

Appetite-controlling molecule could prevent 'rebound' weight gain after dieting

February 15 2018



Credit: Monash University

Scientists have revealed how mice control their appetite when under stress such as cold temperatures and starvation, according to a new study by Monash University and St Vincent's Institute in Melbourne. The results shed light on the metabolic processes behind why people tend to regain much of their weight after dieting and could lead to treatments to help them keep the weight off for good.

"Most weight-loss strategies focus on creating a negative energy balance, where you burn more calories than you consume, but these strategies frequently fail because of compensatory increases in appetite," explains first author Dr. Sandra Galic from St Vincent's Institute of Medical Research (SVI), Australia.

"The underlying mechanisms that link energy demand to increased appetite are not fully understood and so we set out to learn more about them."

The team focused their study on a molecule called AMPK, which is known to control how the body generates and uses energy under different conditions. But the other molecules that AMPK works with to achieve these effects are largely unknown.

Lead author Professor Bruce Kemp, also from SVI, says: "One theory is that AMPK switches off another molecule called ACC as an essential step in regulating appetite and heat generation. To investigate this further, we engineered [mice](#) with mutated ACC, which made them insensitive to the effects of AMPK, and studied them under various conditions."

They found that the engineered mice were slightly leaner than [normal mice](#). The team first thought this might be due to different [energy expenditure](#) in the mice. But when they found this wasn't the case, they looked at whether there were differences in food intake instead, and this is where they saw marked changes.

Under cold conditions, normal mice increased their food intake to meet the energy demands of increasing body temperature, yet the mutated mice did not. Instead, the mutated mice adapted their metabolism to burn more fat instead of carbohydrate, unlike those kept in normal temperatures. This suggests that under conditions of stress, the lack of

ACC control by AMPK increased the animals' tendency to utilise fat, rather than intake more calories.

"We then noticed that the mutated mice had increased levels of ghrelin, known as the 'hunger hormone' for its role in boosting appetite," says co-author Zane Andrews, Associate Professor of Physiology at Monash University, Australia.

"Although this hormone was increased, food intake was still suppressed, which led us to wonder if blocking AMPK-ACC somehow affects the normal response to ghrelin."

Indeed, when they gave supplementary ghrelin to the mutated mice, they saw little increase in food intake, suggesting the mice were unable to respond to this appetite-inducing signal.

Ghrelin also promotes obesity regardless of [food intake](#) and is responsible for the renowned 'rebound' weight gain seen after diet-induced weight loss.

To study ghrelin's longer-term effects on weight, they gave the hormone to the mice for two weeks and measured their weight gain. Remarkably, although the normal mice increased in weight by 4 percent (equivalent to 2.8 kg in a 70-kg person), the [mutant mice](#) did not show any significant [weight gain](#).

"We have identified a distinct signalling pathway that is involved in regulating [appetite](#) and fat metabolism distinct from [energy](#) expenditure," concludes Dr. Galic.

"Our results could pave the way for therapies to prevent the regain of weight that so often follows the initial success of diet-induced [weight](#) loss, by suppressing hunger signals caused by prolonged calorific

deficits."

This research is published in *eLife*.

More information: Sandra Galic et al. AMPK signaling to acetyl-CoA carboxylase is required for fasting- and cold-induced appetite but not thermogenesis, *eLife* (2018). DOI: [10.7554/eLife.32656](https://doi.org/10.7554/eLife.32656)

Provided by Monash University

Citation: Appetite-controlling molecule could prevent 'rebound' weight gain after dieting (2018, February 15) retrieved 21 May 2024 from <https://medicalxpress.com/news/2018-02-appetite-controlling-molecule-rebound-weight-gain.html>

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