The ancient clock that rules our lives – and determines our health

October 5 2017, by Russell Foster

Credit: AI-generated image (disclaimer)

Our lives are ruled by time; we use time to tell us what to do. But the alarm clock that wakes us in the morning or the wristwatch that tells us we are late for supper are unnatural clocks. Our biology answers to a profoundly more ancient beat that probably started to tick early in the evolution of all life.

Embedded within the genes of us, and almost all life on earth, are the instructions for a biological clock that marks the passage of around 24 hours. Biological clocks or "circadian clocks" help time our sleep patterns, alertness, mood, physical strength, blood pressure and much more.

Under normal conditions, we experience a 24-hour pattern of light and dark, and our circadian clock uses this signal to align biological time to the day and night. The clock is then used to anticipate the differing demands of the 24-hour day and fine-tune physiology and behaviour in advance of the changing conditions. Body temperature drops, blood pressure decreases, cognitive performance drops and tiredness increases in anticipation of going to bed. While before dawn, metabolism is geared-up in anticipation of increased activity when we wake.

A circadian clock also stops everything happening at the same time, ensuring that biological processes occur in the appropriate sequence. For cells to work properly they need the right materials in the right place at the right time.

Thousands of genes have to be switched on and off in order and in harmony. Proteins, enzymes, fats, carbohydrates, hormones, nucleic acids and other compounds have to be absorbed, broken down, metabolised and produced in a precise time window. Energy has to be obtained and then allocated to growth, reproduction, metabolism, locomotion and cellular repair.

All of these processes, and many others, take energy and all have to be timed to the correct time of the day. Without a clock, our biology would be in chaos.

The pioneering research of Jeffrey Hall, Michael Rosbash and Michael Young – awarded the 2017 Nobel Prize in Physiology or Medicine

earlier this week – provided our first clear understanding of how a biological clock ticks in any organism; in this case, a fruit fly.

How the clock works

At the heart of the clock is a "negative feedback loop" which consists of the following sequence of events. The clock genes produce messages that are translated into proteins. The proteins then interact to form complexes and move from the cytoplasm of the cell into the nucleus and then inhibit their own genes. These inhibitory clock protein complexes are then broken down and the clock genes are then once more free to make more messages and fresh protein – and the cycle continues day after day.

This negative feedback loop generates a near 24-hour rhythm of protein production and degradation that drives the internal biological day.

> Our biological clock helps to regulate sleep patterns, feeding behavior, hormone release and blood pressure #NobelPrize pic.twitter.com/NgL7761AFE
>
> — The Nobel Prize (@NobelPrize) October 2, 2017

Based on the findings of Hall, Rosbash and Young in the fruit fly, very similar clock genes were then discovered in mice, humans and many other animals. So the biological clocks that "tick" in us are broadly similar to the clocks found in insects, worms, fish and birds.

We now know that the morning and evening preferences of individuals who describe themselves as either "larks" or "owls" also appear to be related to small changes in some of these clock genes that either speed up or slow down our circadian rhythms.

Do not disturb

An understanding of how circadian clocks work and the central role they play in our biology has led to advances in many areas, not least an appreciation that when circadian rhythms are disrupted our overall health and well-being can be severely affected.

Shift workers try to sleep during the day, but sleep is usually shorter and of poorer quality than when sleep occurs at night because, although desperately tired, the circadian system is instructing the body that it should be awake. They then work during the night at a time when the circadian system has prepared the body for sleep, and alertness and performance are low. In effect, they work when they are sleepy and sleep when they are not.

Short-term circadian rhythm disruption can have a big negative impact on memory, problem solving, emotional responses and attention. And years of night-shift work has been shown to increase the risk of heart disease, infection, cancer, type 2 diabetes and obesity. So we ignore our circadian rhythms at our peril.

Circadian rhythm disruption is also a feature shared by some of the most challenging diseases of our time. Sufferers of mental illnesses such as schizophrenia, bipolar disorder and depression; neurological conditions like Alzheimer's, stroke and multiple sclerosis; developmental disorders such as autism; and serious disorders of the eye (including the development of cataracts) all exhibit circadian-rhythm disruption.

The future of circadian rhythms research is to understand how this disruption comes about, and, based on this knowledge, develop new drugs and treatments that will help us regulate internal time across the health spectrum. We truly live in exciting times.