Pituitary vasopressin signaling realigns biological clock for jet lag recovery: Study

November 27 2023

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Jet lag is all in the mind. What exactly lags has more to do with the hypothalamus than the jet.

A misalignment of the body's internal clock following jet travel across multiple time zones causes sleep deprivation and physical discomfort. The master clock in the tiny suprachiasmatic nucleus—or SCN in the anterior part of the hypothalamus—keeps the departure time and requires several days to adjust to the destination time.

While the exact cause of jet lag remains a mystery, a team of researchers from Kyoto University and Kansai University has revealed the pivotal vasopressin signaling in neuroendocrine circuits of the hypothalamus and anterior pituitary may provide clues as to its role in the SCN's pacemaker. The work has been published in the *Proceedings of the National Academy of Sciences*.

"The role of rhythm generation by the extra-SCN neuroendocrine-anterior pituitary system might have gone unnoticed had it not been for the advent of intercontinental jet travel in the 50s, which caused an artificial and uniquely human experience," says Research Fellow Hitoshi Okamura of KyotoU's Graduate School of Medicine.

Subsequent studies revealed that SCN lesions abolished all circadian rhythms in the body, and that isolated SCNs can generate robust circadian rhythms. This discovery has led researchers to believe that only neuronal circuits of SCN clockwork can adjust jet lag to new light-dark cycles.

Previous research found that global inhibition of vasopressin receptors

V1a and V1b signaling eliminated jet lag. Okamura's team is now trying to identify the critical sites in those receptor systems. Thus far, the researchers have determined that vasopressin and its receptor V1b in the hypothalamic-anterior pituitary systems can help maintain the original time during jet lag.

To date, there are no effective medications for the syndrome, mainly because current drugs target only the SCN. The revelation that the hypothalamus-pituitary systems are orchestrating a synchronized response to the body's shaken circadian rhythm has inspired the development of more effective treatments.

"The development of vasopressin inhibitors on multiple targets—not only V1a in the SCN but also V1b in the pituitary—could significantly help mitigate jet lag," says Yoshiaki Yamaguchi of Kansai University's Faculty of Chemistry, Materials, and Bioengineering.

"Addressing the different parts of the neuroendocrine systems work collectively on the cellular clockwork in SCNs is an important step towards a deeper understanding of how our biological clocks maintain time even during rapid light fluctuations," says Okamura.

More information: Yoshiaki Yamaguchi et al, An intact pituitary vasopressin system is critical for building a robust circadian clock in the suprachiasmatic nucleus, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2308489120

Provided by Kyoto University