Lack of sleep, body clock disruption leads to impaired insulin sensitivity

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A new study by the University of Colorado shows that the longer people are awake during the time their biological clock is telling them to sleep the worse their sensitivity to insulin, which is a precursor to diabetes.

The study showed that a disruption, or circadian misalignment of a person's internal clock induced by five-hour 'short-sleep' schedules,

resulted in morning wakefulness during the biological night when melatonin levels were still high, said CU-Boulder Professor Kenneth Wright, lead study author. Melatonin is a sleep-promoting hormone produced naturally by the pineal gland and controlled by the brain's master clock, while insulin, produced in the pancreas, regulates blood sugar.

"We found the longer you are awake during the biological night, the worse your insulin sensitivity is," said Wright, who directs CU-Boulder's Sleep and Chronobiology Laboratory. "This is important because impaired insulin sensitivity can lead to both pre-diabetes and type 2 diabetes."

While the study participants all ate healthy diets during several days and nights of baseline measurements, they were allowed to eat the types and amounts of foods they wanted during the short-night sleep testing periods in order for the researchers to better understand insulin changes, said Wright.

"We found the body is not prepared for food intake during the biological night, nor is it prepared to be physically active," said Wright. "We are supposed to be resting and recovering during that time."

A paper on the subject was published online Nov. 5 in the journal *Current Biology*. The study included co-authors from CU-Boulder and from the University of Colorado Anschutz Medical Campus in Aurora, Colorado.

The team tested two groups of eight healthy men and women in their early 20s, all of whom were given both oral and intravenous tests in which they drank or were infused with a sugary liquid, after which their baseline insulin levels were tested. Insulin helps fat and muscle cells absorb glucose from the bloodstream, lowering blood-sugar levels.

Impaired insulin sensitivity occurs when those cells cannot easily absorb glucose, causing the pancreas to produce more insulin.

During the sleep disruption part of the study one group had just five hours of available sleep time each night for five days—simulating a workweek with too little sleep—before transitioning into five days with nine hours of available sleep time. The other group did the opposite, starting with nine hours of available sleep time for the first five nights, then switching to just five hours per night for the next five nights.

The team found that the simulated five-day workweek of five hours of sleep per night resulted in a 20 percent reduced oral and intravenous insulin sensitivity in otherwise healthy people. It took three consecutive nights of nine hours of available sleep time to restore oral insulin sensitivity in test subjects, Wright said.

"Our study and other previous studies have shown sleep loss reduces sensitivity to insulin," said Wright. "But we also found in this study that the test subjects with sleep loss had to release a lot more insulin to keep their blood sugar levels normal."

Wright said further testing could reveal a lot more about insulin sensitivity.

"These were young and very healthy people we studied," said Wright. "We don't know how much this might affect middle-aged or elderly people. One good follow-up study would be to see if improving the sleep of older people could improve their metabolic health."

Study co-authors included Research Associate Christopher Depner, former Research Associate Mark R. Smith and former graduate students Rachel Markwald and Andrew McHill of CU-Boulder, as well as first author Dr. Robert Eckel, Dr. Leigh Perreault and Associate Professors

Janine Higgins and Edward Melanson of the University of Colorado Anschutz Medical Campus.

The National Institutes of Health, the Howard Hughes Medical Institute and the Biological Sciences Initiative/Undergraduate Research Opportunities Program at CU-Boulder funded the study.

"This collaboration was a perfect fit," said Wright. "The Anschutz Medical Campus researchers are experts in diabetes, obesity and nutrition, and CU-Boulder has expertise in sleep and circadian rhythms. We needed to bring all these people together to generate this kind of science."

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