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Model of Internal Clocks Reveals How Jet Lag Disrupts the System

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Contact Information

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Description

Symptoms of extreme jet lag may result from the body overshooting as it tries to adjust to particularly large leaps forward in time, suggests new research that models circadian rhythms in rats. For a smooth transition to a new time zone, advancing in chunks of four hours or fewer is recommended. Implications for rotational shift workers, such as nurses are discussed.

Newswise — Symptoms of extreme jet lag may result from the body overshooting as it tries to adjust to particularly large leaps forward in time, suggests new research from the University of Massachusetts Amherst that models circadian rhythms in rats. To transition smoothly to a different time zone, the researchers recommend advancing in chunks of not more than four hours, thus allowing the body's clocks to remain coordinated. The work also has implications for rotational shift workers, such as nurses and airline attendants, as some shifts will be much harder for the body to adjust to than others.

The analytical model, by UMass Amherst's Hava Siegelmann, appears in the current issue of the *Journal of Biological Rhythms*. Tanya Leise of Amherst College co-authored the work.

The body's sleep and wakefulness patterns are just two of the physiological processes that run on a roughly 24-hour-cycle, or circadian clock, explains Siegelmann. These and other processes are coordinated by the master pacemaker, or clock, an area of the brain with a natural cycle that is approximately 24 hours long. In mammals, the master clock is a group of cells called the suprachiasmatic nucleus (SCN), which lies at the base of the hypothalamus. The SCN receives information on daylight sent from the eyes' optic nerve and can be reset by environmental cues such as light.

Recent research suggests that every cell in the body actually has its own clock—liver cells prepare for digestion at particular times of day; patterns of hormone production and brain activity exhibit cyclic peaks and valleys, says Siegelmann.

"The circadian system is really fundamental, it affects our behavior, our physiology and emotions," she says. "The clock organizes the whole body into a very nice dance, and it organizes people together into a larger social orchestra."

The so-called “local clocks” have natural circadian cycles that range from 21 to 26 hours, says Siegelmann. They are synchronized by the SCN, but the pathways and mechanisms by which this coordination happens aren’t fully understood. Evidence has recently emerged that the SCN itself is compartmentalized. One clump of cells responds to and processes information about light, they then alert an intermediate group of cells that transmit the information to more peripheral components.

This hierarchy within the circadian system introduces a time-delay in getting the entire body adjusted to a new environment, suggests Siegelmann. The delay is based, in part, on the strength of the connections between the different parts of the SCN, between the SCN and the peripheral clocks, and on the differing rhythms of the local clocks, she says.

To explore the dynamics of the system and how it responds to disruption Siegelmann and Leise designed a model with parameters reflecting this hierarchical nature. The model accounts for the SCN’s light-responsive component, its intermediate component, and the various peripheral components. It incorporates behavioral data, physiological data and what’s known about differences in natural circadian rhythms in the peripheral tissues. In rats, for example, internal organs such as the liver and lungs take a relatively long time to become synchronized with the SCN.

Simulations of the model revealed certain properties about both the stability and adaptability of the system, Siegelmann says. The light sensitive compartment of the master clock responds quickly, providing flexibility, whereas the intermediate compartment of the SCN seems to act as a buffer against small perturbations in the cycle.

The simulations suggest that the system gets most out of whack when the master clock is shifted forward between five and eight hours. After such a large leap, it appears that the master clock actually overshoots the desired time. Then, following a slight delay, the intermediate component and some of the peripheral components overshoot as well, depending on their inherent circadian time and their connectivity with the master clock. For example, the peripheral components that already tend to lag actually try to catch up by backtracking, achieving a leap forward of six hours by delaying themselves 18 hours.

So what is the best strategy for reducing jet lag? Consider the system dynamics, says Siegelmann, and aim for the largest shift of the master clock that still leads to coordinated shifting. Their analysis suggests that a four–hour advance pushes the entire system in the right direction, causing all components to advance smoothly and quickly. And while their model addressed the system in on rats, a nocturnal animal, the researchers note the general principle is likely to be widely applicable.

“Jet lag isn’t a horrible thing that we have to conquer—and our clock is a very important regulator at a basic level— medications to target the clock may be counter-productive if they affect future oscillatory behavior,” she says. “Instead, take a stopover if you are traveling for more than 6 hours—relax for a day and then continue. Understand and go with your body’s natural oscillations.”

The work also has implications for rotational shift workers, such as nurses and airline attendants, says Siegelmann. There are shifts that are much harder for the body than others, and if employers are expected be alert and functional, a 9 p.m. to 3 a.m. shift might bode better than a midnight to 6 a.m. shift.

“I think people will pay more attention to this as we learn more,” she says. “If you are flying to a meeting where you need to be alert and able to concentrate, you can prepare your body for those particular goals by making the shift gradually.”