MedicalXpress

Eating and weight gain not necessarily linked, study shows

June 3 2008

You may not be what you eat after all. A new study shows that increased eating does not necessarily lead to increased fat. The finding in the much-studied roundworm opens the possibility of identifying new targets for drugs to control weight, the researchers say.

The discovery reveals that the neurotransmitter serotonin, already known to control appetite and fat build-up, actually does so through two separate signaling channels. One set of signals regulates feeding, and a separate set of signals regulates fat metabolism. The worm, known scientifically as Caenorhabdtis elegans, shares half of its genes with humans and is often a predictor ofhuman traits.

The signaling pathways are composed of a series of molecular events triggered by neurons in the brain that ultimately "instruct" the body to burn or store fat.

If the "separate-channel" mechanism is also found in humans, weight-loss drugs might be developed to attack just the fat-deposition channel rather than the hunger-dampening pathway that has met with limited success, says Kaveh Ashrafi, PhD, assistant professor of physiology at UCSF and senior author on the scientific paper reporting the study.

"It's not that feeding isn't important," Ashrafi says. "But serotonin's control of fat is distinct from feeding. A weight-loss strategy that focuses only on eating can only go so far. It may be one reason why diets fail."

The research is being reported online June 3 by the journal "Cell Metabolism" and in the print edition June 4.

The finding does not challenge the view that hunger, feeding and fat are all linked in a feedback loop under the influence of serotonin and other neurotransmitters that act on neurons in the brain. But the discovery shows that this is not the whole story, according to Ashrafi.

Various weight-loss drugs have been developed to boost serotonin and thereby suppress appetite. But the cutback in eating tends to be short-term – often a matter of days, based on animal research, Ashrafi says. Drugs that block the brain's separate fat-deposition signaling pathway might be a boon to controlling obesity, type 2 diabetes, cardiovascular disease and other threats, he adds.

The scientists studied more than 250 genes to identify those that underlie serotonin's effects on fat and feeding. They found that serotonin controls feeding by docking with receptors on neurons that are distinct from those that control fat. In turn, these fat- controlling neurons send signals to sites of fat storage to rev up metabolism.

It is widely believed that environments that encourage excessive food intake and little physical activity promote development of obesity. However, extensive studies have revealed that body weight is not merely a passive consequence of environmental conditions but that a physiological system coordinates the complex mechanisms that regulate food intake and energy expenditure, Ashrafi says.

This physiological system is thought to involve genes that operate in various tissues such as fat, muscle, and brain. In fact, the genetic contribution to body weight is estimated to be between 40 and 70 percent. The molecular mechanisms that link excess fat to various diseases such as type 2 diabetes are not understood.

To help decipher the complex relationships between behavioral and metabolic pathways that control body weight, Ashrafi and his team began analyzing serotonin-induced regulation of fat and feeding in the microscopic C. elegans worm. They took advantage of a powerful and relatively new technique known as RNA interference, or RNAi, which allowed them to inactivate hundreds of genes one at a time to determine the effect of these gene inactivations on serotonin's actions on fat regulation.

"Obesity and thinness are not solely determined by feeding behavior," the scientists conclude in their paper. "Rather, feeding behavior and fat metabolism are coordinated but independent responses of the nervous system to the perception of nutrient availability."

Source: University of California - San Francisco