

Body's circadian rhythm tightly entwined with blood sugar control

October 5 2009

Scientists have long struggled to understand the body's biological clock. Its tick-tock wakes us up, reminds us to eat and tells us when to go to bed. But what sets that circadian rhythm?

New research now shows that daily fluctuations in powerful hormones called glucocorticoids directly synchronize the biological clock as an integral part of our mechanism for regulating [blood sugar](#).

"The most surprising part of our findings is that our internal biologic rhythms are embedded directly into another pathway, one that is essential to regulate metabolism," said senior study author Brian Feldman, MD, PhD, assistant professor of pediatric endocrinology at the Stanford University School of Medicine. Feldman also practices at Lucile Packard Children's Hospital.

The new findings give the first in vivo evidence of a direct link between glucocorticoid hormones and genes that regulate our biological clock. The research may eventually help doctors reduce disabling side effects of glucocorticoid drugs such as prednisone, Feldman said. The work could also help diabetics control their blood sugar levels and may shed light on why night-shift workers are at risk for obesity and diabetes.

The study will be published online Oct. 5 in [Proceedings of the National Academy of Sciences](#). Feldman worked previously at the University of California-San Francisco, where much of the research was conducted.

Feldman's team began their experiments by applying a synthetic glucocorticoid to dishes of mouse and human stem cells to see which genes responded. To the team's surprise, three genes known to control the biological clock changed their activity in a direct response to the hormone.

Next, the researchers tested how the hormone's effect on the biological clock is linked with its other functions. The scientists gave the synthetic glucocorticoid to genetically engineered mice lacking a specific gene involved in regulating biologic rhythms. As the team expected, genetically normal control mice responded to the glucocorticoid with blood glucose changes associated with increased diabetes risk. In contrast, the genetically engineered mice were protected from harmful side effects on blood sugar levels. The result shows that blood sugar regulation and the [biological clock](#) are closely entwined.

The close link between daily cycles of glucocorticoids, the body's daily rhythms and blood sugar fluctuations should prompt doctors to examine how they use glucocorticoid drugs, Feldman said. For instance, prednisone is a powerful immune-suppressing glucocorticoid used to treat everything from severe asthma to cancer. Unfortunately, its side effects include poor regulation of blood sugar, weight gain and diabetes.

"Some very simple modifications in how we use glucocorticoids may change whether these drugs cause diabetes," Feldman said. Giving prednisone in a daily pattern that matches the body's natural glucocorticoid cycle -- with a daily peak in the early morning -- might help solve the problem, he said. And because prednisone is already approved for human use, clinical trials of this idea would be fast and simple.

Feldman's findings might also be applied to aid people who already have diabetes, possibly making it easier for them to artificially control their

blood sugar with medications. And the work provides the beginnings of a concrete explanation for the down side of night-shift work.

"We know that disturbed sleep patterns predispose people to metabolic syndrome," or a combination of obesity and elevated diabetes risk, Feldman said. "But our molecular understanding has been poor. Now we're fleshing out the beginnings of those molecular details."

Source: Stanford University Medical Center ([news](#) : [web](#))

Citation: Body's circadian rhythm tightly entwined with blood sugar control (2009, October 5) retrieved 18 April 2024 from

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