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EDITORIAL

Detecting activities of multiple neurotrophins to see the complex effect of acute sleep deprivation on mood and behavior in humans

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Sleep is necessary for humans and animals to keep optimal functions of the brain and body, to adapt themselves efficiently to the environment, and to achieve maximal survival. Experiments in animals have shown that complete sleep deprivation for prolonged periods results in death. Sleep deprivation and sleep restriction in humans under pathological or experimental conditions are associated with impairment of brain functions over performance, vigilance, attention, and concentration, as well as a variety of physical adverse effects including metabolic and cardiovascular problems or mortality [1]. Impaired brain and cognitive functions in humans after sleep deprivation have been estimated to be a consequence of neural dysfunction or cell loss due to the activation of the stress-related cascades including corticosterone [2].

Sleep deprivation makes another unique reaction in humans. When acute sleep deprivation is applied to patients with major depression, it shows rapid antidepressant effects, consisting of an improvement of depressive mood and an amelioration of some physical symptoms [3]. The rapid antidepressant effects of acute sleep deprivation in depressed patients have been well described in clinical literature. However, the mechanism underlying therapeutic sleep deprivation has yet to be elucidated. Some researchers postulate that an upregulation of hippocampal neurogenesis similar to acutely sleep-deprived animals provides a possible explanation for the therapeutic effect, likewise decreased hippocampal volume in depressive patients recovers after antidepressant therapy [4].

Among the messengers possibly involved in neurogenesis, a group of specific proteins called neurotrophins have expected to play crucial roles in the central nervous system. Brain-derived neurotrophic factor (BDNF), a member of the neurotrophin family, is located in the brain and increases its expression associated with neuronal maintenance, plasticity, and neurogenesis [5]. Some researchers assume that BDNF may be differentially involved in neurogenesis and stress caused by sleep deprivation, because its expression in the brain is increased after acute sleep deprivation in animals in contrast with chronic one. Therapeutic sleep deprivation was reported to improve depressive symptoms and increase serum BDNF levels in patients with major depression [3]. In a study, acute sleep deprivation in animal models of depression had behavioral antidepressant-like effects, which were associated with increased BDNF levels and hippocampal neurogenesis [6]. Such bi-directional responses to acute or chronic sleep deprivation have not been clearly described in non-depressive healthy subjects.

In the current issue of Sleep and Biological Rhythms, Dr. Yasemin and the coauthors published an article on the effects of acute sleep deprivation on neurotrophines, in which seventeen healthy young adults underwent 36 h total sleep deprivation [7]. They found that serum levels of three neurotrophins including glial cell line-derived neurotrophic factor (GDNF), brain-derived neurotrophic factor (BDNF), and vascular endothelial growth factor (VEGF) were increased after acute sleep deprivation, together with changes of subjective status indicating acute effects of sleep disruption and its related stress.

There were several methodological limitations in this article with respect to the sample size, observation period of neurotrophines after sleep deprivation, and confirmation of behaviors during sleep deprivation. However, the current report still seemed to propose several potential clues for the future studies aiming to understand the mechanisms of antidepressant sleep deprivation therapy. First, it confirmed an increase of serum BDNF and GDNF after acute sleep deprivation in healthy subjects as observed in depressive patients, which in turn contrasted with its decrease after chronic sleep deprivation. Second, the elevation of GDNF after acute sleep deprivation suggests that a link between sleep deprivation

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and the dopaminergic system might be common in healthy and depressive subjects. Third, the increase of VEGF in the study indicates that interaction or combined action of different neurotrophines may be helpful to understand the complex mechanism underlying antidepressant effects.

Declarations

Conflict of interest The author has consulted for Idorsia Pharmaceuticals Japan, Kao Corporation, Taisho Pharmaceutical and Takeda Pharmaceutical.

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