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### Original Article

# Association between stress-related sleep reactivity and cognitive processes in insomnia disorder and insomnia subgroups: preliminary results



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#### ABSTRACT

*Objective*: Stress-related sleep reactivity, sleep-related cognitions, and psychological factors play an important role in insomnia. The aim was to investigate their possible association in Insomnia Disorder, insomnia subgroups, and healthy subjects.

Methods: The cross-sectional study consisted of 93 subjects who met diagnostic criteria for Insomnia Disorder according to Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) and of 30 healthy subjects. Survey instruments included the Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Ford Insomnia Response to Stress Test (FIRST), Dysfunctional Beliefs about Sleep scale (DBAS), Beck Depression Inventory (BDI), and Zung Self-Rating Anxiety Scale (SAS). Descriptive statistics, Pearson correlations,  $\chi^2$ -test, and multiple linear regression were performed.

Results: FIRST and SAS best determined the insomnia subjects vs good sleepers (FIRST  $\chi^2$  = 109.6, p < 0.001, SAS  $\chi^2$  = 120.3, p < 0.001). FIRST was best predicted by DBAS (p < 0.001), PSQI (p < 0.001), and SAS by PSQI (p < 0.001), ISI (p < 0.05), BDI (p < 0.001). In the sleep onset subgroup FIRST was related to ISI, PSQI, and DBAS and in the combined subgroup with DBAS. In both subgroups SAS was related to PSQI, ISI, and BDI. Conclusions: Findings suggest potential implications: (1) among the factors that may contribute to insomnia, stress-related sleep reactivity, and psychological factors, such as anxiety symptoms, may distinguish insomnia subjects from good sleepers; (2) sleep reactivity and sleep-related cognitions seem interrelated, unhelpful beliefs may affect the stress reactivity; (3) psychological factors may influence sleep quality and the severity of insomnia; (4) these important sleep-related variables may have similar associations in insomnia subgroups; they may constitute the core factors for insomnia development and maintenance.

#### 1. Introduction

Chronic insomnia is a highly prevalent health problem. Population-based estimates indicate that about one-third of adults report insomnia symptoms [1–3] that are related to a wide spectrum of comorbid conditions, including psychiatric and neurodegenerative disorders as well as neuroendocrine and cardiovascular disease [4–11].

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Understanding the mechanisms involved in the development and maintenance of insomnia, could be particularly useful for prevention and treatment strategies of insomnia and its comorbid conditions. Recently, there has been growing interest in studying insomnia subgroups: this strategy might provide novel pathways for clinicians to assess and adequately treat insomnia [12,13].

Stress has been considered a common precipitating factor of insomnia in predisposed individuals [14]; subjects suffering from insomnia report increased cognitive and physiological responses to stress challenges according to the hyperarousal model [15,16] which may contribute to the development and persistence of insomnia [15,16]. In turn, hyperarousal in insomnia has been related to 'Sleep reactivity' [17–22] which is defined as the degree of sleep

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disruption in response to stressful events [17–21] and may favor the progression of insomnia [17,18,21–25].

In addition, cognitive processes such as unhelpful beliefs and attitudes about sleep are presumed to play an important role in the development and maintenance of insomnia: previous studies have consistently shown that subjects with insomnia have more dysfunctional sleep-related thoughts than good sleepers [26–29]. Cognitive processes, such as cognitive intrusion at sleep onset, worry, unhelpful beliefs, expectation, and safety behaviors have been shown to be correlated with insomnia severity and have an influence on treatment response [27,29]. Maladaptive cognitions may lead to increased arousal and attention toward sleep-related threats, thus generating a vicious cycle that impairs the ability to initiate and maintain sleep [25–27,29–31], and further contributing to the chronicity of the disorder.

While studies have shown cognitive intrusions and unhelpful sleep-related beliefs to be associated with the stress-related sleep disturbance in contributing to the development of insomnia [24,32,33], no previous studies have examined their possible relationship in subjects with Insomnia Disorder (ID).

Several studies have attempted to discover and create insomnia subgroups. Patients with insomnia may present with sleep initiation or maintenance difficulties, early morning awakening, or some combination of the three. Edinger et al. [12] identified naturally occurring subgroups indicating only initiation or only maintenance problems to fall into separate subgroups than individuals presenting with multiple insomnia symptoms. These findings suggest that a variety of clinically distinct subgroups can be identified and might be relevant for differential treatments.

Studies have also shown a role of psychological factors in insomnia: depressive and anxiety symptoms are highly comorbid and showed a mutual relationship with insomnia [5,7,33–35]. Particularly, individuals with only sleep initiation difficulties have been shown to be more likely to be depressed [34,36]. Other studies showed all insomnia subtypes to be strongly associated with depressive symptoms, anxiety and pain [37]. Initiation and maintenance combined disorders have been shown to have the highest percentage of comorbid psychiatric illnesses compared to other insomnia subtypes [38].

Little is known about the differences between insomnia subgroups based on cognitive factors. It has been suggested that worrying about sleep difficulties sleeping may be a specific feature of individuals belonging to the sleep-onset subgroup [39].

Although a great deal of research has investigated the psychological determinants of insomnia [34–38], only a few studies examined the potential contribution of sleep reactivity and cognitive processes within different insomnia subgroups. In particular, it is unclear whether there are different cognitive, psychological, and sleep reactivity profiles between different insomnia subgroups.

On this basis, the primary aim of this study was to evaluate stress-related sleep reactivity, cognitive processes and psychological factors in a group of subjects with ID and in a group of healthy controls with the objective of determining which variables among them may predict insomnia. The second aim of the study was to evaluate the possible predictors of these variables. The association between all these variables was studied in two different insomnia subgroups such as (1) difficulty initiating sleep – the sleep onset insomnia subgroup, and (2) multiple insomnia symptoms subgroup, ie, difficulty maintaining sleep and early morning awakenings insomnia combined subgroup, as it was less studied in previous research.

To these aims we also used a set of variables generally used to assess insomnia, which included the evaluation of insomnia severity of the sleep quality. As psychological factors, anxiety state and depressive symptoms were evaluated.

#### 2. Methods

2.1. Subjects selection and psychometric questionnaire administration

From January 2012 to May 2014, consecutive outpatients attending the Sleep Center of the Psychiatry Unit II, University of Pisa, Italy, who met diagnostic criteria for ID according to the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) [2] and a group of healthy subjects were recruited. All subjects underwent a face-to-face evaluation conducted by a psychiatrist (L.P.). Sleep disorders were assessed by clinical evaluation and the use of sleep-related questionnaires. The evaluation also concerned insomnia severity, sleep quality, stress-related sleep reactivity, and unhelpful sleep-related beliefs and attitudes about sleep, anxiety levels, and depressive status. Inclusion criteria for subjects with insomnia disorders [2] were: (1) difficulty in initiating and/or maintaining sleep and/or early morning awakening; (2) the sleep disturbance causes clinically significant distress or impairment in important areas of functioning; (3) the sleep disturbance has been ongoing for at least three months; (4) subjects without a sleep-disruptive medical/psychiatric condition, substance abuse, and/or other sleep disorder. Only individuals who reported sleep difficulties for at least three nights a week were enrolled in the study.

Item 1 (a, b, and c) of the Insomnia Severity Index (ISI) [26] was used to create the insomnia subgroup categories, following the definition previously adopted [40]. Item 1 is divided into three questions investigating the severity of initiating sleep (a), staying asleep (b), and problems with waking up too early (c). Participants were divided into two subgroups using the score 3 (moderatesevere) or above as a threshold. Subjects who endorsed only initiation difficulties were labeled as (1) 'sleep onset' insomnia group, and those who endorsed difficulty maintaining and early morning awakening difficulties as (2) combined insomnia group. Exclusion criteria for subjects with ID were: cognitive impairment, previous or current diagnosis of other psychiatric disorders, sleep disorders (ie, obstructive sleep apnea syndrome, restless legs syndrome, etc.).

Healthy individuals were recruited from the hospital and the university personnel. Subjects underwent a face to face evaluation and the administration of questionnaires. The inclusion criteria were: less than 30 min of wake after sleep onset or wake time after sleep onset in usual nocturnal sleep [41]. The exclusion criteria were the following: (1) previously or currently diagnosed as having cognitive impairment, sleep disorders or psychiatric disease; (2) habitually users of hypnotics or of bedtime alcohol; (3) engaged in shift work; and (4) failed to complete questionnaires.

Cognitive impairment was ruled out through a face-to-face evaluation and the administration of the Mini-Mental State Examination (sum score >26 for a normal cognitive activity) [42]. Previous or current diagnosis of other psychiatric disorders was ruled out through a face-to-face evaluation and the administration of the Structured Clinical Interview for DSM IV Axis I Disorders [43]. Sleep disorders were assessed through a face-to-face interview on sleep disorders and the administration of Sleep Disorder Screening Questionnaire Italian version [44].

In particular, subjects with a score of 1 or more on item 10 of the Pittsburgh Sleep Quality Index (PSQI) [45] regarding self-reported symptoms or symptoms reported by the patient's roommate that were compatible with other sleep disorders were excluded according to the guidelines of the International Classification of Sleep Disorders, third edition [2].

The study conformed to the Declaration of Helsinki. All subjects provided written informed consent prior to entering the study.

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