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Original Research

Efficiency moderates the relationship between sleep-onset insomnia and resting-state electroencephalogram microstate

Xiaoqian Ding[1], Fengzhi Cao[1], Shenghan Wang[1], Yunshu Zhang[1], Lijing Yu[1], Xinshu Wang[2,3], Rongxiang Tang[4], Yiyuan Tang[5,*]

[1]College of Psychology, Liaoning Normal University, 116029 Dalian, Liaoning, China
[2]Institute of Psychology, Chinese Academy of Science, 100101 Beijing, China
[3]Department of Psychology, University of Chinese Academy of Science, 100049 Beijing, China
[4]Department of Psychiatry, University of California San Diego, La Jolla, CA 92093, USA
[5]College of Health Solutions, Arizona State University, Tempe, AZ 85281, USA
*Correspondence: yiyuan@asu.edu (Yiyuan Tang)

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Abstract

Background: Overactivation of the salience network (SN) causes hyperarousal in insomnia patients and is associated with sleep-onset insomnia (SOI). Resting-state microstate 3 (RS-MS3) duration is closely related to SN overactivation. However, whether RS-MS3 duration is a biomarker for SOI has not yet been reported in the literature. In addition, SN activity is also associated with efficiency. However, it is not clear whether there are individual differences in the neural mechanisms of SOI in different efficiency groups. **Methods**: Considering that RS-MS3 duration characterizes the stability and persistent activation of the SN in the resting state, the current study investigated the link between SOI measured by sleep latency of Pittsburg Sleep Quality Index (PSQI), efficiency measured by Kirton Adaption-Innovation Inventory (KAI), and RS-MS3 in a Chinese healthy (subclinical) student population, using electroencephalography (EEG) microstate analysis. **Results**: We found that RS-MS3 duration was positively correlated with sleep latency and efficiency. The interaction between sleep latency and efficiency was significant. Simple slope analysis showed that high sleep latency was positively correlated with longer RS-MS3 duration in participants with higher efficiency scores. This correlation did not exist in participants with low efficiency scores. **Conclusions**: RS-MS3 duration may serve as a biomarker for SOI. There is heterogeneity in the relationship between SOI and RS-MS3 duration between individuals with high and low efficiency.

Keywords: sleep-onset insomnia; efficiency; sleep latency; resting-state microstate 3

1. Introduction

Sleep-onset insomnia (SOI) is a key subtype of insomnia disorder (ID) [1,2]. ID is caused by sleep-related disturbances characterized by an impaired ability to initiate or maintain sleep and early morning awakening. The ability to initiate sleep is often represented by sleep latency, where the longer the sleep latency, the more severe the SOI [3]. Insomnia is the second most common psychiatric disorder [4]. Insomnia causes a wide range of distressful dysfunctions in life by definition [5], and is associated with an increased risk of developing and dying from cardiovascular disease [6], and acts as a risk factor for later diagnoses of major depression disorder [6] and anxiety disorder [7].

The salience network (SN) is an executive neural network consisting of the dorsal anterior cingulate cortex (dACC) and the anterior insula (AI) [3], and is closely related to SOI. Previous studies have shown that patients with ID exhibit significantly increased SN connectivity in the resting state [8]. From a neural network perspective, a recent review suggested that the overactive SN as a main culprit of hyperarousal in ID during sleep [4]. AI's coactivation of the entire SN is enhanced even during sleep initiation in patients with ID [3]. It was reported that SOI shares a common physiological mechanism of hyperarousal with other ID subtypes, which manifests as increased activity and connectivity of SN in the resting state [8]. Moreover, the lateral rostral ACC volume is positively associated with sleep latency in people diagnosed with insomnia, implying either a compensatory effect or a risk physiological trait [9]. Therefore, brain imaging evidence of SOI suggests that excessive activation of SN causes hyperarousal in patients with insomnia, which is associated with SOI.

Efficiency is a subscale of the Kirton Adaption-Innovation Inventory (KAI). The KAI is used to measure an individual's propensity to solve problems, and efficiency reflects an individual's stable preference for doing things precisely, efficiently, and reliably. Individuals with high efficiency have higher precision, reliability, and conscientiousness [10]. Efficiency is highly consistent to conscientiousness in the Big-Five personality traits (r = 0.73), and the neural mechanisms of conscientiousness point to the SN. Previous studies have shown that SN is also the main neural basis of conscientiousness [11,12]. SN is responsible for integrating internal and external signals, rank-

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ing the importance of the current tasks, coordinating an extensive neural network to constantly monitor priorities, updating salience rankings, and initiating behavioral adjustments [13,14]. Toschi *et al*. [12] found that conscientiousness was associated with the coherence between the dACC and the insula in resting state; in addition, the entire network was responsible for the prioritization and execution of goals. Thus, we hypothesized that efficiency may be related to brain features representing SN neural activity.

High-efficiency individuals demonstrate precision, reliability, and high conscientiousness when doing things. Compared with low-efficiency individuals, high-efficiency individuals have a higher perception of self and therefore show social overcommitment [15], guilt about their daytime job [16], intentional planning and reflection at bedtime [17], and other characteristics. These manifestations are associated with individual SOI [1]. Therefore, we hypothesized that there might be individual differences in the neural basis of SOI. Specifically, unlike the low-efficiency group, the neural mechanisms of SOI development in the high-efficiency group may be associated with self-related SN neural activity [1,18,19].

Electroencephalography is a noninvasive method consisting in detection and registration of electrical activity of the brain using electrodes attached to the scalp. EEG offers high temporal resolution which is not possible with MRI. Presently, EEG is most often used by neurologists to differentiate functional from organic brain diseases, to diagnose sleep disorders [20]. Spontaneous brain activity can be studied by resting-state EEG microstates [21,22]. Resting-state microstates (MS) are the basic, semi-stable categories of resting-state EEG topographic fragments at the microsecond scale, each lasting about 100 ms and alternating with each other [23]. Among the four microstate categories, MS3 is closely related to SN. Previously, RS-MS3 was observed to be associated with activation of the dACC and AI. These brain regions constitute the SN and are thought to manage problems related to the self [18,19]. Among these, the duration of resting-state RS-MS3 reflects the stability and persistent activation of SN in the resting state [24]. Based on the close relationship between SN and SOI, we speculated that RS-MS3 duration may be a biomarker for SOI.

In summary, based on the relationship between RS-MS3 and SOI, we hypothesize that (1) sleep latency is positively correlated with RS-MS3 duration. Based on the fact that SN is a neural mechanism of conscientiousness and SN is related to RS-MS3, we hypothesize that (2) efficiency is positively correlated with RS-MS3 duration. Unlike the low-efficiency group, the high-efficiency group is characterized by a high focus on the self. The more self-related the cognition/perception, the more difficult it is to initiate sleep. Further, dealing with self-related problems is a function of RS-MS3. Based on the above, we hypothesize that (3) efficiency moderates the relationship between sleep latency and RS-MS3 duration. In individuals with high efficiency, sleep latency is positively correlated with RS-MS3 duration.

In this study, we used Pittsburg Sleep Quality Index (PSQI) to measure sleep latency and KAI to measure efficiency; additionally, combined with resting-state EEG microstate analysis, we explored the relationship between sleep latency and RS-MS3 duration, the relationship between efficiency and RS-MS3 duration, and the regulatory effect of efficiency on the relationship between sleep latency and RS-MS3 duration.

2. Materials and methods

2.1 Subjects

We recruited 62 subjects from Liaoning Normal University to participate in this study, one of whom was excluded due to substandard EEG data quality. Our Study data were obtained from the remaining 61 subjects (64% male, 36% female; mean age = 20.84, SD = 1.53). Their Efficiency and Sleep Latency were measured using the Kirton Adaptation-Innovation Inventory (KAI) and Pittsburgh sleep quality index (PSQI). EEG microstate analysis was conducted on their resting-state EEG datasets. All materials and procedures were approved by the Ethics in Human Research Committee of the first author's university. All participants gave informed consent to participate in the study and received a gift as compensation for their time.

2.2 Materials

2.2.1 Kirton Adaption-Innovation Inventory (KAI)

The KAI is widely used to measure the innovative personality and cognitive style of an individual [25,26]. It has good reliability and content validity and is considered to have three dimensions: Originality, Efficiency, and Conformity [27]. The efficiency subcomponent in Kirton Adaption-Innovation Inventory (KAI) measures the personality adaption which emphasizes the tendency to "do things better" versus "do things differently" [28]. The dimension we focus on is efficiency. Efficiency is a sum of seven questions' score. Each question uses Likert's 5-point scale of 1 to 5. The higher efficiency score, the more rigorous, reliable and disciplined people are.

2.2.2 Pittsburgh Sleep Quality Index (PSQI)

The PSQI is a self-rated questionnaire that assesses sleep quality and disturbances over an l-month time interval. Nineteen individual items generate seven "component" scores: Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction [29]. The dimension we focus on is sleep latency. The sleep latency is obtained by adding item 2 and item 5a of PSQI. Item 2 refers to the time it takes to fall asleep, i.e., how many minutes it usually takes to fall asleep each night over the past month (The scoring formula is 0 scores for less than or equal to 15

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minutes, 1 score for 16~30 minutes and 2 scores for 31~60 minutes). Item 5a refers to difficulty falling asleep, i.e., the number of times of inability to fall asleep within 30 minutes per week for the last month (The scoring formula is 0 scores for 0 time/week, 1 score for 1 time/week, 2 scores for 2 times/week, 3 scores for 3 times/week or more than 3 times/week). The cumulative score of sleep latency is 0 (scores for 0), 1 (scores for 1~2), 2 (scores for 3~4), and 3 (scores for 5~6). The higher scores indicate a greater tendency to take longer to fall asleep and to have difficulty falling asleep [29].

2.2.3 RS-EEG data acquisition and preprocessing

The resting-state data were collected when the subjects' eyes were open and closed for 5 minutes each. EEG data were processed with the EEGLAB toolbox, Matlab (Swartz Center for Computational Neuroscience Inc., La Jolla, CA, USA) [30]. The preprocessing was conducted on continuous EEG data. Raw data were visually inspected by an experienced data analyzer to remove significant artifacts caused by body movements, amplifier clipping, or bursts of EEG activity. The online sampling rate was 500 Hz, and we resampled the time series to 250 Hz. Then, channels with excessive artifacts were interpolated using the spherical spline method [31]. Basic filters embedded in EEGLAB were applied in the following order: 50 Hz notch filter, 1 Hz high-pass filter, and 30 Hz low-pass filter. Independent Component Analysis (ICA) was performed on filtered data using the Infomax ICA algorithm [32] to spatially filter out the eye blink, horizontal eye movement, muscle activity, and electrocardiography artifacts, which were automatically recognized by ICA label Toolbox (Swartz Center for Computational Neuroscience and Department of Electrical and Computer Engineering Inc., La Jolla, CA, USA) [33].

The global field power (GFP) of all the subjects at each data point was calculated to determine the point with the highest terrain signal-to-noise ratio (SNR). K-means was performed to analyze the microstates with the polarity of each topographical map being disregarded, which is a clustering analysis method. According to our data, four clusters (MS1, MS2, MS3, and MS4) were found, and explained variance was 0.721 ± 0.039, which was the same as that found in most studies of RS-EEG microstate [18,34,35].

The global map dissimilarity (GMD) was used as a criterion to fit all original maps of each subject into the four prototype maps, where each time point was fitted and labeled with the one cluster it correlated with the best [36]. Finally, the labeled data were used to compute the temporal characteristics, namely, duration, occurrence, and contribution of each microstate, as well as the probability of transition between them. We focus on the duration of RS-MS3.

Table 1. The relationships between efficiency, sleep latency, and Duration of RS-MS3 (n = 61).

	M	SD	1	2	3
Efficiency	25.670	3.730	-		
Duration of RS-MS3	0.080	0.020	0.252*	-	
Sleep latency	0.800	0.749	–0.083	0.293*	-

*$p < 0.05$. RS-MS3, resting-state microstate 3; M, mean; SD, standard deviation.

2.2.4 Statistical analysis

The efficiency scores of the KAI, sleep latency of PSQI and the duration of RS-MS3 were imported into SPSS 24.0 (SPSS Inc., Chicago, IL, USA) for correlation analysis. Then, the modulating role of efficiency in the relationship between the score of sleep Latency and the duration of RS-MS3 was analyzed using Model 1 of PROCESS 3.0 (SPSS Inc., Chicago, IL, USA) [37] with a statistical threshold of $p < 0.05$.

Fig. 1 is a flow chart to show the full process of data acquisition, processing and statistical analysis in a visual format.

3. Results

3.1 The relationships between efficiency, sleep latency, and duration of RS-MS3

Pearson correlation analysis was performed for Efficiency, Duration of RS-MS3, and Sleep Latency (see Table 1). The results showed that there was a significant positive correlation between Efficiency and the Duration of RS-MS3 ($r = 0.25$, $p < 0.05$), but no correlation with Sleep Latency. The Duration of RS-MS3 was positively correlated with Sleep Latency ($r = 0.29$, $p < 0.05$).

3.2 The modulating role of efficiency in sleep latency

The results showed that interaction of the sleep latency × efficiency was significant [F (1,57) = 5.52, $p < 0.05$, $R^2 = 0.074$]. Thus, we visualized the relationships between duration of RS-MS3 and sleep latency in Fig. 2 at high and low (one SD above and below the mean) levels of efficiency (see Fig. 2). Simple slope analysis results showed that compared to college students with short efficiency, college students with long efficiency have a longer duration of RS-MS3.

In addition, when the total efficiency score was higher (mean + 1 SD), the total score of sleep latency was significantly positively correlated with the duration of RS-MS3 (βsimple = 0.605, $t = 3.579$, $p < 0.001$) and when the total Efficiency score was lower (mean – 1 SD), the total score of Sleep latency was not significantly correlated with the Duration of RS-MS3 (βsimple = 0.108, $t = 0.738$, $p = 0.463$). To summarize, for college students with long Efficiency, a higher level of Sleep Latency is associated with a longer Duration of RS-MS3. In other words, compared to the short Efficiency group, the effect of Sleep Latency on the RS-MS3 is stronger in the long Efficiency group.

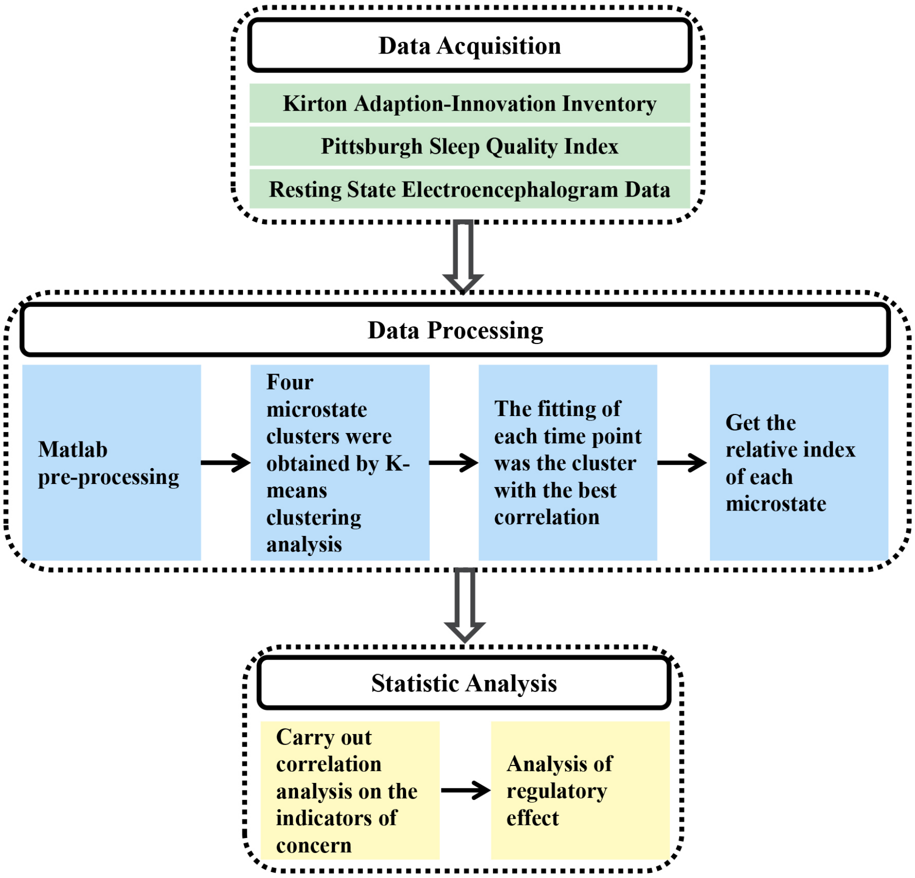

Fig. 1. RS-EEG data acquisition and preprocessing.

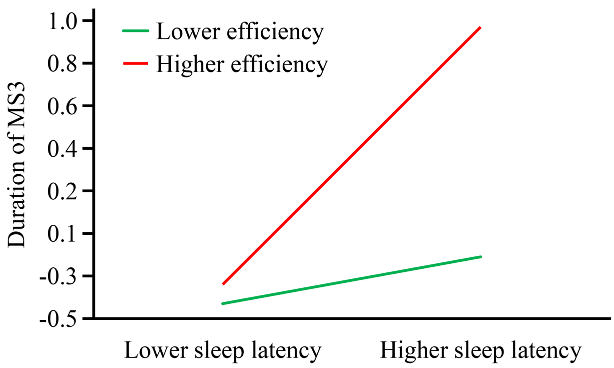

Fig. 2. Effects of sleep latency on duration of RS-MS3 at different efficiency. Two levels of efficiency graphed include one standard deviation above and below the mean, respectively. The graph is for description only. All inferential analyses keep continuous data of sleep latency and duration of RS-MS3. The units of the three variables are as follows. Duration of MS3: millisecond; Efficiency: score; Sleep latency: score.

These results suggest that Efficiency moderates the relationship between Sleep Latency and Duration of RS-MS3. Additionally, when Efficiency was longer, the Duration of RS-MS3 was higher only in higher sleep latency people.

4. Discussion

We investigated the correlations between efficiency, sleep latency, and RS-MS3 using PSQI and KAI in combination with resting-state EEG microstate analysis. We found that RS-MS3 duration was positively correlated with sleep latency and efficiency. Furthermore, efficiency moderated the relationship between sleep latency and RS-MS3 duration. Sleep latency was positively correlated with RS-MS3 duration in individuals with high efficiency, and no significant correlation was observed in individuals with low efficiency.

Sleep latency serves as an indicator of SOI where a longer sleep latency indicates a more severe impairment in the ability to initiate sleep, i.e., a greater susceptibility to SOI [3]. A number of previous studies have shown a close relationship between SN and SOI. Individuals with SOI have significantly increased SN connectivity and activity in the resting state. Moreover, co-activation of the entire SN by AI is also increased when individuals with insomnia begin to sleep [3]. Studies have also shown that RS-MS3 was associated with SN activation including the dACC and AI [18]. This study showed that sleep latency is positively correlated with RS-MS3 duration, i.e., individuals with longer RS-MS3 duration have more difficulty falling asleep. The results of this study are consistent with previous findings on the presence of an overactive SN in the ID population [16,34,38]. This validates our initial hypothesis that RS-MS3 duration may serve as a biomarker for SOI.

Efficiency is highly positively correlated with conscientiousness [39,40]. The neural mechanisms of conscientiousness and SN both point to dACC and AI, and both emphasize prioritizing current tasks [11,13,14]. Therefore, based on the corresponding relationship between SN and RS-MS3, we found that the RS-MS3 duration was positively correlated with efficiency. This may reflect the fact that SN is the neural mechanism of efficiency, and individuals with higher SN activation also have higher efficiency.

Typically, individuals with high efficiency (or high conscientiousness) [39,40] have a higher perception of self. High-efficiency individuals tend to organize their lives, work hard to achieve their goals, and adhere to the norms and rules of life more than low-efficiency individuals [16]. However, they tend to have more cognitive activities at bedtime, such as paying more attention to their worries, problems, and environmental noises [40]; this is likely due to strong body sensations [41], social overcommitment [15], guilt about their daytime jobs [16], and intentional planning and reflection at bedtime [17]. RS-MS3 corresponds to SN, which is the brain region reflecting self-cognition/perception [42]. Moreover, based on the corresponding relationship between RS-MS3 and SN, significant activation of SN also promotes the development of SOI [3]. Our study found that only in high-efficiency individuals, RS-MS3 duration was positively correlated with sleep latency, which might reflect that unlike the low-efficiency individuals, the neural mechanisms of SOI in high-efficiency individuals were associated with self-related cognitive/perceptual neural activities.

Additionally, our study found that in low-efficiency individuals, sleep latency was not correlated with RS-MS3 duration. This may reflect the fact that low-efficiency individuals have different neural mechanisms of SOI from high-efficiency individuals. Low-efficiency individuals have higher levels of negative emotions [16]. Low-efficiency individuals lead more spontaneous and chaotic lives; they more often fail to fulfill interpersonal responsibilities and resist temptations and experience unpleasant situations resulting from not doing their part, such as impaired relationships and unachieved goals, which lead them to experience more negative influences [16]. Negative emotions of low-efficiency individuals may increase their regurgitated thoughts before sleep, making it more difficult for them to fall asleep [43]. We speculate that SOI in low-efficiency individuals may be related to negative emotions and sleep hygiene problems. Findings from individuals with different efficiencies suggest that RS-MS3 duration may only be a biomarker for SOI in high-efficiency individuals.

To our knowledge, this study was the first to explore the relationships between efficiency, sleep latency, and RS-MS3 duration, as well as the regulatory effect of efficiency on the relationship between sleep latency and RS-MS3 duration using resting-state EEG microstates. Based on these results, we found that RS-MS3 duration might be a biomarker for SOI development in high-efficiency individuals. In addition, SOI development in high-efficiency individuals might be associated with neural mechanisms of self-related cognition/perception, while SOI development in low-efficiency individuals has another neural mechanism that differs from that in high-efficiency individuals.

Although we have important and compelling evidence to understand the relationship between sleep latency and RS-MS3 duration, certain limitations still need to be considered. First, with the progress of microstate research, although some research progress has been made on the physiological and psychological significance of some of its indicators, more indicators still need to be explored. Therefore, the unknown indicators should be explored more carefully in the future. Second, we should further investigate the neural and psychological mechanisms of SOI in different populations. Third, in the future, empirical studies can be used to directly focus on the time period before sleep onset to verify the multiple hypotheses about the neurological and psychological states before sleep onset proposed in this study based on the resting state data. Fourth, although efficiency significantly moderated the relationship between sleep latency and RS-MS3 duration in this study, considering that people with higher conscientiousness (efficiency) had better self-evaluation of their health [39], efficiency may have a confounding effect on self-reported sleep latency in conjunction with insomnia where accurate recall may be affected. Future studies can measure the sleep latency from a physiological perspective to avoid the confounding effect caused by self-report. Finally, the extent to which the results are applicable to clinical patients with insomnia needs further investigation.

5. Conclusions

In conclusion, this study was the first to use RS-EEG to explore the relationship between sleep latency, RS-MS3 duration and efficiency, providing a new reference for the study of SOI. This study found that higher efficiency and longer sleep latency were associated with longer RS-MS3 duration by EEG microstate analysis without differentiating groups. After differentiating groups, SOI development in high-efficiency individuals was associated with RS-MS3 duration, i.e., the longer sleep latency of high-efficiency individuals, the longer the RS-MS3 duration, which might be associated with self-related cognitive/perceptual function presented by RS-MS3. Conversely, SOI development in low-efficiency individuals might originate from a different neural mechanism. Based on the results of this study, we propose that RS-MS3 duration may be a biomarker for SOI. But given the small sample size, limited indicators, and confounding factors associated with self-reported sleep latency in this study, so this preliminary result requires further validation before reaching a conclusion. The results of this study provide preliminary physiological evidence for the microstate of sleep latency, an indicator of sleep, and provide reference for further understanding the microstate indicators of insomnia patients in the future. Future studies should further expand the sample size and focus on insomnia population, and combine sleep monitoring technology with microstates to explore the relationship between physiological indicators of sleep and different microstates, so as to provide theoretical support for medical treatment of insomnia from multiple perspectives.

Abbreviations

dACC, dorsal Anterior Cingulate Cortex; AI, Anterior Insula; EEG, electroencephalography; GFP, Global Field Power; GMD, global map dissimilarity; ICA, Independent Component Analysis; ID, Insomnia Disorder; KAI, Kirton Adaptation-Innovation Inventory; MS, Microstates; MS3, resting-state microstate 3; PSQI, Pittsburgh sleep quality index; SN, Salience Network; SNR, signal-to-noise ratio; SOI, sleep onset insomnia.

Author contributions

XD and YT designed the research study. XD performed the research. SW, YZ, LY and XW provided help and advice. XD and FC analyzed the data. XD, FC, SW and YT wrote the manuscript. XD, FC, RT, and YT contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study involving human participants was reviewed and approved by the Liaoning Normal University ethics committee. Our protocol approval number is LL2021043. The participants provided their written informed consent to participate in this study.

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Conflict of interest

The authors declare no conflict of interest. YT is serving as one of the Editorial Board members of this journal. We declare that YT had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to RF.

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