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Study: Mice fed a high fat diet show evidence of neuron rewiring

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Lab mice like this one showed major changes after eating a diet high in fat (Image: Rama, Wikipedia Commons)

A recent study by Alexandre Benani and colleagues published in the *Journal of Neuroscience* shows evidence that feeding adult mice a high-fat diet quickly remodels neuronal circuits within a part of the brain called the hypothalamus and also causes these mice to limit their caloric intake.

In this study, mice were given either high-fat or standard mouse chow ad libitum, which means they were able to gorge themselves to their hearts' content. At day one, the high-fat-food mouse group ate significantly more calories than the mice eating standard food. However, the mice in the high-fat-food group quickly adjusted to their new diet and ate a similar number of calories as the control mice after eight days. This adjustment suggests that eating high-fat food spurred fast changes in the hypothalamic circuits that control calorie intake.

Consistent with this idea, the researchers found significant increases in the expression levels of several genes involved in the extension and/or retraction of neuronal endings (cytoskeleton genes) and the forming of new neuronal connections (synaptogenesis and cell-interaction related genes) in the hypothalami of mice fed the high-fat diet. Remarkably, mice that had only eaten the high-fat food for one day showed significant increases for many of these genes. Hypothalamic levels of polysialic acid (PSA) —a molecule known to promote reorganization of neuronal connections—also increased in these mice.

Changes in gene levels don't necessarily mean that circuits are rewired. To see if neuronal connections were functionally changed after exposure to a high-fat diet, the authors measured the electrical activity of a particular subset of hypothalamic neurons—POMC neurons— and determined that a high-fat diet significantly increased one component of this activity (excitatory postsynaptic currents) and decreased another component (inhibitory postsynaptic currents). These results support a significant rewiring of the neurons that contact the POMC neurons in the mice that ate the high-fat diet. Injection of a drug that inhibits PSA action prevented the increase in excitatory currents in the mice fed the high-fat food—suggesting that PSA plays a significant role in remodeling the hypothalamic circuits responsible for controlling food intake. Even after a week of eating the high-fat diet, mice receiving the injections continued to overeat the high-fat food and gained significantly more weight than the mice that were fed the high-fat food but who did not receive the injections.

These results are noteworthy because they highlight how quickly neuronal rewiring can take place with almost immediate behavioral consequences. They also show how perturbation of a single molecule, PSA in this case, can throw an entire system out of whack—an idea that may have relevance for treating human obesity.