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Original article

Links between sleep and body mass index in bipolar disorders: An exploratory study☆

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ABSTRACT

Study objectives: Obesity and excess bodyweight are highly prevalent in individuals with bipolar disorders (BD) and are associated with adverse consequences. Multiple factors may explain increased bodyweight in BD including side effects of psychotropic medications, and reduced physical activity. Research in the general population demonstrates that sleep disturbances may also contribute to metabolic burden. We present a cross-sectional study of the associations between body mass index (BMI) and sleep parameters in patients with BD as compared with healthy controls (HC).
Methods: Twenty-six French outpatients with remitted BD and 29 HC with a similar BMI completed a 21-day study of sleep parameters using objective (actigraphy) and subjective (PSQI: Pittsburgh Sleep Quality Index) assessments.
Results: In BD cases, but not in HC, higher BMI was significantly correlated with lower sleep efficiency ($P = 0.009$) and with several other sleep parameters: shorter total sleep time ($P = 0.01$), longer sleep onset latency ($P = 0.05$), higher fragmentation index ($P = 0.008$), higher inter-day variability ($P = 0.05$) and higher PSQI total score ($P = 0.004$).
Conclusions: The findings suggest a link between a high BMI and several sleep disturbances in BD, including lower sleep efficiency. Physiological mechanisms in BD cases may include an exaggeration of phenomena observed in non-clinical populations. However, larger scale studies are required to clarify the links between metabolic and sleep-wake cycle disturbances in BD.

1. Introduction

Bipolar disorders (BD), defined as recurrences of major depressive and (hypo)manic episodes, affect at least 1% of the population [22]. Inter-episode residual depressive symptoms, sleep disturbances and somatic comorbidities, particularly obesity or metabolic syndrome, contribute to poor quality of life, functional impairment and clinical outcomes [18].

Whilst sleep disturbance is one of the diagnostic criteria for both depressive and manic episodes, it is often evidence during periods of remission as well. Persistent sleep problems and insomnia are frequent euthymic BD cases, with polysomnography and actigraphy studies showing disturbances in sleep continuity and duration [12]. Furthermore, insomnia is a robust prodromal symptom of BD relapse [15].

Obesity is frequent among those who suffer from severe mental disorders [19]. BD cases are four times more likely than individuals with no psychiatric condition to be obese or overweight [9], and

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their life expectancy is reduced by about 10 years due to cardiovascular and metabolic diseases [30]. High body mass index (BMI) impacts negatively on clinical and functional outcomes in BD. Indeed bipolar patients with obesity reported greater impairment in quality of life than non-psychiatric individuals with obesity and than non-obese psychiatric patients [17]. Furthermore, high BMI negatively influences treatment response to mood stabilizers such as lithium and valproate, and the likelihood of remission [16]. In BD, the pathophysiology of weight gain is incompletely understood. Genetic susceptibility, recurrent depressions, low activity levels, poor dietary habits, poor medical care, and side effects of antipsychotics/mood-stabilizers medication may all play a part [21].

Links between sleep disturbances and weight gain are already well documented in the general population, with an association reported between shorter sleep duration and risk of being overweight [26]. More specifically among remitted patients with BD, an association between evening chronotype and higher percentage of body fat composition had been suggested [33] and shorter sleep duration was associated with low HDL cholesterol [34].

To our knowledge, there are no published data on any associations between BMI and sleep parameters in BD cases who are in remission. Our first hypothesis was that BMI would be inversely related to sleep efficiency assessed by actigraphy in BD cases as compared with healthy controls (HC). In addition, we undertook subsidiary, exploratory analyses, to see if similar relationships existed between BMI and other sleep parameters in both cases and controls.

2. Methods

2.1. Sample

With ethical approval, written informed consent was obtained from 26 BD outpatients who were currently in remission and 29 HC. The BD cases were recruited from the Paris Est University-affiliated psychiatric department whilst the HC were recruited from the general population via advertisements posted at blood donor centres between January and August 2012.

As the study focused on ecological sleep-wake patterns, primary exclusion criteria for both groups related to confounders of sleep-wake cycle, including: shift work, recent trans-meridian travel (with a $>$ 3-hour time difference), pregnancy, child birth or recent bereavement occurring within two months before the study.

Included cases met DSM-IV criteria for BD (diagnosed using the Diagnostic Interview for Genetic Studies [DIGS]) [25], whilst HC had no personal history of a DSM-IV mental disorder (assessed using the DIGS), and no first-degree relative with a mood or psychotic disorder, or suicide attempts (assessed with the Family Interview for Genetic Studies: FIGS) [20]. Mood symptoms were measured in both groups using the Young Mania Rating Scale (YMRS) [38], and the Montgomery Asberg Depression Rating Scale (MADRS) [24].

For BD cases, remission was defined as the absence of a current or recent (within 3 months) major mood episode (according to the DIGS mood section), plus a score $<$ 8 on both the MADRS and the YMRS. Cases were also excluded if in the 3 months prior to interview they had been hospitalized for a major mood episode (DSM-IV criteria), and/or had any change in psychiatric medications.

2.2. Sleep and BMI assessment

2.2.1. Actigraphy measure of sleep

Actigraphy allows the prospective and objective monitoring of sleep (inactivity) and activity patterns, and can capture the variability in sleep-wake patterns over several consecutive days. For the purposes of this study, we selected sleep efficiency as our primary as it is widely reported in sleep and circadian studies and in those with physical and mental disorders; sleep efficiency and BMI are known to be correlated in healthy populations [23]; also, it is a composite measure that takes into account time in bed and total sleep time, all of which can be measured objectively using an actiwatch.

All study participants were asked to wear an actiwatch (AW-7 CamNtech®) continuously on the non-dominant wrist for 21 consecutive days. An actiwatch is a device that contains an accelerometer and detects, scores, and stores information about the intensity and timing of wrist movements over consecutive 24-hour intervals. Participants were instructed to press the event-marker when they went to bed to sleep and when they got out of bed to start the day (and concurrently to complete a sleep diary). Data were sampled in one-minute epochs and analyzed with the sleep detection algorithm provided by Actiwatch software (Actiwatch Activity & Sleep Analysis Ltd CamNtech® 7.28). The following sleep scoring procedure was used: (i) information provided by the event-marker was given priority, (ii) if participants forgot to press the event-marker, missing information about bed- and/or rise-times was retrieved from the sleep diary, (iii) visual inspection was used to correct any inconsistencies between the times provided by the event-marker, the diary and/or the recorded signal [5]. The definitions of the actigraphy parameters of interest are summarized in Table 1.

2.2.2. Sleep questionnaires

Participants completed the French version of the Pittsburgh Sleep Quality Index (PSQI) [2] and the French version of the Berlin Questionnaire [31]. The PSQI is a 19-item self-rated questionnaire that measures subjective sleep quality. A total score $>$ 5 is regarded as indicating clinical significant levels of sleep disturbances. As discrepancies between objective and subjective measure of sleep are common in BD [13], we regarded the examination of the associations between BMI and PSQI total score as secondary analysis. The Berlin Questionnaire is a validated assessment of an individual's risk of Obstructive Sleep Apnea (OSA) [31]. Since a substantial proportion of obese individual and patients with BD who are overweight are known to present with OSA [35], we included this as a putative moderating variable in our analysis. The Berlin Questionnaire identifies three risk categories for OSA and individuals can be classified into high risk (if they have positive scores for $\geq$ 2 categories) or low risk (if they have a positive score $\leq$ 1 category).

Table 1
Definitions of the actigraphy parameters.

Actigraphy parameters	Definitions
Sleep efficiency	Ratio of time spent asleep (total sleep time) to the amount of time spent in bed
Total sleep time	Time period from sleep onset to wake up time
Sleep onset latency	Time period from lights out/bedtime to sleep onset
Wake after sleep onset (WASO)	Total amount of time awake excluding sleep onset latency
Intra-day variability	Variation in activity levels within one day
Fragmentation index	Ratio of the number of phases of 1-minute immobility to the total number of immobility phases of all duration multiplied by 100