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Study of fruit fly 'brain in a jar' reveals mechanics of jet lag

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Drosophila sp fly. Credit: Muhammad Mahdi Karim / Wikipedia. GNU Free Documentation License, Version 1.2

Long the stuff of science fiction, the disembodied "brain in a jar" is providing science fact for UC Irvine researchers, who by studying the whole brains of fruit flies are discovering the inner mechanisms of jet lag.

To do this, Todd C. Holmes, professor of physiology & biophysics in the UCI School of Medicine, and colleagues used imaging technology to make movies of fruit fly brains kept alive for six days in a petri dish. The scientists captured the activity of individual circadian clocks at single-cell resolution with an extremely sensitive low-light camera in order to determine how the circadian clock circuit is "reset" by light.

The study marks the first time researchers have seen in real time how specific neurons in intact circadian neural networks react to light cues that are comparable to rapid travel across time zones, such as flying from Los Angeles to Chicago. Study results appear online in *Current Biology*.

Most organisms make daily adjustments to their activity and metabolism to synchronize with environmental signals - daylight being the most powerful circadian cue. The scientists found that desynchronization of circadian neurons is a key feature of light-induced jet lag and suggest that treatments accelerating this desynchronization before travel may speed recovery afterward.

"Remarkably, our work indicates that the way you feel while jet-lagged exactly reflects what your nervous system is experiencing: a profound loss of synchrony," Holmes said.

He explained that a single light pulse cues the biological clock of the fruit fly brain to shift two hours ahead of its original schedule through a process the researchers call "phase retuning." This is characterized by a circadian circuit-wide pattern of brief desynchrony followed by the gradual emergence of a new state of network synchrony.

The scientists propose that temporarily weakening synchronization among neurons governed by circadian patterns allows for more rapid adaptation (an estimated two days) by enabling phase retuning to a new time zone's cues. Normally, Holmes said, circadian circuit light response

- i.e., jet lag recovery - takes place over four days for the time shift tested. A larger time shift, such as the one experienced in flying from Los Angeles to London, would likely require a longer time for recovery.

"That two-day difference is quite a bit if it means you feel great from the beginning of your arrival, say, in Italy," Holmes noted. "You're going to feel bad on the plane in any event, so it's best to get the adjustment over with so you can enjoy your destination. I'm certain this will lead to treatments that'll have a big impact on our travel practices."

"These results literally and figuratively bring the inner workings of biological clocks 'into the light,'" said Logan Roberts, a graduate student researcher in Holmes' lab and the study's first author.

"This work illustrates in realtime how the network of daily clocks in the brain adjusts to synchronize with the local light cycle," added Erik Herzog, a circadian biology expert at Washington University in St. Louis who was not involved in the study. "With extraordinary cellular resolution, the researchers show that some cells shift faster than others following a pulse of light. This might become a useful therapy in treating jet lag or the growing problem of 'social jet lag,' where people keep different schedules during the week than on the weekends."

Provided by University of California, Irvine

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