# Brain response to sleep-related attentional bias after cognitivebehavioral therapy in individuals with insomnia symptoms

## Xiao Nie<sup>1</sup>, Xi-Jian Dai<sup>2</sup>

<sup>1</sup>Department of Radiology, Central Hospital of Yiyang, Yiyang 413000, China; <sup>2</sup>Department of Medical Imaging, Jinling Hospital, Medical School of Nanjing University, Nanjing 210002, China

*Correspondence to:* Xi-Jian Dai. Department of Medical Imaging, Jinling Hospital, Medical School of Nanjing University, 305# Eastern Zhongshan Rd, Nanjing 210002, China. Email: daixjdoctor@126.com.

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Almost half of adult population was reported to have subjective experience of insomnia symptom, making it one of the most common sleep disorders (1). The most widely accepted model of the psychophysiological insomnia is hyperarousal theory, which states difficulties in initiating and/or maintaining sleep due to global increases in cortical and physiological arousal across the sleep-wake cycle (2,3).

Psychophysiological insomnia, considered to be a learned insomnia, caused by a condition process, whereby hyperarousal and sleep-related condition are paired. Poor sleep in individuals with insomnia symptoms increases sleep-related anxiety with heightened vigilance to sleeprelated stimuli, which further exacerbates hyperarousal and in turn affects sleep. Recently more and more neurobiological researches have revealed the existence of sleep-related attentional bias, which was defined as the tendency to selectively attend to sleep-related information in comparison to neutral information, and has been suggested to be an important factor for the maintenance in individuals with insomnia symptoms (4-8).

Functional magnetic resonance imaging (fMRI), one of the hot research areas in neuroimaging field, is suitable for the mechanism exploration for central nervous system due to its abilities in detecting the spontaneous neuronal brain activity (9), which may help us to elucidate the mechanisms underlying sleep related attentional bias by investigating the brain activation in response to sleep-related and neutral pictures or words. Baglioni *et al.* observed increased amygdala activity in response to insomnia-related pictures in insomnia patients (10). Spiegelhalder *et al.* didn't find any threat- or craving-related brain reactivity in response to sleep-related words in patients with chronic insomnia compared with good sleepers (11). However, these studies are too few and diverse in tasks to draw a definitive conclusion.

Cognitive behavior therapy (CBT) is a structured, didactic and goal-oriented form of therapy (12). The CBT is a safe and effective treatment approach, and has been gradually accepted for clinical first-line treatment for a large proportion of individuals with chronic insomnia symptoms with longer time effect than hypnotic medications (13,14). Furthermore, the CBT was also used to manage various psychiatric disorders, such as mild to moderate depression and other disorders, such as anxiety, obsessive compulsive disorder, and panic disorder (15-17). Individuals with insomnia symptoms are expected not to have difficulties in initiating and/or maintaining sleep, and are expected not to overreact to sleep-related stimuli as before, due to the positive clinical effect of the CBT. Previous study found that the prefrontal lobe was hypo-activated during a verbal fluency task and was recovered after the CBT (18). The brain region of the visual area and the amygdala showed an increased functional connectivity before the CBT, whereas the functional connectivity between the two areas was decreased after the CBT (19). These findings suggest that the individuals with chronic insomnia symptoms have an overreaction to visual stimuli before the CBT while it was recovered after the CBT. However, there is a lack of

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longitudinal study to explore the brain responses to sleeprelated stimuli before and after the CBT for individuals with chronic insomnia symptoms.

Recently, Kim et al. using a longitudinal data aimed to explore the changes in brain activities in response to visual sleep-related stimuli and neutral stimuli in 14 drug-free psychophysiological insomnia before and after the CBT for insomnia (CBT-I) (20). In their study, psychophysiological insomnia showed higher brain responses to sleeprelated stimuli in several brain areas before the CBT, including the prefrontal lobe, precentral gyrus, fusiform gyrus, and posterior cingulate cortices, whereas these increased responses in brain areas were reduced after the CBT. Additionally, the increased brain response in the precentral gyrus was associated with longer wake time after sleep onset, and the clinical improvements after the CBT were correlated with decreased brain responses in the insula, precentral cortex and paracentral cortex in response to sleep-related stimuli. The observed results suggest that the CBT may decrease the hyper-responses of psychophysiological insomnia by normalizing the exaggerated brain activation, and provide evidence of the existence of therapeutic effect of the CBT on improvements for the hyper-responses to sleep-related stimuli in psychophysiological insomnia. These findings could significantly advance our understanding of the psychological mechanisms underlying sleep-related attentional bias in psychophysiological insomnia.

Some factors are worthy of notice concern for these studies. First, to state whether these changes of the brain response to sleep-related stimuli before and after the CBT were caused only by the CBT itself, we should introduce a new control group with sham treatment to exclude the effects similar to placebo due to the sensitive brain response on blood oxygen level dependent signal. Second, larger sample sizes allow us to draw a definitive and credible conclusion more easily. Future studies with larger sample sizes are appreciated. Third, as mentioned in Kim et al.'s study, only a small number of samples used a new version of the sleep-related stimuli which is different with the version for most of the subjects, because there were no previous sleep-related pictures other than one emotional insomniarelated picture set. Whether the two versions of sleeprelated pictures have a potential effect on the final results is unclear. Fourth, it's better to present the visual sleeprelated stimuli with black background in a dark bedroom to simulate real-life situation. Finally, we would better use some objective clinical measurements to evaluate the

changes of sleep and behavior before and after the CBT.

In conclusion, the present study by Kim *et al.* provide an innovative method to investigate the sleep-related attentional bias behavior by exploring brain response to the sleep-related stimuli in psychophysiological insomnia, and whether the CBT has the abilities to extinctive the sleeprelated attentional bias behavior and further improve their sleep efficiency. This study may extend our understanding of the comprehensive neurobiological mechanisms of psychophysiological insomnia and forward us to draw a possible theory that the CBT may play its therapeutic effect by reducing brain hyper-responses to sleep-related attentional bias behavior.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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