

Brain response to sleep-related attentional bias in patients with chronic insomnia

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Comment on: Spiegelhalder K, Baglioni C, Regen W, *et al.* Brain Reactivity and Selective Attention to Sleep-Related Words in Patients With Chronic Insomnia. *Behav Sleep Med* 2016;1-15.

Submitted Mar 20, 2017. Accepted for publication Apr 20, 2017.

doi: 10.21037/jtd.2017.05.23

View this article at: <http://dx.doi.org/10.21037/jtd.2017.05.23>

Patients with chronic insomnia, prevalent in 10–15% of the adult population, who underwent the subjective experience of chronically disturbed sleep, sleep loss, non-refreshing sleep, and heightened arousal in bed with impaired quality of life, showed a decreased ability to disengage from external information processing at sleep on-set (1-3). They frequently experience intrusive thoughts, described as worrisome and negatively toned, and paid too much attention to sleep-related information. Sleep-related attentional bias is defined as the tendency to selectively attend to sleep-related information in comparison to neutral information (4). Sleep-related attentional bias has been suggested to represent an important factor for the inability to maintain sleep or fall asleep in patients with chronic insomnia (4,5). Recently, more and more researchers paid their attention to the neuroimaging studies of sleep-related attentional bias. However, what drives the sleep-related attentional bias is still unclear.

On one hand, patients with chronic insomnia strongly crave to get good sleep quality. They always demonstrated signs of craving in response to sleep-related stimuli (4), perhaps in the similar manner one might toward substances following a period of substance deprivation for individuals with substance dependence. On the other hand, patients with chronic insomnia always showed signs of threat and/or anxiety in response to sleep-related cues because of the long-term poor sleep quality. Previous meta-analytical data demonstrated that the craving hypothesis is associated with amygdala and insula (6), and the threat hypothesis is associated with ventral striatum and posterior cingulate

cortex (PCC) (7). Recently Huang found decreased functional connectivity between the amygdala and the insula, striatum and thalamus in patients with primary insomnia compared with good sleepers using resting-state functional connectivity analysis (8). Our previous neuroimaging studies also found that insufficient sleep resulted in abnormal regional brain activity in the threat-related brain areas and craving-related brain areas (9-14). These findings may be regarded as supporting both the craving hypothesis and threat hypothesis of sleep-related attentional bias in patients with chronic insomnia. Therefore, we hypothesize that the sleep-related attentional bias is associated with both threat hypothesis and craving hypothesis, and the two hypotheses represent positive and negative sleep-related attentional bias respectively. However, whether in response to sleep-related cues represent a craving hypothesis or threat hypothesis, or both hypotheses in patients with chronic insomnia, is still unknown. Thus, it will have important clinical value to find a biological indicator for early diagnosis by explore its imaging characterization and find the target brain areas or network indicator.

Previous research has validated a set of sleep-related and neutral pictures or words can be used to study the sleep-related attentional bias in patients with chronic insomnia (15). Recently, Spiegelhalder *et al.* (16) utilized functional magnetic resonance imaging to investigate brain reactivity to sleep-related and neutral words in 20 patients with primary insomnia and 35 good sleepers, so as to explore whether craving hypothesis or threat hypothesis drives the sleep-related attentional bias. However, they found,

contrary to the hypotheses, patients with chronic insomnia did not differ from good sleeper controls in terms of threat- or craving-related brain reactivity to sleep-related words. It's the first study investigating sleep-related attentional bias in insomnia with neuroimaging techniques, although no definite conclusions can be drawn, it provided a new perspective for us to explore the sleep-related attentional bias in insomnia.

Furthermore, some factors are worthy of notice, which may be the important cause of no significant differences in the brain reactivity in response to the sleep-related stimuli. First, as mentioned in this study, future studies may use pictorial stimuli for investigating sleep-related information processing in insomnia. Undoubtedly, the author gave us a sage advice. In brief, whether the sleep-related word showed a weaker effect than sleep-related pictorial stimuli is still unknown, thus, using pictorial stimuli is worth having a try. Second, the group of the insomnia sample was mild insomnia (mean insomnia severity index score of 14.7 ± 3.9 ; mean Pittsburgh Sleep Quality Index score of 10.4 ± 3.2), which may not display significant symptom of sleep-related attentional bias such as craving and threat. However, whether other types of insomnia will show significant differences in the brain reactivity in response to the sleep-related stimuli is unknown. Therefore, larger sample sizes and moderate to severe types of insomnia patients may give us a more comprehensive understanding about the brain reactivity in response to the sleep-related stimuli. Third, only nine patients have never used sleep medication before, and the other insomnia patients have taken sleep medication prior or during this study, which may disturb the results. Fourth, in the insomnia sample, two patients suffered from sleep-onset insomnia, six from sleep-maintenance insomnia, one from nonrestorative sleep, and 11 from mixed insomnia. However, whether the complex sample type have an effect on brain activity in response to sleep-related information is still unclear, which needs to be explored in the future. Fifth, only ten sleep-related words were used in the block design. Alternatively, complete random design will be more suitable for these studies. Furthermore, using more than 20 sleep-related words may be more convictive.

In conclusion, although there are no significant differences in the brain reactivity in response to the sleep-related information, the study by Spiegelhalter *et al.* provided an innovative and feasible method to investigate the sleep-related attentional bias with a new perspective. The attentional bias to sleep-related stimuli may be a core feature of chronic insomnia, worthy of exploring in the

future with more factors taken into account.

Acknowledgements

Funding: This study was supported by the Jiangxi Provincial Department of Science and Technology Support Program (grant No: 20141BBG70026).

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Dai XJ. Brain response to sleep-related attentional bias in patients with chronic insomnia. *J Thorac Dis* 2017;9(6):1466-1468. doi: 10.21037/jtd.2017.05.23