Researchers pinpoint neurons that control obesity in fruit flies

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A team of scientists from the California Institute of Technology have pinpointed two groups of neurons in fruit fly brains that have the ability to sense and manipulate the fly's fat stores in much the same way as do neurons in the mammalian brain. The existence of this sort of control over fat deposition and metabolic rates makes the flies a potentially useful model for the study of human obesity, the researchers note.

Their findings were published in the August 13 issue of the journal *Neuron*.

By manipulating neural activity in fruit fly brains using transgenic techniques, the researchers found that, "just as in mammals, fly fat-store levels are measured and controlled by specific neurons in the brain," says Caltech postdoctoral scholar Bader Al-Anzi, the Neuron paper's first author. "Silencing these neurons created obese flies, while overactivating them produced lean flies."

Mammalian brains are given information about the body's fat stores by hormones such as leptin and insulin, and respond to that information by inducing changes in food intake and metabolism to maintain a constant body weight. The researchers found that similar behavioral and metabolic changes occurred in the fruit flies, though which changes occurred depended on which of the two sets of newly identified neurons was silenced.

For instance, silencing one group of neurons led to an increase in food intake, a decrease in metabolism, and an increase in the synthesis of fatty acids (the building blocks of fat). Silencing the other group led to a similar decrease in metabolism and increase in fatty-acid synthesis, as well as to a defect in the flies' ability to utilize their fat stores.

Increasing activity in either of the groups of neurons, on the other hand, resulted in depletion of fat stores by increasing the flies' metabolism and decreasing their synthesis of fatty acids.

The next step is to "see exactly how neurons regulate fat storage, and how the two different groups of neurons identified in this study work," says Kai Zinn, professor of biology at Caltech, who led the research group. "They clearly regulate fat storage using different mechanisms."

The paper is the result of research originally led by Caltech biologist Seymour Benzer, a pioneer in the study of genes and behavior. Zinn continued this research after Benzer's death in late 2007.

"The goal was to establish a model system for obesity in humans," Zinn explains. "This could, at some point, eventually define new drug targets."

The search for a model system is critical, adds Al-Anzi. With obesity on the rise—statistics say that more than a third of adults in Western society are overweight—efforts to find its roots in human brains or human genes have similarly increased. Unfortunately, Al-Anzi notes, these efforts "have not been extremely successful."

In addition, says Al-Anzi, "While mammalian models such as the mouse have provided progress in the field, they tend to be difficult and expensive research subjects."

Thus, he notes, "The obesity research field would benefit greatly if another model organism could be used, one that is accessible for easy, fast, and affordable biomedical research methods. We believe the fruit fly can be such an organism.

"There is a surprising amount of overlap between the simple fruit fly and more complex mammals in many basic biological processes," Al-Anzi adds. "This is why it's an excellent model system for exploring such medically relevant issues as Alzheimer's disease, alcoholism, and addiction. Our results thus far suggest that body-weight regulation will be no different."

Having now established that fruit flies are indeed similar to mammals in the way they control fat deposition via the brain, researchers can begin to test antiobesity dietary or drug treatments on flies whose fat-regulating neurons have been silenced. "Treatments that cause these flies to return to normal body weight could then be retested for their effectiveness in a mammalian obesity model," Al-Anzi notes.

Knowing the neurons involved in the regulation of fat storage could also lead to identifying the genes that allow for the critical communications between the brain and the fat stores. "This can be done by identifying the genes that are selectively expressed only in those neurons," he explains.

In addition, this research should help researchers determine if the mechanisms behind appetite and body-weight regulation in fruit flies have been conserved over evolutionary time and throughout the animal kingdom. "This has been shown to be the case for genes that regulate behavioral phenomena like learning and circadian rhythms," notes Al-Anzi, "and we hope that body-weight and appetite regulation will be no different."

More information: *Neuron* paper: "Obesity-blocking neurons in Drosophila"

Source: California Institute of Technology (news : web)