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PERSPECTIVE

Is Insomnia a Brain Disorder Arising From Aberrant Brain Structure, Brain Function, or Both?

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Insomnia is a common, distressing, and clinically important symptom. Insomnia disorder (ID) is the most common sleep disorder in the general population. The diagnostic criteria for ID are difficulty falling and/or maintaining sleep, or early morning awakening at least three times per week over at least 3 months, not attributable to sleep-disrupting external conditions accompanied by subjective daytime impairment, including fatigue, mood disturbance, poor concentration, or memory impairment. ID is diagnosed based on subjective symptoms. The pathogenesis of ID is thought to be associated with psychological, behavioral, and physiological factors. Although the underlying neurobiological pathophysiology of insomnia is poorly understood, a neurobiological model of insomnia including affect and arousal as key elements has been proposed (the hyperarousal theory) [1]. The hyperarousal theory posits that insomnia results from the dysregulation of arousal networks, including in the hypothalamus, brain stem, and cortical areas. Numerous physiological studies on insomnia support the hyperarousal model. Patients with insomnia have significantly higher heart rates during sleep and wake states than those in control groups [2]. Moreover, a cortical arousal study indicated that beta electroencephalogram frequencies increase during non-rapid eye movement sleep in patients with insomnia [3].

Recent neuroimaging studies have attempted to reveal the neurobiological basis of ID. A positron emission tomography study demonstrated altered brain metabolism in patients with insomnia [4]. Brain structure studies have reported that cortical and subcortical brain structures play key roles in the pathophysiology of ID, including volume changes in the frontal cortex and hippocampus [5]. Moreover, previous functional magnetic resonance imaging (fMRI) research has demonstrated that disruptions in the functional connectome of the brain may be related to insomnia [5]. Insomnia patients exhibit changes in functional connectivity during specific tasks [5]. In addition, Baglioni et al. [6] reported that patients with ID present with heightened activity in the amygdala in response to insomnia-related pictures. In a previous study, regional brain activity in response to sleep-related sounds was reduced in insomnia patients after cognitive behavioral therapy for insomnia (CBT-I) [7]. Furthermore, brain activity in response to sleep-related pictures was significantly higher in the bilateral precentral, left prefrontal, left fusiform, and bilateral posterior cingulate cortices in the insomnia group, and decreased after CBT-I [8]. Resting-state fMRI studies suggest that the default mode network (DMN), salience network (SN), and limbic circuit, which includes key nodes from both the SN and DMN, are neural systems of particular interest in patients with ID [5]. Increased DMN connectivity in patients with insomnia seems to be associated with subjective sleep disturbances, dysfunctional coping with hyperarousal, maladaptive emotion regulation (particularly rumination), and enhanced (negative) memory retrieval [9]. Increased SN connectivity in patients with insomnia may be associated with heightened sensitivity to negative internal and external stimuli, impaired integration of emotional and physiological states, and poor coordination of neural resources. Although the role of the limbic circuit as a mediator between DMN and SN is not fully understood, primary limbic structures are assumed to be key to the impaired interplay between the networks.

However, most previous studies had relatively small samples and used a single-center design, which limits the generalizability of the results. The ENIGMA-Sleep Working Group performed a large-scale collaborative study investigating the effect of insomnia on different brain regions; differences between subjects with and without insomnia were analyzed [10]. Moreover, machine

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learning methods have been successfully applied for fMRI-based prediction of differential brain activity patterns in patients with insomnia [5].

According to the above results, ID can be a brain disorder caused by changes in the structure and function of the brain. Therefore, advancements in brain imaging studies are needed to identify the more specific neural correlates of ID, to identify a candidate of target region for new therapeutic techniques such as neuromodulation. Because CBT-I or medication is not proven to treat all insomnia patients successfully. Moreover, insomnia is particularly closely related to conditioning mechanisms; thus, task-based research is needed to explore the underlying mechanism. Research exploiting the task-based metaverse may provide more insight into the brain mechanisms of insomnia, which could in turn improve treatments.

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Conflicts of Interest

The author has no potential conflicts of interest to disclose.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

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