



# Sleep disturbances, functioning, and quality of life in euthymic patients with bipolar disorder

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## ABSTRACT

There is scarce knowledge about the impact of sleep disturbances on functioning and quality of life (QoL). This study aims to investigate the links between sleep satisfaction and duration, and functioning and QoL in euthymic BD patients. We made a secondary analysis of a cross-sectional, naturalistic, multicenter study. Inclusion criteria: DSM-IV BD diagnosis; age > 17 years; written informed consent. Sample: 119 Spanish euthymic BD outpatients. Hierarchical multiple regressions were performed controlling for confounding factors. We found that almost half of the patients reported at least one sleep complaint, nighttime awakenings (60.5%) and difficulty falling asleep (31.9%) were the most frequent. Long sleep duration was associated with worse global functioning, and also with worse occupational functioning along with caffeine consumption. Sleep satisfaction was negatively associated with worse QoL in the mental health subscale and the summary mental. In both cases, the use of benzodiazepines negatively affects these QoL domains. In conclusion, euthymic bipolar patients frequently present sleep disturbances that seem to contribute to the impairment of their functioning and QoL. Also, the use of benzodiazepines negatively affects the QoL of these patients. Thus, a detailed sleep evaluation should be performed, and the use of benzodiazepines should be reduced to the minimum.

## 1. Introduction

Bipolar disorder (BD) is a severe, recurrent disorder with a high prevalence of comorbidities (Leboyer et al., 2012) and mortality (Kupfer, 2005), and with a significant impact on daily functioning and quality of life (QoL), even when in clinical remission (Deckersbach et al., 2016; Rosa et al., 2012; Sierra et al., 2005). Moreover, Carta and Angst (2016) discuss the hypothesis of identifying BD as an issue of clinical and public health interest, including sub-threshold cases.

Several lines of evidence highlight sleep disruptions as a key feature of the disorder. First, sleep disturbances have been identified as an early indicator of emerging BD (Duffy et al., 2007; Ritter et al., 2015), and once the diagnosis is made, they are described as the most common prodrome of mania and the sixth most common symptom occurring before the onset of a depressive episode (Harvey et al., 2005b). Second, experimentally induced sleep deprivation is linked to the onset of manic episodes and improvement of depressed mood in unipolar depression (Colombo et al., 1999; Wu and Bunney, 1990). Third, there are multiple lines of evidence suggesting that sleep disturbances contribute to

relapse in BD (Bauer et al., 2006; Gruber et al., 2009; Harvey et al., 2009). Fourth, sleep disturbances have been identified as the most prominent correlates of mood episodes and inadequate recovery (Harvey, 2008). Finally, it has been estimated that between 15 and 100% of BD patients experience sleep disturbances during the euthymic phase (Iyer and Palaniappan, 2017; Millar et al., 2004; Sylvia et al., 2012).

Although it is well documented that sleep is disturbed, there is less knowledge about how it is disturbed (Harvey, 2008). The pathological sleep pattern of persons with BD depends mostly on the type of episode. Depressive episodes are typically characterized by increased nighttime awakenings and more severe insomnia or hypersomnia, while manic episodes are usually characterized by more severe insomnia or what is often described as a decreased 'need for sleep,' with increased energy levels (Harvey et al., 2005). Furthermore, during euthymia, it has been estimated that between 15 and 100% of individuals experience sleep disturbances (Millar et al., 2004; Sylvia et al., 2012), and one third have circadian rhythm sleep-wake disorders (Takaesu et al., 2018).

There are conflicting results in studies on sleep disturbances and

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their impact on functioning in euthymic individuals with BD. While some studies have shown an association between sleep disturbances and functional impairment (Keskin et al., 2018; Boland et al., 2015; Rosa et al., 2013), a recent study by Samalin et al. (2017) found that they are only indirectly associated via residual depressive symptoms and perceived cognitive performance. Other studies have described a negative impact of sleep disturbances on functioning (Cretu et al., 2016; St-Amant et al., 2013), but their results should be interpreted with caution due to methodological problems, mainly the lack of psychometric instruments for assessment both sleep problems and functioning (sleep items from HDRS, and GAF and the daytime functioning item of PSQ).

QoL has consistently been shown to be decreased in BD patients (Sierra et al., 2005). Furthermore, two studies, one in symptomatic patients (Gruber et al., 2009) and one in euthymic patients (Giglio et al., 2009), have demonstrated that sleep disturbances are another factor that contributes to the low quality of life in BD patients.

Given the scarce and conflicting literature, this paper aims to investigate the impact of two sleep parameters (satisfaction and duration) on daily functioning and QoL in a sample of adults with BD during the euthymic phase. In contrast to previous studies, we employed psychometrically valid and reliable instruments for assessing these domains. We hypothesized that dissatisfied sleepers would have a lower functioning and would report worse health-related QoL. We also hypothesized that given the literature on the general population and acute phases of BD, long and short sleepers would exhibit worse daily functioning and poorer QoL.

## 2. Methods

### 2.1. Subjects

This paper is a secondary analysis of a huge study for developing a staging model for BD supported by the Spanish Ministry of Health, Social Services and Equality (Ref. PI11/02493).

Subjects were recruited at four sites in Spain [Oviedo (1 center), Barcelona (2 centers), and Valencia (1 center)]. Inclusion criteria were (1) BD diagnoses confirmed with the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) (First et al., 2002); (2) older than 17 years of age; (3) receiving outpatient treatment at one of the four sites; and (4) written informed consent to participate in the study. Exclusion criteria were designed to be minimal and consisted only of refusal to participate.

The study was approved by the Research Ethics Committee of the Principality of Asturias (Ref. 36/12) and was conducted in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice. All patients received extensive information about the study and provided written informed consent before they were enrolled.

### 2.2. Clinical assessment

Trained researchers performed all assessments. The assessments included an ad-hoc questionnaire for collecting demographic and clinical information (comorbidity, somatic illness, and treatments). Also, the Spanish versions of the following psychometric instruments were used: Young Mania Rating Scale (YMRS) (Colom et al., 2002), Hamilton Depression Rating Scale (HDRS) (Bobes et al., 2003), and Clinical Global Impression Scale (CGI) (Guy, 1976). Euthymia was defined as a score of  $\leq 7$  for depression on the HDRS and  $\leq 6$  for hypomania or mania on the YMRS. Additionally, the use of legal and illegal substances was recorded based on patients self-report. We employed the Spanish version of the ASI-6 (Diaz Mesa et al., 2010) for alcohol and illicit drugs, and an ad-hoc questionnaire for caffeinated drinks and tobacco consumptions. Caffeine consumer was defined as drinking at least one cup of caffeinated coffee daily and tobacco user as smoking at least one cigarette per

day.

#### 2.2.1. Sleep characteristics

Sleep was measured using the Oviedo Sleep Questionnaire (OSQ) (Bobes et al., 2000). The OSQ is a brief semi-structured interview on sleep characteristics that has recently been validated in patients with severe mental disorders (García-Portilla et al., 2009). It consists of 15 items, 13 of which generate scores in the following three dimensions: (1) subjective satisfaction with sleep (ranging from 1 = very dissatisfied to 7 = very satisfied), (2) insomnia (no/yes), and (3) hypersomnia (no/yes) according to either ICD-10 or DSM IV-TR diagnostic criteria.

Based on the subjective sleep satisfaction dimension score, the sample was divided into two groups: satisfied patients (scores ranging from 5 = satisfied to 7 = very satisfied) ( $n = 72$ ) and dissatisfied patients (from 1 = very dissatisfied to 4 = more or less dissatisfied) ( $n = 47$ ).

Furthermore, the OSQ requires patients to estimate an average total sleep time (TST) per night in the past month. TST was used to divide the sample into three sleep duration groups: normal sleepers (NS) (6.5–8.5 h slept per night) ( $n = 65$ ); short sleepers (SS) ( $\leq 6$  h slept per night) ( $n = 12$ ); and long sleepers (LS) ( $\geq 9$  h slept per night) ( $n = 33$ ) (Gruber et al., 2009). These cutoff scores have been used in others studies (Aeschbach et al., 1996; Gruber et al., 2009; Monk et al., 2001).

#### 2.2.2. Functioning and quality of life

The level of functioning was measured with the Functional Assessment Short Test (FAST) (Rosa et al., 2007) and the Global Assessment of Functioning (GAF) (Association, 1987).

The FAST was specifically developed and validated for use in patients with BD. It consists of 24 items that evaluate 6 specific areas of functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure time. All items are rated using a Likert scale that ranges from 0 (highest level of functioning) to 3 (lowest level of functioning). It provides scores for each area of functioning and a global functioning score that is the sum of the scores in the six areas and ranges from 0 to 72. The higher the score, the poorer the functioning.

The GAF scale provides a general rating of the patient's current level of functioning (psychological, social, and occupational) on a scale from 1 = lowest functioning to 100 = highest functioning.

Patient perception of QoL was examined using the SF-36 Health Survey Short-Form (Ware and Sherbourne, 1992). This is a structured, self-report questionnaire and one of the most widely used generic measures of health-related QoL. Its 36 items constitute the following eight subscales: physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning, and mental health. There is no single general score for the SF-36. Instead, it generates eight subscale scores and two summary scale scores: physical and mental. The scores range from 0 to 100, and the higher the value, the greater the QoL.

### 2.3. Analyses

All analyses were performed using SPSS statistical software (version 23.0). To detect group differences in demographic, clinical, functioning, and QoL variables between satisfied and dissatisfied patients and among sleep duration groups, independent samples *t* tests and ANOVA with Tukey post-hoc or chi-square were used. For all tests, the significance level was set at  $p < 0.05$ .

No significant differences were found between satisfied and dissatisfied patients in demographic, clinical, pharmacological treatment, or substance use variables. Significant statistical differences were found among sleep duration groups in the following variables: age, pharmacological treatment, and caffeine consumption. Therefore, subsequent ANCOVA analyses were done using these three variables as covariates.

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