Hormone found to switch off hunger could help tackle obesity

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A hormone that can suppress food intake and increase the feeling of fullness in mice has shown similar results in humans and non-human primates, says a new study published today in *eLife*.

The hormone, called Lipocalin-2 (LCN2), could be used as a potential treatment in people with obesity whose natural signals for feeling full no longer work.

LCN2 is mainly produced by bone cells and is found naturally in mice and humans. Studies in mice have shown that giving LCN2 to the animals long term reduces their food intake and prevents weight gain, without leading to a slow-down in their metabolism.

"LCN2 acts as a signal for satiety after a meal, leading mice to limit their food intake, and it does this by acting on the hypothalamus within the brain," explains lead author Peristera-Ioanna Petropoulou, who was a Postdoctoral Research Scientist at Columbia University Irving Medical Center, New York, US, at the time the study was carried out, and is now at the Helmholtz Diabetes Center, Helmholtz Zentrum München, Munich, Germany. "We wanted to see whether LCN2 has similar effects in humans, and whether a dose of it would be able to cross the blood-brain barrier."

The team first analyzed data from four different studies of people in the US and Europe who were either normal weight, overweight or living with obesity. The people in each study were given a meal after an overnight fast, and the amount of LCN2 in their blood before and after the meal was studied. The researchers found that in those who were of normal weight, there was an increase in LCN2 levels after the meal, which coincided with how satisfied they felt after eating.

By contrast, in people who were overweight or had obesity, LCN2 levels decreased after a meal. Based on this post-meal response, the researchers grouped people as non-responders or responders. Non-responders, who showed no increase in LCN2 after a meal, tended to have a larger waist circumference and higher markers of metabolic disease—including BMI, body fat, increased blood pressure and increased blood glucose. Remarkably, however, people who had lost weight after gastric bypass surgery were found to have a restored sensitivity to LCN2—changing their status from non-responders before their surgery, to responders afterwards.

Taken together, these results mirror those seen in mice, and suggest that this loss of post-meal LCN2 regulation is a new mechanism contributing to obesity and could be a potential target for weight-loss treatments.

After verifying that LCN2 can cross into the brain, the team explored whether treatment with the hormone might reduce food intake and prevent weight gain. To do this, they treated monkeys with LCN2 for a week. They saw a 28% decrease in food intake compared with that before treatment within a week, and the monkeys also ate 21% less

than their counterparts who were treated only with saline. Moreover, after only one week of treatment, measurements of body weight, body fat and blood fat levels showed a declining trend in treated animals.

"We have shown that LCN2 crosses to the brain, makes its way to the hypothalamus and suppresses food intake in non-human primates," concludes senior author Stavroula Kousteni, Professor of Physiology and Cellular Biophysics at Columbia University Irving Medical Center. "Our results show that the hormone can curb appetite with negligible toxicity and lay the groundwork for the next level of LCN2 testing for clinical use."

More information: Peristera-Ioanna Petropoulou et al, Lipocalin-2 is an anorexigenic signal in primates, *eLife* (2020). DOI: 10.7554/eLife.58949