Researchers discover new way to improve internal clock function

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Overnight flights across the Atlantic, graveyard shifts, stress-induced insomnia are all prime culprits in keeping us from getting a good night's sleep. Thanks to new research from McGill University and Concordia University, however, these common sleep disturbances may one day be put to bed.

The rotation of the earth generates day and night. It also confers daily rhythms to all living beings. In mammals, something known as a

"circadian clock" in the brain drives daily rhythms in sleep and wakefulness, feeding and metabolism, and many other essential processes. But the inner workings of this brain clock are complex, and the molecular processes behind it have eluded scientists—until now.

In a new study published in *Neuron*, researchers have identified how a fundamental biological process called protein synthesis is controlled within the body's circadian clock—the internal mechanism that controls one's daily rhythms. Their findings may help shed light on future treatments for disorders triggered by circadian clock dysfunction, including jet lag, shift work disorders, and chronic conditions like depression and Parkinson's disease.

"To understand and treat the causes and symptoms of circadian abnormalities, we have to take a closer look at the fundamental biological mechanisms that control our internal clocks," says study co-author Dr. Shimon Amir, professor in Concordia University's Department of Psychology.

To do so, Amir and co-author Dr. Nahum Sonenberg, a James McGill professor in the Dept. of Biochemistry, Faculty of Medicine, at the Goodman Cancer Research Centre at McGill University, studied how protein synthesis is controlled in the brain clock. "We identified a repressor protein in the clock and found that by removing this protein, the brain clock function was surprisingly improved," explains Dr. Sonenberg.

Because all mammals have similar circadian clocks, the team used mice to conduct their experiments. They studied mice that lacked this specific protein, known as 4E-BP1, which blocks the important function of protein synthesis. They found that the mice that lacked this protein overcame disruptions to their circadian clocks more quickly.

"In modern society, with the frequency of trans-time zone travel, we often deal with annoying jet lag problems, which usually require a couple of weeks of transition," says Dr.Ruifeng Cao, a postdoctoral fellow who works with Drs. Sonenberg and Amir, "However, by inducing a state like jet lag in the mice lacking that protein, we found they were able to adapt to time zones changes in about half of the time required by regular mice."

Furthermore, the researchers found that a small protein that is critical for brain clock function, vasoactive intestinal peptide or VIP, was increased in the mice lacking the protein 4E-BP1. The results indicate that the functioning of the circadian clock could be improved by genetic manipulations, opening doors on new ways to treat circadian clock-related disorders.

"A stronger clock function may help improve many physiological processes, such as aging," says Cao. "In addition, understanding the molecular mechanisms of biological clocks may contribute to the development of time-managing drugs," Amir concurs, noting that "the more we know about these mechanisms, the better able we will be to solve problems associated with disruptions to our bodies' internal clocks".

Provided by McGill University

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