Scientists pinpoint anorexia's neurologic origins

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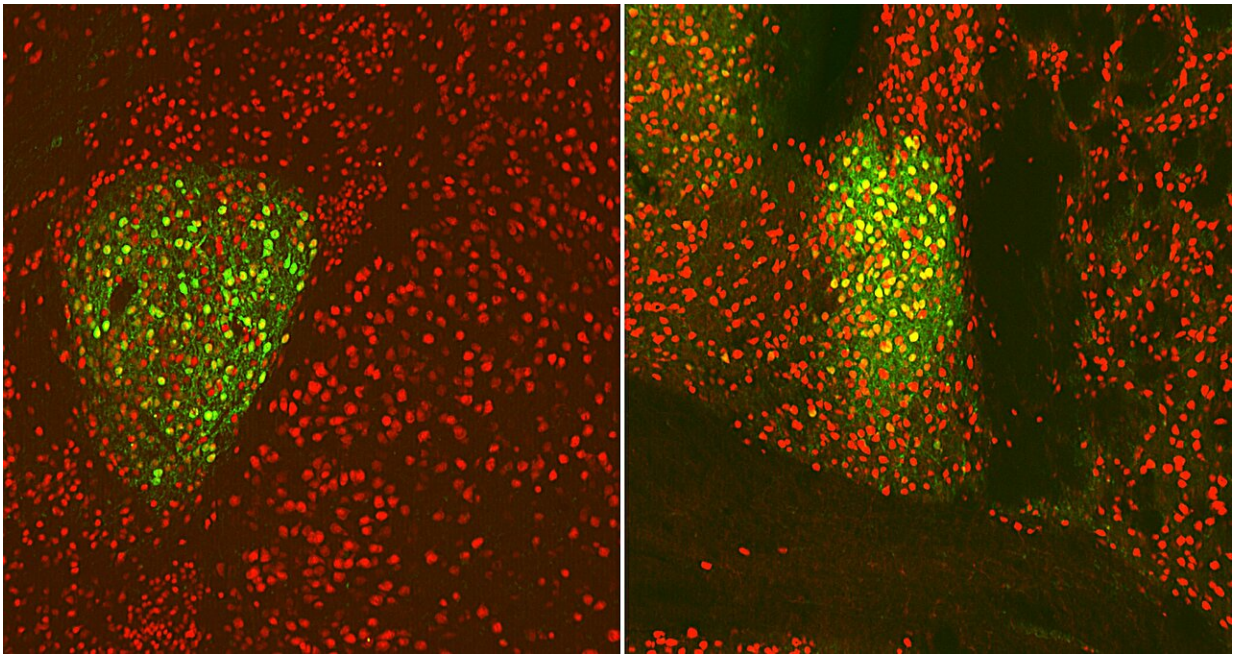

On the left is the central amygdala and on the right is the oval region of the bed nucleus of the stria terminalis. PKC-delta neurons glow green in this image. When the research team turned off those neurons in both regions, mice recovered from anorexia. Scientists sought out anorexia's origins in the amygdala, the brains emotion center, because the disorder is often associated with anxiety and depression. Credit: Haijiang Kai

Anorexia nervosa, a mental health disorder in which people dangerously restrict their eating or purge their stomachs soon after a meal, is one of

the deadliest psychological diseases.

Yet, what exactly happens biologically in the anorexic brain has remained unclear, and therapies are limited.

Scientists have been tailing a lead for years, though. They've known that the disorder is often associated with anxiety and depression, hinting that the biological basis for anorexia could be regulated by neurons somewhere in the brain region that controls emotion, called the amygdala.

That's exactly where Haijiang Cai, a University of Arizona associate professor in the Department of Neuroscience and BIO5 Institute member, and his team found it: Anorexia is caused by a combination of two subregions in the amygdala, according to new research published in *Cell Reports*.

One knot of neurons in the central nucleus of the amygdala pumps the brakes on your appetite when you get full, feel nauseous or taste something bitter. The other is in the oval region of the bed nucleus of the stria terminalis, which also halts eating due to inflammation and sickness.

Cai and his research team found that when they destroyed a certain type of brain cell, called PKC-delta neurons, in both of these regions, they could prevent anorexia development.

They also found that PKC-delta neurons become more active in response to eating during the anorexia development. What's more, when they artificially activated these neurons, they caused a suppression in eating habits and increased exercise.

"This study suggests two important insights to treat anorexia," Cai said.

"One is that we need to target multiple brain regions to develop therapies. We also need to treat multiple conditions. For example, maybe one drug will target nausea and another drug target will target inflammation, and you have to combine them, like a cocktail therapy, to have better therapeutic effects."

The team relied on mice models for their research.

"There's no animal model that can mimic human disease completely, but this is as close as we can get," Cai said. "For example, there are multiple common features, including a warped body image, a very low body weight, limited food intake and excessive exercise. We can't know if an animal has a warped body image, but we can measure the other three features."

One future step—since researchers cannot destroy neurons for human treatment—is to develop a method to silence the neurons temporarily, using drugs or some other method to test if that can prevent anorexia development or speed up recovery for people who have already developed the disorder.

More information: Wesley Ilana Schnapp et al, Development of activity-based anorexia requires PKC-δ neurons in two central extended amygdala nuclei, *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.113933

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