Study identifies food-related clock in the brain

May 22 2008

In investigating the intricacies of the body's biological rhythms, scientists at Beth Israel Deaconess Medical Center (BIDMC) have discovered the existence of a "food-related clock" which can supersede the "light-based" master clock that serves as the body's primary timekeeper.

The findings, which appear in the May 23 issue of the journal *Science*, help explain how animals adapt their circadian rhythms in order to avoid starvation, and suggest that by adjusting eating schedules, humans too can better cope with changes in time zones and nighttime schedules that leave them feeling groggy and jet-lagged.

"For a small mammal, finding food on a daily basis is a critical mission," explains the study's senior author Clifford Saper, MD, PhD, Chairman of the Department of Neurology at BIDMC and James Jackson Putnam Professor of Neurology at Harvard Medical School. "Even a few days of starvation is a common threat in natural environments and may result in the animal's death."

The suprachiasmatic nucleus (SCN), a group of cells in the brain's hypothalamus, serves as the body's primary biological clock. The SCN receives signals about the light-dark cycle through the visual system, and passes that information along to another cell group in the hypothalamus known as the dorsomedial nucleus (DMH). The DMH then organizes sleep-wake cycles, as well as cycles of activity, feeding and hormones.

"When food is readily available," explains Saper, "this system works

extremely well. Light signals from the retina help establish the animals' circadian rhythms to the standard day-night cycle." But, if food is not available during the normal wake period, animals need to be able to adapt to food that is available when they are ordinarily asleep.

In order to survive, animals appear to have developed a secondary "food-related" master clock. "This new timepiece enables animals to switch their sleep and wake schedules in order to maximize their opportunity of finding food," notes Saper, who together with lead author Patrick Fuller, PhD, HMS Instructor in Neurology and coauthor Jun Lu, MD, PhD, HMS Assistant Professor of Neurology, set out to determine exactly where this clock was located.

"In addition to the oscillator cells in the SCN, there are other oscillator cells in the brain as well as in peripheral tissues like the stomach and liver that contribute to the development of animals' food-based circadian rhythms," says Saper. "Dissecting this large intertwined system posed a challenge."

To overcome this obstacle, the authors used a genetically arrhythmic mouse in which one of the key genes for the biological clock, BMAL1, was disabled. They next placed the gene for BMAL1 into a viral vector which enabled them to restore a functional biological clock to only one spot in the brain at a time. Through this step-by-step analysis, the authors uncovered the feeding entrained clock in the DMH.

"We discovered that a single cycle of starvation followed by refeeding turns on the clock, so that it effectively overrides the suprachiasmatic nucleus and hijacks all of the circadian rhythms onto a new time zone that corresponds with food availability," says Saper. And, he adds, the implications for travelers and shift workers are promising.

"Modern day humans may be able to use these findings in an adaptive

way. If, for example, you are traveling from the U.S. to Japan, you are forced to adjust to an 11-hour time difference," he notes. "Because the body's biological clock can only shift a small amount each day, it takes the average person about a week to adjust to the new time zone. And, by then, it's often time to turn around and come home."

But, he adds, by adapting eating schedules, a traveler might be able to engage his second "feeding" clock and adjust more quickly to the new time zone.

"A period of fasting with no food at all for about 16 hours is enough to engage this new clock," says Saper. "So, in this case, simply avoiding any food on the plane, and then eating as soon as you land, should help you to adjust – and avoid some of the uncomfortable feelings of jet lag."

Source: Beth Israel Deaconess Medical Center