Scientists unwind circadian clocks at cell level

Research proves that desynchronization of individual cellular clocks disrupts circadian rhythm - mechanism could be behind jet lag, shift-work fatigue

A team of Japanese scientists have shed light on the circadian rhythms, one of the least understood aspects of animal biology. Circadian rhythms are the 24-hour cycles in the physiological processes of most organisms, ranging from simple bacteria to plants and animals. These rhythms, the researchers found, originate in the cells themselves, and disrupting them can have serious physiological effects.

The scientists, including several from a research team led by Hiroki Ueda at the RIKEN Center for Developmental Biology in Kobe, were studying the dynamics of so-called "cellular clocks." In particular, they sought to understand a phenomenon known as singularity behavior, in which the cellular clock is disrupted by, for example, a pulse of bright light.

In order to study this, the scientists made normal mammal cells sensitive to light by introducing a substance known as melanopsin into the cells by using DNA transfer. Melanopsin, a photopigment discovered in 1998, is found in specialized photosensitive cells in the retina in mammals, including humans. These retinal cells are known to be involved in regulating circadian rhythms in mammals.

After making the normal cells responsive to light using melanopsin, the next challenge the scientists faced was how to monitor the cells' circadian rhythms. They did this by inserting a substance which made the cells bioluminesce, or glow in the dark, in response to cell activity. They then measured the amount of light the cells were producing, using a sensitive detector.

They found that if the cells were kept in the dark, a single pulse of bright light had the effect of disturbing the circadian rhythms of the cells over a period of one day. They found that light pulses affect both the timing of the cellular clock, and the level of cell activity.

This type of effect is sometimes experienced by shift workers, when changing from day to night shifts or vice versa. One example of a circadian cycle in humans is body temperature, which normally fluctuates in a predictable way over a 24-hour period. Shift workers, however, often experience difficulty sleeping when their body temperature
clock is telling them it is time to be awake. This phenomenon is called circadian desynchronization, and the scientists found that the cells’ internal clock was upset by light pulses and became out of phase from the normal 24-hour daily cycle. Following this, the scientists studied how circadian rhythms in rats were affected by photo-perturbation, or disruption by light pulses. The rats were kept in normal light-dark conditions for two weeks, followed by a day in the dark. They were then exposed to a series of light pulses, and then kept in constant darkness. The scientists measured how the rats' cellular clocks were affected, and found that they had become desynchronized from their normal circadian rhythm. They also measured the rats' level of physical movement, and found that it had changed following the light pulses. Using the results of these investigations, they were able to construct a mathematical model that helped them understand the effects of circadian desynchronization of many cells in a complex organism like a rat. This work represents a significant advance in understanding how cellular clocks operate.

Original work:

For more information, please contact:

RIKEN Public Relations Office
Email: koho@riken.jp