

Scientists find mechanism to reset body clock

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Researchers from The University of Manchester have discovered a new mechanism that governs how body clocks react to changes in the environment.

And the discovery, which is being published in *Current Biology*, could provide a solution for alleviating the detrimental effects of chronic shift work and jet-lag.

The team's findings reveal that the enzyme casein kinase 1epsilon (CK1epsilon) controls how easily the body's clockwork can be adjusted or reset by environmental cues such as light and temperature.

Internal biological timers (circadian clocks) are found in almost every species on the planet. In mammals including humans, circadian clocks are found in most cells and tissues of the body, and orchestrate daily rhythms in our physiology, including our sleep/wake patterns and metabolism.

Dr David Bechtold, who led The University of Manchester's research team, said: "At the heart of these clocks are a complex set of molecules whose interaction provides robust and precise 24 hour timing. Importantly, our clocks are kept in synchrony with the environment by being responsive to light and dark information."

This work, funded by the Biotechnology and Biological Sciences Research Council, was undertaken by a team from The University of Manchester in collaboration with scientists from Pfizer led by Dr Travis Wager.

The research identifies a new mechanism through which our clocks respond to these light inputs. During the study, mice lacking CK1epsilon, a component of the clock, were able to shift to a new light-dark environment (much like the experience in shift work or long-haul air travel) much faster than normal.

The research team went on to show that drugs that inhibit CK1epsilon were able to speed up shift responses of normal mice, and critically, that faster adaption to the new environment minimised metabolic disturbances caused by the time shift.

Dr Bechtold said: "We already know that modern society poses many challenges to our health and wellbeing - things that are viewed as commonplace, such as shift-work, sleep deprivation, and jet lag disrupt our body's clocks. It is now becoming clear that clock disruption is increasing the incidence and severity of diseases including obesity and diabetes.

"We are not genetically pre-disposed to quickly adapt to shift-work or long-haul flights, and as so our bodies' clocks are built to resist such rapid changes. Unfortunately, we must deal with these issues today, and there is very clear evidence that disruption of our body clocks has real and negative consequences for our health."

He continues: "As this work progresses in clinical terms, we may be able to enhance the clock's ability to deal with shift work, and importantly understand how maladaptation of the clock contributes to diseases such as diabetes and chronic inflammation."

Provided by University of Manchester

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