Multiple phenotypes of resting-state cognition are altered in insomnia disorder

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ABSTRACT

Background: Research has supported the role of cognitive processes in the development and maintenance of insomnia, yet a standardized characterization of mind-wandering experiences in insomniacs is lacking.
Objectives: The aim was to understand the quantitative nature of thoughts and feelings during mind wandering in insomniacs and healthy controls and their relationship with sleep-related parameters.
Methods: We used the 5-minute eyes-closed wakeful rest as an experimental model condition of mind wandering. Forty-seven individuals with insomnia disorder according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (48.66 ± 15.62 years; 31 women) and 29 healthy controls (50.66 ± 15.14 years; 17 women) participated in the experiments and completed the Amsterdam Resting-State Questionnaire (ARSQ) immediately after the resting session. Participants also completed the Insomnia Severity Index (ISI), the Pittsburgh Sleep Quality Index (PSQI), the Dysfunctional Beliefs and Attitudes About Sleep Scale (DBAS). Statistical analyses included multiple regression to elucidate the independent determinants of ARSQ phenotypes.
Results: Participants with insomnia presented higher ISI, PSQI, and DBAS scores than did healthy controls. Insomniacs had strikingly different scores on most dimensions of the ARSQ, in particular Discontinuity of Mind, Self, Sleepiness, and Health Concern, that correlated positively with ISI and DBAS. Multiple regressions highlighted that for insomniacs, ISI was the best predictor of both Discontinuity of Mind and Health Concern.
Conclusions: Resting-state activity in insomnia is altered and it seems to be related to unhelpful beliefs and insomnia severity. Resting-state neuroimaging in combination with the ARSQ could reveal important associations between these aberrant cognitive scores and their underlying systems-level brain mechanisms.

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Introduction

Chronic insomnia is a highly prevalent health problem worldwide, affecting almost one-third of the adult population.[1] It is related to a wide spectrum of sequelae and cormorbid conditions, which include psychiatric, neurodegenerative disorders, neuroendocrine, and cardiovascular diseases.[2-4] Moreover, insomnia is involved in the development of cognitive impairment,[5,6] it is an independent risk factor for work disability and reduced work performance,[7] and it is associated with high direct and indirect costs for the health care system and society.[8] Understanding the mechanisms involved in the development and maintenance of insomnia may thus be particularly useful for the design of prevention and treatment strategies for insomnia and its comorbid conditions.

Research has supported the role of cognitive processes in the development and maintenance of insomnia. Previous studies have consistently shown that participants with insomnia have more unhelpful sleep-related thoughts than good sleepers.[9,10] According to Harvey's Cognitive Model of Insomnia,[9] those with sleep difficulties can suffer from repetitive thinking throughout the 24-hour period. This mental activity has been described to focus on unhelpful beliefs and attitude about sleep, worries about sleep, or daytime rumination on the possible consequences of insomnia, which may interfere with sleep, thus contributing to perpetuating insomnia.[9,10] Previous studies have also shown that participants with insomnia have more

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unhelpful sleep-related thoughts on a metacognitive level compared with good sleepers and participants with other sleep disorders.[11]

Spontaneous cognition, that is, the activity of the brain during a "rest" period with no ongoing task to perform, has been associated with the activation of a specific brain network called "default mode network" (DMN[12]). The DMN is purported to maintain the most basic cognitive activities of the human brain in a condition of "resting state," including perceiving the outside world and monitoring mental conditions.[13] From a cognitive perspective, the resting state may be viewed as a model system for states in which attention drifts away from any task at hand toward inner mentation—also referred to as stimulus-independent thought,[14] daydreaming, or mind wandering.[15,16] Estimates suggest that the human brain engages in mind wandering for approximately half of its waking day, thereby generating thoughts and feelings unrelated to current external demands.[15,16] Altered connectivity between regions of the DMN has been associated with a variety of mental disorders including depressive and anxiety disorders.[12,13,15,17-19] In particular, overactivity of the DMN has been related to rumination in depression.[19] Recent studies have also suggested that structural abnormalities in insomnia may be linked to alterations in the DMN.[20-22]

In this view, a self-report tool, the Amsterdam Resting-State Questionnaire (ARSQ[23,24]), has been developed to quantify thoughts and feelings during wakeful rest along different dimensions. The ARSQ consists of 50 statements on thoughts and feelings that one may experience at rest, and this questionnaire has been validated with data gathered from studies measuring resting-state functional magnetic resonance imaging ([25,26]) and electroencephalography,[23,27] and with measures of mental health such as depression, anxiety, and sleep quality.[23-25] At least 10 cognitive phenotypes have been labeled such as Discontinuity of Mind, Theory of Mind, Self, Planning, Sleepiness, Comfort, Somatic Awareness, Health Concern, Visual Thought, and Verbal Thought.[24,25]

The primary objective of this study was to evaluate the mind-wandering activity during wakeful rest in individuals suffering from insomnia and in healthy controls. Based on previous literature showing higher level of daytime rumination in insomniacs (see Palagini et al[28]), as well as on studies showing a positive association between frequency of mind-wondering episodes and poorer sleep quality,[29,30] we hypothesized that insomniacs would present higher scores relative to controls in resting-state phonotypes associated with sleep (ie, Sleepiness), health (ie, Health Concern), and cognitive and somatic arousal (ie, Discontinuity of Mind and Somatic Awareness). The second aim was to explore the possible associations between mind-wandering activity during the resting state and other aspects that may contribute to the development and maintenance of insomnia such as unhelpful beliefs and attitude about sleep. We hypothesized that resting-state phenotypes that are altered in insomniacs would also be predictive of sleep-related cognitions as scored by established scales such as the Pittsburgh Sleep Quality Index (PSQI), the Insomnia Severity Index (ISI), the Dysfunctional Beliefs and Attitudes About Sleep Scale (DBAS), the Zung Self-Rating Anxiety Scale (SAS), and the Beck Depression Inventory (BDI). To the best of our knowledge, this is the first report using the ASRQ to characterize the aberrant content and quality of thoughts and feelings in a clinical cohort.

Methods

Participants enrollment and psychometric questionnaire administration

From January 2014 to January 2015, consecutive outpatients attending the Sleep Center of the Psychiatry Unit II, University of Pisa, Italy, who met the diagnostic criteria for insomnia disorder according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*[1] were included in the study.

All participants underwent a face-to-face evaluation conducted by a medical doctor with an expertise in the sleep field (L.P.). Sleep disorders were assessed by clinical evaluation coupled with sleep questionnaires following the recommendations for a standard research assessment of insomnia.[31] Inclusion criteria for participants with insomnia disorder were as follows: (i) difficulty in initiating and/or maintaining sleep and/or early morning awakening, (ii) the sleep disturbance causes clinically significant distress or impairment in important areas of functioning, (iii) for at least 3 months, and (iv) without a sleep disruptive medical/psychiatric condition, substance abuse, and/or other sleep disorder.[1] Only individuals who reported sleep difficulties for at least 3 nights per week were enrolled in the study.[1]

Exclusion criteria for individuals with insomnia disorder were the presence of cognitive disorders, previous or present diagnosis of psychiatric disorders, and other sleep disorders (eg, obstructive sleep apnea syndrome, restless legs syndrome). In particular, participants with a score of 1 or more on item 10 of the PSQI[32] regarding self-reported symptoms or symptoms reported by the patient's roommate that were compatible with other sleep disorders (eg, sleep apnea) were excluded according to the *International Classification of Sleep Disorders–Third Edition* guidelines.[1]

Healthy individuals were recruited from the hospital and the university personnel. Participants underwent a face-to-face assessment and completed the same set of questionnaires used for the potential insomniacs. Inclusion criteria of the healthy participants were less than 30 minutes of sleep onset latency or wake time after sleep onset in usual nocturnal sleep.[33] The exclusion criteria were the following: (i) previously or currently diagnosed as having cognitive impairment, sleep disorders, or psychiatric diseases; (ii) habitual use of hypnotics or bedtime alcohol; (iii) engaged in shift work; and (iv) failed to complete the questionnaires.

For each participant, the presence of previous or current diagnosis of psychiatric disorders was assessed by means of the Structured Clinical Interview for *DSM IV-TR* Axis I Disorders.[34]

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

Resting-state cognition assessment

Resting-state cognition was evaluated using the ARSQ.[23,24] The ARSQ is a self-report questionnaire consisting of 50 Likert-type statements relating to thoughts and feelings that may be experienced during rest. Participants were seated in a quiet and isolated room of the laboratory and asked to find a comfortable position and relax with the eyes closed for 5 minutes. Laboratory personnel took care that they were not interrupted or disturbed during the resting state period. Participants were instructed that an acoustic "beep" would notify the end of the rest session. Afterwards, participants were instructed to fill out the ARSQ. Specifically, they were asked to report their level of agreement to all the ARSQ statements, which refer to the feelings and thoughts participants may have experienced during the 5-minute resting state. The level of agreement of all statements in the questionnaire was scored on a 5-point ordinal scale with the labels "Completely Disagree," "Disagree," "Neither Agree nor Disagree," "Agree," and "Completely Agree" corresponding to scores of 1 to 5, respectively. Ten cognitive phenotypes were computed using the mean score of the 3 items belonging to each cognitive phenotype.[24,25] The 10 dimensions and example items are Discontinuity of Mind ("I had busy thoughts," "I had difficulty holding on to my thoughts"), Theory of Mind ("I thought about other," "I thought about people I like"), Self (eg, "I thought about my behavior," "I thought about myself"), Planning ("I thought about my work/study," "I thought about solving