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Resting-state quantitative EEG characteristics of insomniac patients with depression☆



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A B S T R A C T
Insomnia is known to show hyperarousal in the central nervous system. However, depression that often coexists with insomnia exhibits hypo-activity in the frontal lobe, which is very different from insomnia. In the present study, we examined wake resting state EEG of insomniac patients with depression to investigate whether they could be conceptualized as spectrum of insomnia or significantly different from insomnia. We compared the absolute power values of EEG spectra of three groups: 15 insomniacs with comorbid depression (CD), age- and sex-matched 15 comorbid-free insomniacs (CFI), and 15 good sleep controls (GSC). As a result, CD and CFI showed no significant difference in the EEG power spectrum analysis. Compared with GSC, however, both CD and CFI groups showed increased high frequency EEG amplitude. From these results, we have confirmed that CD

1. Introduction

Depressive symptoms are commonly observed in patients with insomnia disorder. Although there are many studies on the psychophysiological mechanism of each disorder, few studies have focused on the coexistence of the two disorders. Neurophysiological studies on the coexistence of insomnia and depression are needed to provide differential diagnosis and appropriate treatment for patients with comorbidity.

The most widely supported psychopathological theory used to explain chronic insomnia is the hyperarousal theory. According to the theory, insomnia is defined as a disorder of hyperarousal, which includes an increase in physical, psychological, and cortical activity (Bonnet and Arand, 1998; Levenson et al., 2015). Substantial neurophysiological evidences have been reported for cortical hyperarousal, especially at night. In regard to many electroencephalograph (EEG) studies, insomnia patients commonly have increased high-frequency EEG activities such as beta or gamma amplitude and decreased slow waves such as theta amplitude in the pre- and post-sleep periods and NREM sleep, which is considered to be an EEG-based index of cortical hyperarousal (Levenson et al., 2015; Merica et al., 1998; Wołyńczyk-Gmaj and Szelenberger, 2011). Several polysomnographic studies have examined the EEG characteristics of insomnia patients, mainly places on the central scalp area; recent studies have shown that increased high-frequency EEG waves occur in the global cortical regions (Riedner et al., 2015). Brain-imaging studies also have revealed evidence of cortical hyperarousal. The results of positron emission tomography (PET) study demonstrated that patients with insomnia did not show decreased glucose metabolism in the medial temporal cortex, amygdala, insula, and anterior cingulate cortex, which would normally be lower during sleep. As a result, the number of instances of wakefulness after sleep onset was positively correlated with cerebral glucose metabolic rate (Nofzinger et al., 2004; Nofzinger et al., 2006).

shows cortical hyperarousal similar to insomnia in the daytime resting state. In conclusion, it would be reasonable to understood insomniac patients experiencing depression as a continuum of insomnia patients.

> Hyperarousal was observed not only at nighttime but also at daytime, hence, the hypothesis of the 24-hour hyperarousal of insomnia patients was raised. Insomniacs showed an increase in 24-hour wholebody metabolism rate compared to controls (Bonnet and Arand, 1995; Bonnet and Arand, 1998). According to Colombo et al. (2016a), patients with insomnia, compared with the control group, demonstrated increased beta and gamma amplitudes over a wide cortical area when their eyes closed during the day.

> However, neuro-pathophysiology of depressive disorder is different from insomnia disorder. A consistent decrease in prefrontal activation and reduction in gray matter volume in patients with depression has been widely reported (Sacher et al., 2012). In particular, a decreased activation in the dorsolateral prefrontal cortex and increased activation

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of the subcortical regions such as anterior cingulate cortex and amygdala in the resting state are considered to be closely related to the depressive symptoms (Northoff et al., 2011). In regard to the EEG studies, asymmetry between right and left hemispheres is observed. The decreased cortical activation in the left prefrontal cortex was apparent, but the activation change of the right prefrontal cortex was not clear (Henriques and Davidson, 1991). This asymmetrical cortical activation pattern can be confirmed by resting EEG alpha asymmetry phenomenon. In the depressed patients, the alpha amplitude in the left frontal region shows higher alpha power than in the right frontal region (Debener and Beauducel, 2000; Henriques and Davidson, 1991).

Studies regarding insomnia have consistently reported cortical hyperarousal, while research on depression has demonstrated hypoarousal in the prefrontal region; the neurophysiological studies between insomnia and depression have indicated incompatible results. Paradoxically, insomnia and depression frequently coexist in clinical settings. In the present study, we investigate whether insomnia with depression could share core neurophysiological mechanism with comorbid-free insomnia. Therefore, the purpose of the present study is to compare brain activation pattern between insomnia with comorbid depression (CD), comorbid-free insomnia (CFI), and good sleep controls through an EEG power spectrum analysis.

2. Methods

2.1. Participant

Participants were recruited through the internet and poster advertising for male and female, whose ages ranged from 18 to 65 years from Seoul and Kyoungki province of South Korea. The participants were divided into comorbid-free insomnia (CFI), insomnia with comorbid depression (CD) and good sleeper control (GSC) groups according to the selection criteria.

CFI met the following criteria: (1) meet the criteria for diagnosis of insomnia disorder in Diagnostic and Statistical Manual of mental disorders-fifth edition (DSM-5; American Psychiatric Association, 2013), (2) a score \geq 5 on the Pittsburgh Sleep Quality Index (PSQI), (3) a score ≥ 8 on the Insomnia Severity Index (ISI), (4) do not meet the criteria for diagnosis of mental disorders other than insomnia confirmed by Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), (5) no symptoms of clinical depression and a score < 21 on the Beck Depression Inventory-II (BDI-II; Beck et al., 1996; Husby et al., 2016). The criteria for the CD were as follows: (1) meet the criteria for diagnosis of insomnia disorder in DSM-5, (2) a score \geq 5 on PSQI, (3) a score ≥ 8 on ISI, (4) do not meet the criteria for diagnosis of mental disorders other than insomnia and depressive disorder through SCID-I. GSC fulfilled the following criteria: (1) a score < 5 on PSQI, (2) a score < 8 on ISI, (3) no diagnosis of mental disorders by SCID-I, (4) no symptoms of clinical depression and a score < 21 on BDI-II (Beck et al., 1996; Husby et al., 2016).

The participants were excluded on the basis of the following criteria: (1) history of psychotic or substance use disorders, (2) history of head injury or systemic disease that may have neurological effects, (3) drug use (including antidepressants) that can affect sleep–wake cycle for the past month, (4) conditions that can affect the sleep–wake cycle including travel to a different time zone or shift work experience within the 6 months prior to the experiment or drink > 4 cups of coffee per day, (5) a body mass index (BMI) \geq 30, which causes a high risk of snoring or obstructive sleep apnea syndrome, (6) left-handed that can affect the EEG pattern.

In the final, the number of participants for each CFI, CD, GSC is 15 respectively. The study protocol was reviewed and approved by the Institutional Review Board at Duksung Women's University. All participants were given an explanation of the experiment and informed consent was signed.

2.2. Measures

2.2.1. SCID-I (First et al., 2000)

SCID-I is designed to provide axis 1 diagnosis of DSM-IV through semi-structured interviews. A trained clinical psychologist carried the interview and it took an average of 1 h.

2.2.2. Pre-sleep Arousal Scale (PSAS; Nicassio et al., 1985)

PSAS is a self-report scale developed to evaluate somatic and cognitive arousal before falling asleep. The 5-point Likert scale consists of two factors, 8 items of somatic arousal and other 8 items of cognitive arousal. The higher the score, the higher level of arousal and total scores range from 16 to 80.

2.2.3. PSQI (Buysse et al., 1989)

PSQI is a self-report scale to assess sleep quality and sleep disturbance. The scale is divided into seven categories: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. It consists of 18 items and patients evaluated from 0 to 3 points for each item. The range of total scores is from 0 to 24; poor sleeper is defined as total scores of 5 or more and good sleep for scoring of 4 or less.

2.2.4. ISI (Morin and Barlow, 1993)

A self-report scale, ISI, measures the severity of insomnia according to DSM-IV and International Classification of Sleep Disorder (ICSD) criteria. It consists of 7 questions: severity of sleep onset, sleep maintenance, and early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others, and distress caused by the sleep difficulties. Total scores range 0 to 24 and total scores of 8 or more suggest insomnia.

2.2.5. Epworth Sleepiness Scale (ESS; Johns, 1991)

The ESS measures daytime sleepiness as a form of self-report scale. Participants were asked to rate from 0 to 3 while engaged in 8 different activities. The possible score range is 0 to 24 and the higher the score, the greater the sleep propensity in daily life. Total scores of 9 or more suggest a sleep disorder.

2.2.6. BDI-II (Beck et al., 1996)

To evaluate the severity of depression, Beck et al. (1996) modified and supplemented the self-report scale BDI (Beck et al., 1961) according to DSM-IV criteria for depression. It is composed of 21 questions including cognitive, emotional, motivational, and physical symptoms of depression and each question is scored from 0 to 3. Total scores of 21 and above classified as clinical depression.

2.2.7. Electroencephalogram (EEG)

EEG was recorded in a laboratory where is designed to minimize noise and artifact from the outside. Participants sat on a comfortable chair during EEG assessment. EEG was measured using a 19-channel full-cap with 19 electrodes placed in accordance with the International 10/20 system and a reference electrode was attached to both ear lobes. The data were recorded at a sampling rate of 256 Hz with Discovery 20 (Brain Master Technology Inc.). EEG data were filtered with a 4th-order bandpass Butterworth filter in the band 0-60 Hz, and a notch filter of 60 Hz to prevent intermixing of the artifact due to the power supply.

To minimize the artifact, participants were requested to store electronic products such as cell phones and accessories outside the laboratory. Participants were instructed to take a comfortable position to relax. In addition, the explanation about procedure and safety on the experiment along with instruction of minimizing muscle and eye movements that may affect EEG measurement was given. EEG was measured four times in each 2-minute of eye-open (EO) and eye-closed (EC) condition. The order combination of EO and EC was determined Download English Version:

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