Study elucidates mechanisms of longer and deeper sleep after an all-nighter

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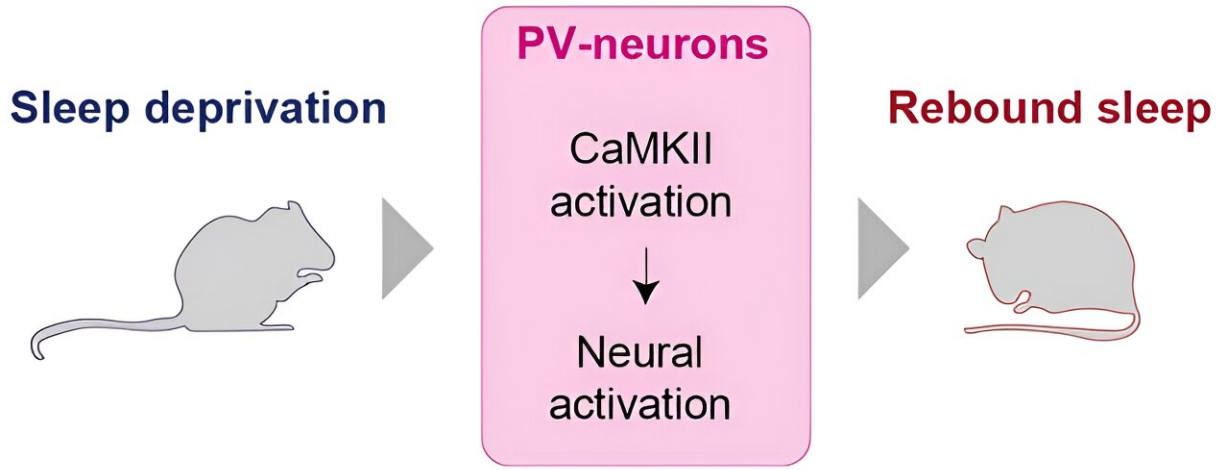

The model of sleep homeostasis regulation proposed in this study. Prolonged wakefulness activates CaMKII in PV-expressing neurons. The activated CaMKII then activates PV-expressing neurons, leading to rebound sleep. Credit: Department of Systems Pharmacology, Graduate School of Medicine, UTokyo

Professor Hiroki R. Ueda , Dr. Kazuhiro Kon and their colleagues at Graduate School of Medicine, The University of Tokyo, have published a study in *Nature Communications* on the importance of proper regulation of the activity of parvalbumin (PV)-expressing neurons, the major inhibitory neurons in the cerebral cortex, in the long, deep sleep (rebound sleep) that occurs after prolonged wakefulness.

We have all experienced at one time or another that when we are sleep deprived, such as when we pull an all-nighter, we feel a strong sense of sleepiness, and our subsequent sleep is longer and deeper than usual.

This indicates that the brain has a mechanism (sleep homeostasis) that records the history of wakefulness and compensates for the sleep needed based on that history. However, the mechanism of sleep homeostasis in the brain is not well understood.

By experimentally depriving mice of sleep, this research group showed that PV-expressing neurons in the cerebral cortex are activated when sleepiness increases and rebound sleep occurs. Furthermore, they elucidated that the activation of calcium/calmodulin-dependent kinase II (CaMKII), a protein phosphorylation enzyme, causes rebound sleep by activating PV-expressing neurons in response to sleepiness.

This study reveals a part of the molecular and neural mechanisms of sleep homeostasis, one of the major mysteries of sleep science. These results are expected to lead to the development of methods to appropriately control sleepiness while quantitatively monitoring it.

This result was obtained from JST Strategic Basic Research Programs ERATO: Research Project "UEDA Biological Timing." The project aims to elucidate the biological timing mechanisms underlying sleep-wake cycles by applying state-of-the-art technology in mouse genetics and human sleep measurement techniques.

More information: Kazuhiro Kon et al, Cortical parvalbumin neurons are responsible for homeostatic sleep rebound through CaMKII activation, *Nature Communications* (2024). DOI: 10.1038/s41467-024-50168-5

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