

Scientists discover link between anxiety and weight loss

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JUPITER, FL – Jan. 17, 2019 – Scripps Research scientists have published a study revealing a shared mechanism for both anxiety and weight loss. Their research, published in the journal *Cell Metabolism*, describes a key molecule that triggers anxiety in the brain, while also increasing metabolism and fat burning.

"We've found a relationship between anxiety and weight loss," says Baoji Xu, PhD, professor on the Florida campus of Scripps Research and senior author of the study. "This research could guide new therapies for anxiety and help researchers design treatments for obesity."

Anxiety disorders are the most common types of mental health disorders in the world. Along with the psychological effects, many people have noticed that weight changes accompany periods of anxiety and stress.

Xu, a long-time obesity researcher, noticed the same phenomenon in a group of mice engineered to lack a molecule called brain-derived neurotrophic factor (BDNF). These mice showed anxiety-like symptoms and stayed lean.

"Even on a high-fat diet, these mice were really lean," says Xu. "Could the same thing be happening in humans?"

Answering that question required a study of how BDNF works. Normally scientists simply turn off a gene to find out what it does. There was a challenge with BDNF, though: Previous work had shown it is mandatory for brain development, learning and memory. They needed a mouse model that had normal BDNF in some areas of the brain, but not the areas they wanted to study.

When they deleted the BDNF gene only in the brain's cortex, hippocampus and amygdala, their model worked as expected. The mice developed anxiety-like symptoms and that same tendency to stay lean.

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With the new model, the researchers discovered that the lack of BDNF meant they could not dampen busy “excitatory” signaling in those brain circuits. They could not take advantage of an important neurotransmitter called GABA, a molecule that normally slows signaling in the brain and promotes relaxation.

Next, the researchers studied how a lack of BDNF kept the mice lean. They found that these anxious mice had an elevated basal metabolic rate, the rate of energy expended to keep the body functioning. In addition, these mice produced more brown fat—a kind of fat that releases more energy and leads to faster weight loss.

Interestingly, the researchers discovered that deleting BDNF just in the amygdala, a brain region that plays a primary role in anxiety, could increase energy expenditure in mice.

The researchers had found a molecule—and a brain region—that link anxiety and weight loss. Xu and his team are now considering how to apply this work to help patients. No one would ever want to trigger anxiety in humans, Xu says. But it may be possible to harness this knowledge to develop obesity therapies able to target just the parts of the pathway involved in energy expenditure, Xu says.

“In this way, we could help obese people lose weight,” says Xu.

He also hopes to further study the neurons that BDNF targets to relieve anxiety. This knowledge could be useful to design additional therapies for people with anxiety disorders.

Xu says the environment at Scripps Research is a great place to try to answer these basic questions about the brain. “At Scripps Research, we have the freedom to pursue any research direction we think is important,” says Xu.

Additional authors of the study, “Activation of Anxiogenic Circuits Instigates Resistance to Diet-Induced Obesity via Increased Energy Expenditure,” were Xiangyang Xie (first author), Juan Ji An, Jessica Houtz, Ji-Wei Tan, Haifei Xu, Guey-Ying Liao and Zhi-Xiang Xu of Scripps Research; and Haili Yang, previously at Scripps Research and now at Southwest University,

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Chong Qing.

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