

The importance of circadian rhythms

Richard Béliveau

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The Nobel Prize for medicine and physiology in 2017 was awarded last Monday to three scientists who discovered the mechanisms controlling the biological clock. It is a richly deserved honor, because these circadian rhythms play a crucial role in the harmonious function of the human body.

Not only is the **sun** essential for life on Earth, but it also controls the rhythm with which that life flows. All living beings, whether they are bacteria, plants or animals, have evolved a way of coordinating their activity with the day-night cycle caused by the Earth's rotation. These "circadian rhythms" (from the Latin *circa* [around] and *diem* [day]) allow the synchronization of biological activities to precise moments of the day: the flowering of plants, the migrations of birds and butterflies, or even certain physiological activities such as the secretion of diverse hormones are all examples of phenomena which depend on appropriate circadian rhythms in each living species. This biological clock which exists inside each cell thus represents a fundamental mechanism of life on Earth, carefully conserved over billions of years of evolution.

In the more advanced animals such as humans, this biological clock is directed by a group of neurons located in the hypothalamus of the brain. These cells are particularly sensitive to the intensity of the light captured by the retina of the eye and are capable of integrating this information to control the sleep-wake cycle as well as several aspects of metabolism. This appears to be a phenomenon of very great importance because the majority of our genes exhibit fluctuations related to the time of day, which establishes the circadian rhythms as one of the most important mechanisms controlling activities within the human body.

BROKEN RHYTHMS

The importance of this biological clock is vividly illustrated by the discomfort which arises when it is perturbed, such as following travel by air across several time zones. The sudden change in luminosity which results means that certain physiological functions which normally occur at specific times of the day must now be time-shifted to the new local time, which perturbs the normal physiological activities.

Several studies have shown that our lifestyle can also derange the biological clock and lead to harmful effects on health over the long term. Over the course of evolution, our species has adapted to eating and sleeping according to rhythms dictated by the day-night cycle: since *Homo sapiens* first saw light in Africa, close to the equator, this means that our metabolism has evolved such that it functions optimally with days and nights of roughly equal lengths (12 hours each). The arrival of electric lighting has completely modified our day-night cycles and thus changed the activities of humans, for example by promoting the consumption of foods during these prolonged periods and decreasing the duration of



sleep. This excessive nocturnal illumination, sometimes referred to as light pollution, has several noxious consequences on flora and fauna (the artificial light perturbs pollination, for example) and the risky situation appears to be getting worse with the arrival of lighting systems that are even more powerful such as light emitting diodes (LEDs) which result in over-illumination.

PERTURBATION OF METABOLISM

In humans, one of the best documented results from perturbing the day-night cycle is its effect on glycaemia. During the night, when no food is consumed, the liver produces glucose and secretes it into the circulation, whereas during the day this system is silenced due to the sufficient quantities of glucose being provided from food. Thanks to a sophisticated system of regulatory genes whose expression follows a very elegant choreography, the biological clock thus allows the body to control, in a completely autonomous fashion, the level of blood sugar. On the other hand, when the day-night cycle is perturbed, this system becomes ineffective and the fluctuations in glycaemia which result can, with time, affect the production of insulin and result in type 2 diabetes. These observations explain why a very large number of studies have shown that people with abnormal day-night cycles, such as night shift workers, are at greater risk of obesity and of diabetes.

ADJUSTING THE CLOCK

Over the past few years, several studies have found that a simple means of avoiding these perturbations in metabolism is to concentrate the intake of food during a short period of the day. This new concept, called "time-restricted feeding", consists of limiting the consumption of food to a period limited by the day and particularly to avoid eating at night. In practice, this seeks to renew the way that humans have eaten throughout evolution, i.e. alternating periods of eating with periods of fasting for 12 hours, which coincides with the daytime. Studies performed to date indicate that this type of feeding prevents or slows the progression of several diseases, including atherosclerosis, diabetes, some cancers, and neurodegenerative disorders, possibly by regularizing the circadian rhythms and optimizing the effectiveness of metabolism¹. Understanding the role of circadian rhythms thus is not only a major advance in comprehension of a mechanism that is absolutely necessary for life, but also opens the way to new perspectives for the treatment of several chronic diseases caused by the perturbation of these circadian rhythms.

⁽¹⁾ Panda, S. Circadian physiology of metabolism. *Science* 2016;354:1008-1015.