MedicalXpress

Brain chemical boosts body heat, aids in calorie burn, research suggests

July 6 2010

New findings by UT Southwestern Medical Center researchers suggest that an enzyme in the brain known as PI3 kinase might control the increased generation of body heat that helps burn off excess calories after eating a high-fat meal.

The increase in energy expenditure, called a thermogenic response, burns calories even in the absence of exercise, so understanding how it is regulated could aid efforts to combat obesity, said Dr. Joel Elmquist, professor of internal medicine, psychiatry and pharmacology at UT Southwestern and co-senior author of the mouse study, which appears online and in the current issue of Cell Metabolism.

"We found that the mice with reduced PI3 kinase activity in specific neurons in the brain gained weight because they were unable to produce this thermogenic response," said Dr. Elmquist, adding that the physical activity levels of the mice with reduced PI3 kinase did not change. "These mice were more susceptible to diet-induced obesity."

It's still unclear whether the findings in mice are translatable to humans, because one of the tissues that mediates the thermogenic response is brown adipose tissue, a type of fat uncommon in adult humans.

"Brown adipose tissue is found in babies - that's why they're so warm - but it's unclear whether the tissue has the same physiological role in adult humans that it does in rodents. Recent studies have suggested that humans do have brown fat, which may have physiological importance,"

Dr. Elmquist said. "What is clear, however, is that specific brain cells and PI3 kinase seem to play a key role in how mice, and potentially humans, respond on a physiological level to a high-fat diet."

Prior research both in mice and in humans has shown that acute exposure to too many calories causes the body to temporarily increase energy expenditure, burning more energy in an effort to use up those excess calories.

For the current study, UT Southwestern researchers generated a type of mouse that has reduced PI3 kinase activity in neurons located in the ventromedial hypothalamus, a small region of the brain known to influence food intake and body weight. The goal was to determine how PI3 kinase signaling in these neurons affects energy balance.

Dr. Yong Xu, instructor of internal medicine at UT Southwestern and co-lead author of the study, said the findings were dramatic but raise many additional questions.

"The animals in this study developed obesity mainly because they didn't produce enough heat after eating, not because the animals ate more or were less active," Dr. Xu said. "A better understanding of this pathway in the brain might lead to ways to activate or enhance it, and perhaps result in a way to combat obesity not by prohibiting eating or increasing physical activity, but by generating more energy expenditure."

The team also found that the neurons in the ventromedial hypothalamus need PI3K in order to mediate the effects of the hormone leptin, which has been shown to activate this pathway and which is known to be a key player in regulating energy use in the body. Other hormones, including estrogen, might also be involved in regulating the system, the researchers said.

The next step, Dr. Elmquist said, is to identify more precisely the relationship between PI3 kinase-expressing neurons and fat-burning, as well as to characterize better the role of leptin and other hormones in the process.

Provided by UT Southwestern Medical Center