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Even your fat cells need sleep, according to new research

In a study that challenges the long-held notion that the primary function of sleep is to give rest to the brain, researchers have found that not getting enough shut-eye has a harmful impact on fat cells, reducing by 30 percent their ability to respond to insulin, a hormone that regulates energy.

Sleep deprivation has long been associated with impaired brain function, causing decreased alertness and reduced cognitive ability. The latest finding — published by University of Chicago Medicine researchers in the Oct. 16 issue of the *Annals of Internal Medicine* — is the first description of a molecular mechanism directly connecting sleep loss to the disruption of energy regulation in humans, a process that can lead over time to weight gain, diabetes and other health problems. The study suggests that sleep's role in energy metabolism is at least as important as it is in brain function.

"We found that fat cells need sleep to function properly," said study author Matthew Brady, PhD, assistant professor of medicine and a member of the Committee on Molecular Metabolism and Nutrition at the University of Chicago Medicine.

Brady said body fat plays an important role in humans.

"Many people think of fat as a problem, but it serves a vital function," he said. "Body fat, also known as adipose tissue, stores and releases energy. In storage mode, fat cells remove fatty acids and lipids from the circulation where they can damage other tissues. When fat cells cannot respond effectively to insulin, these lipids leach out into the circulation, leading to serious complications."

He and the other researchers recruited six men and one woman, all young, lean and healthy. Each volunteer went through two study conditions, at least four weeks apart. In one, they spent 8.5 hours a night in bed for four consecutive nights. In the other, they spent 4.5 hours in bed for four nights. Food intake, strictly controlled, was identical under both study conditions.

On the morning after the fourth night following both the long and short sleep conditions, each volunteer took an intravenous glucose tolerance test, which measures total-body insulin sensitivity. The researchers performed a biopsy, removing abdominal fat cells from the area near each volunteer's navel. Then they measured how these fat cells responded to insulin.

After four nights of short sleep, total-body insulin response decreased by an average of 16 percent. The insulin sensitivity of fat cells decreased by 30 percent. This reduction is comparable to the difference between cells from obese vs. lean participants or from people with diabetes versus non-diabetic controls.

The researchers assessed insulin sensitivity at the molecular level by measuring the phosphorylation of a protein called Akt within fat cells. Akt phosphorylation is a crucial early chemical step in the cell's response to insulin.

They found that the sleep-deprived study participants had a decreased response to a range of doses of insulin. It took nearly three times as much insulin to provoke half of the maximum Akt response in volunteers who had been deprived of sleep.

“Sleeping four to five hours a night, at least on work days, is now a common behavior” said study author and sleep specialist Esra Tasali, MD, assistant professor of medicine at the University of Chicago.

“Some people claim they can tolerate the cognitive effects of routine sleep deprivation,” said co-author Eve Van Cauter, PhD, the Frederick H. Rawson Professor of Medicine and director of the sleep, metabolism and health center at the University of Chicago. “In this small but thorough study, however, we found that seven out of seven subjects had a significant change in insulin sensitivity. They are not tolerating the metabolic consequences.”

The study was one of the first to bring together sleep research experts and biologists focused on energy regulation and metabolism in adipose tissue. The impetus came from a sleep-research graduate student, Josiane Broussard, PhD ’10, lead author of the study and now a Society in Science-Branco Weiss fellow at Cedars-Sinai Medical Center in Los Angeles. She wanted to combine her interest in sleep and metabolism with research at the molecular level.

So she pulled together a team for this project that included the two sleep researchers, Tasali and Van Cauter, plus two specialists from the University of Chicago Kovler Diabetes Center, David Ehrmann, MD, and Brady, who studies how insulin regulates energy storage in fat and liver cells.

They focused on fat cells because of their direct links to metabolic disruption and weight gain. These cells store energy for the body, are exquisitely sensitive to insulin and help regulate appetite.

Witnessing the direct effect of sleep deprivation on a peripheral tissue such as fat at the cellular level “was an eye-opener,” Broussard said. It helps cement the link between sleep and diabetes and “suggests that we could use sleep like diet and exercise to prevent or treat this common disease.”

Brady said the study opens up many new questions.

“What signals from sleep loss affect the fat cell? What effect does dysfunctional fat have at the whole-body level?” Brady wondered. “And if we can deprive healthy people of sleep and make them worse, can we take sick people, such as those with the common combination of sleep apnea, obesity and diabetes, improve their sleep and make them better? That’s the missing link in the sleep-obesity-diabetes connection.”

This study is “a valuable contribution to the understanding of the causal pathways by which reduced sleep duration may directly contribute to diabetes and obesity,” according to an editorial in the journal by Francesco Cappuccio, MD, DSc, and Michelle Miller, PhD, of the University of Warwick, in Coventry, United Kingdom. “These results point to a much wider influence of sleep on bodily functions, including metabolism, adipose tissue, cardiovascular function, and possibly more.”

The paper, “Impaired Insulin Signaling in Human Adipocyes,” appears in the Oct. 16, 2012, issue of the *Annals of Internal Medicine.* Funding for this work was provided by the National Institutes of Health and Society in Science – The Branco Weiss Fellowship.

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