Researchers identify molecular mechanism that regulates wakefulness, sleep

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Researchers at Boston University School of Medicine (BUSM) have, for the first time, identified an intracellular signaling enzyme that regulates the wake-sleep cycle, which could help lead to the development of more effective sleep aid medications. Subimal Datta, PhD, director and principle investigator at the Laboratory of Sleep and Cognitive Neuroscience at BUSM, led the study, which points to a specific enzyme inside neurons in the brain that trigger an important shift in consciousness from sleep to wakefulness and wakefulness to sleep.

The results will be published in the Nov. 23 issue of the Journal of Neuroscience.

According to the National Institute of Neurological Disorders and Stroke, at least 40 million Americans suffer from chronic sleep deprivation each year from disorders such as sleep apnea and insomnia.

"Sleep, one of the most mysterious regular shifts in consciousness, is regulated by a delicate balance between biological processes, the environment and behavior, but the mechanisms involved in the regulation are not well understood," said Datta, who also is a professor of psychiatry and neurology at BUSM. "The ultimate goal of my research is to deepen the understanding of how sleep is regulated at the cellular level , which could lead to finding the causes and cures for a variety of sleep disorders."

There are two main stages of sleep – REM (rapid eye movement) and

non-REM – and both are necessary in order to maintain health and wellbeing. Dreaming generally happens during REM sleep, when the brain is in an active state and the muscles of the body are paralyzed. During non-REM sleep, studies have shown that the body repairs tissue, regenerates cells and improves the function of the body's immune system.

Previous research has shown that pedunculopontine tegmentum (PPT) nuclei in the brain play a key role in the regulation of REM sleep and wakefulness. Datta and his colleagues identified that an enzyme, calcium/calmodulin kinase (CaMKII), plays a crucial role in the intracellular pathway for sleep regulation and is necessary for the promotion of wakefulness and suppression of sleep. During the study when the activation of the CaMKII enzyme was blocked using an inhibitor named KN-93, natural REM and non-REM sleep occurred, whereas when the enzyme was activated, wakefulness occurred. Additionally, very minimal doses of therapeutic agents were required to activate or block the system.

According to Datta, this finding opens up the possibility for a new generation of target-specific drugs that could be effective at lower doses. "Current treatments for sleep disorders do not achieve the ideal behavioral outcome, and are usually accompanied by many undesirable side effects," Datta explained. "A more specific, fine-tuned approach to treating these disorders by promoting alertness and treating insomnia would greatly benefit the public health of our country."

Provided by Boston University Medical Center