether the aim was to describe the clinical characteristics of a population primarily recruited for a smoking cessation intervention trial (Chengappa et al., 2014; Evins et al., 2014); or whether the goal was to examine mechanisms underlying any hypothesized associations, such as oxidative stress and suicide attempts in small homogenous BD sub-groups (Nunes et al., 2014). Few studies have simultaneously examined mental and physical effects of tobacco smoking in BD and/or examined the most robust associations between such factors and smoking in BD. Also, the majority of studies have not considered gender-related differences in the morbidity patterns associated with tobacco smoking in BD (Okoli et al., 2013), the possible impact of subtype of BD on tobacco smoking-related morbidity (Merikangas et al., 2011), or the fact that certain treatments, such as the use of atypical antipsychotics, may directly increase the risk of

metabolic disturbances and diabetes, whether or not the individual is a current tobacco smoker (Vancampfort et al., 2015b; Vancampfort et al., 2016). These characteristics are potentially important, as they could act as confounders and may account for some of the inconsistencies in observations regarding manic symptom burden in tobacco smoking (which may relate to BD I subtype); regarding suicidal behaviour or ASUD (which may relate to gender or BD subtype) (Gonda et al., 2012; Merikangas et al., 2011; Nery et al., 2014); or the cardio-vascular impact (which often shows variations according to gender) (Barrett-Connor, 2013; Smith et al., 2015).

A further gap in our understanding is whether the impact on morbidity of tobacco in BD extends beyond the point of smoking cessation. Most studies compare current smokers with individuals who currently do not smoke, with the latter group including both former smokers and those who never smoked (Ducasse et al., 2015; Ostacher et al., 2009; Slomka et al., 2012). In contrast, fewer studies examine lifetime exposure to tobacco (which combines current and former smokers) compared with no exposure (i.e. those who never smoked) (Waxmonsky et al., 2005). However, it may be more fruitful to classify individuals into three (rather than two) groups, namely: current (CS) and former smokers (FS) and those who have never smoked tobacco (NS).

The present study identified a large, multi-center, representative clinical sample of BD cases recruited from outpatients across France who were consecutively enrolled at the FondaMental Advanced Centers of Expertise in Bipolar Disorders (known as FACE-BD). It focuses on key aspects of the burden of BD in CS, FS and NS, and takes into account any confounding effects of gender or BD subtype. We hypothesized that there would be a ‘dose-response’ type gradation in effects, such that CS would always experience more negative consequences than FS, who in turn would show higher health burdens than NS. To assess these issues, the study focused on two broad goals. First, to assess the burden of tobacco smoking in bipolar disorder by examining four specific sets of putative markers of morbidity: (i) current symptom load and lifetime psychiatric comorbidities; (ii) prevalence of alcohol and substance use disorders; (iii) medication usage; and (iv) level of functioning and physical health parameters. Second, to identify the combination of markers that best differentiated NS from FS, and NS from CS.

2. Material and methods

The local ethical review board approved the recruitment procedure and assessment protocol for the FACE-BD cohort studies (Comité de Protection des Personnes-Ile de France IX, January 18th, 2010), in accordance with the Helsinki Declaration of 1975.

2.1. Sample

We conducted a cross-sectional multicenter study by using data from outpatients being treated at the FACE-BD centers. The inclusion criteria for participants in the current study were: (i) age ≥ 18 years; (ii) currently attending an outpatient clinic for treatment of BD; (iii) met diagnostic criteria for BD type I or II according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) criteria (American Psychiatric Association, 2000); (iv) current tobacco smoking status was clearly described in the case notes (i.e. CS, FS, or NS); and (v) willing and able to give written informed consent. The exclusion criteria for being assessed and treated in FACE-BD centers are: (i) currently fulfilling criteria for a severe depressive or manic episode, or any acute psychiatric or physical state requiring immediate medical management (ii) unable to complete assessments (e.g. due to limited ability to communicate in French).

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