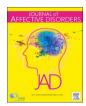
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#### Research paper

## Insomnia and hypersomnia in major depressive episode: Prevalence, sociodemographic characteristics and psychiatric comorbidity in a population-based study



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#### ABSTRACT

*Objectives*: To examine (i) the frequency of different sleep complaints (early wake-up, trouble falling asleep, hypersomnia) and their co-occurrence and (ii) the sociodemographic characteristics and psychiatric comorbidity associated with each type of sleep profiles.

*Methods*: Data were drawn from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions, a nationally representative survey of the US adult population (wave 1, 2001–2002; wave 2, 2004–2005). The primary analyses were limited to 3573 participants who had a DSM-IV-TR diagnosis of major depressive episode (MDE) between the two waves. We used a multiple regression model to estimate the strength of independent associations between self-reported sleep complaints, sociodemographic characteristics and lifetime psychiatric comorbidity.

Results: Most of participants with MDE (92%) reported significant sleep complaints, from whom 85.2% had insomnia and 47.5% hypersomnia symptoms. The prevalence rates were for insomnia "only" of 48.5%, hypersomnia "only" of 13.7%, and their co-occurrence of 30.2%. We found that several sociodemographic characteristics (gender, age, education, individual and familial income, marital status) and psychiatric disorders (bipolar disorders, post-traumatic disorders and panic disorder) were significantly and independently associated with different sleep profiles. The co-occurrence of insomnia (especially early wake-up) and hypersomnia presented with a two-/three- fold increase risk of bipolar disorders.

Limitations: Definitions of sleep complaints were qualitative and subjective.

Conclusion: Sleep complaints are prevalent and heterogeneous in expression during MDE. Sleep disturbance profiles are associated with specific patterns of comorbidity. Our findings highlight the importance of continued research on sleep complaints during MDE while taking into account psychiatric comorbidity.

#### 1. Introduction

Major Depressive Disorder (MDD) is associated with considerable functional and social impairment (Ustün et al., 2004; Wittchen and Jacobi, 2005) and considered as being the most prevalent psychiatric disorder (Waraich et al., 2004). MDD is the second worldwide cause of

disability and is associated with decreased quality of life and increased mortality (Ferrari et al., 2013; Hoertel et al., 2014; Whiteford et al., 2013). Sleep disturbances are observed in nearly 90% of individuals with major depressive episode (MDE) (Tsuno et al., 2005). The most characteristic sleep disturbances in MDE include delayed sleep onset, non-restful sleep, early-morning wakening, daytime fatigue, and

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blunting or reversal of the normal morning peaks in subjective energy and alertness (Hickie and Rogers, 2011). Sleep complaints are also frequently the last symptoms to resolve at the end of a MDE (Wichniak et al., 2012). Several clinical studies have linked sleep disturbances in patients with MDE to increased severity of depressive symptoms (O'Brien et al., 2011), poorer treatment response (Pigeon et al., 2008), and increased risk of suicidal ideation and suicide attempt (Li et al., 2012; Pigeon et al., 2012). Sleep complaints may also persist during MDE remission and are associated with greater risk of recurrence (Kaplan et al., 2011; Perlis et al., 1997; Sylvia et al., 2012), poorer overall functioning and quality of life, and increased risk of metabolic syndrome (Kaplan et al., 2011; Li et al., 2012; van Mill et al., 2010). Advancing our understanding of the mechanisms through which sleep disturbances impact on the prognosis of MDE may have important implications for the management of patients with MDE (Bellivier et al., 2015; Dallaspezia et al., 2015; Harvey et al., 2015).

Along the last decades, growing attention has been paid by clinicians and researchers to better characterize sleep disturbances associated with MDE. Several studies used subjective and objective measures based on actigraphy or polysomnography and showed a short rapid eye movement (REM) sleep latency, an increased REM sleep and a decreased slow wave sleep (Arfken et al., 2014; Berle et al., 2010; Korszun et al., 2002; Lopez et al., 2010; Pillai et al., 2011; Todder et al., 2006). Based on these findings, several chronobiological treatments have emerged to help relieve MDE symptoms, including bright light treatment, melatonin agonists, sleep deprivation, and specific cognitive and behavioural therapies (Al-Karawi and Jubair, 2016; Benedetti and Colombo, 2011; Dallaspezia et al., 2015; Hickie and Rogers, 2011). However, a better understanding of the heterogeneity of sleep complaints observed in individuals with MDE may help refine existing sleep treatments and develop personalized treatment of depression.

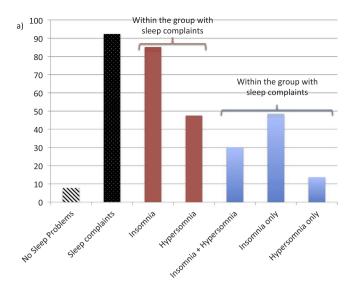
Research on insomnia and hypersomnia in MDE has predominantly focused on sleep complaints as distinct entities despite growing evidence indicating that insomnia and hypersomnia can co-occur (Soehner et al., 2014). In addition, it remains poorly known whether specific sociodemographic and psychiatric comorbidity may be associated with specific sleep complaints in MDE.

In a large sample of individuals with MDE, we sought to examine (i) the frequency of three sleep complaints (i.e., early wake-up, trouble falling asleep and hypersomnia) and their co-occurrence and (ii) the sociodemographic characteristics and psychiatric comorbidity associated with the different types of sleep complaints. By using a large, nationally representative sample, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), we aimed to obtain stable estimates that could be generalized beyond clinical samples.

#### 2. Methods

#### 2.1. Participants

Data were drawn from the Wave 1 and Wave 2 NESARC, a nationally representative survey of the US adult population, conducted in 2001-2002 (Wave 1) and 2004-2005 (Wave 2) by the National Institute on Alcoholism and Alcohol Abuse (NIAAA) and described in detail elsewhere (Grant et al., 2009). The target population included the civilian population, aged 18 years and older, residing in households and group quarters. Face-to-face interviews were conducted with 43,093 respondents. The overall survey response rate for Wave 1 was 81%. In Wave 2, attempts were made to conduct reinterviews with all 43,093 respondents. Excluding respondents ineligible for the Wave 2 interview because they were deceased, deported, on active military duty throughout the follow-up period, or mentally or physically impaired, the cumulative response rate at Wave 2 was 70.2%, reflecting 34,653 completed Wave 2 interviews. Adjustment for nonresponse across sociodemographic characteristics and the presence of any lifetime Wave 1 NESARC substance use disorder or other psychiatric disorder was



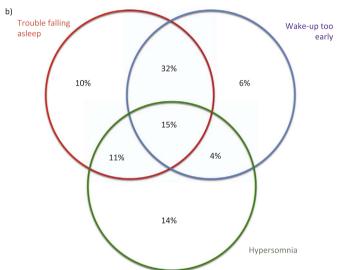


Fig. 1. Prevalence of sleep complaints in participants with major depressive disorder between the two waves of the NESARC. a) Histogram of prevalences of sleep complaints by pattern of sleep disturbance (in red: patterns are not mutually exclusive; in blue: patterns are mutually exclusive); b) Venn diagram of prevalences of types of sleep complaints.

performed at the household and person levels (Grant et al., 2007). Weighted data were then adjusted to be representative of the civilian population of the United States on socioeconomic variables based on the 2000 Decennial Census (Grant et al., 2009). The Wave 2 NESARC weights include a component that adjusts for nonresponse for sociodemographic factors and psychiatric diagnoses (Grant et al., 2009), to ensure that the sample approximates the target population, i.e., the original sample minus attrition between the two waves. In order to test whether this nonresponse adjustment was successful, Wave 2 respondents were compared with the target population (comprising Wave 2 respondents and eligible nonrespondents) in terms of number of baseline (Wave 1) sociodemographic and diagnostic measures (Grant et al., 2009). The resulting comparison indicated that there were no significant differences between the Wave 2 respondents and the target population on socioeconomic status, age, race-ethnicity, sex or the presence of any lifetime substance, mood, anxiety or personality disorder (each examined separately) (Grant et al., 2009). The research protocol, including informed consent procedures, received full human subjects review and approval from the US Census Bureau and the Office of Management and Budget (Grant et al., 2009).

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