Understanding of mechanisms behind post-exercise lack of appetite can open new paths to obesity treatment

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The complex relationship between physical activity and energy balance—food intake versus energy expenditure—is still a challenge for

science, especially in light of the rising worldwide prevalence of overweight and obesity. Some of the medications available on the market to combat obesity work analogously to hormones associated with appetite control, and for some time researchers have focused on understanding how processes involving metabolites (products of cell metabolism) affect hunger and satiety.

A possible combination of mechanisms similar to hormone functions and those of metabolites is found to be a promising route for advances in the treatment of obesity by Henver Simionato Brunetta, a postdoctoral fellow at the State University of Campinas (UNICAMP) in Brazil, and Jens Lund, a professor at the University of Copenhagen in Denmark, in an editorial published in *The Journal of Physiology*. Brunetta and Lund also review a randomized study reported in the same issue investigating the metabolic interaction between carbohydrates and exercise, and its role in acute appetite regulation.

Led by James Frampton, a researcher at Imperial College London in the United Kingdom, the study found two metabolites, acetate and succinate, to be potential novel mediators of exercise-induced appetite and energy intake responses.

"The most interesting point made by the article about their study is that acute exercise suppresses hunger, but hormone function is not sufficient to explain this effect," Brunetta told Agência FAPESP. "Frampton and colleagues investigated the mechanisms by which exercise and dietary conditions alter metabolites, concluding that some of these, such as acetate and succinate, can be considered predictors of satiety. Appetite is regulated to some extent by metabolites, although we don't know exactly how."

The randomized crossover study by Frampton et al. recruited 12 healthy men aged 18-40 between February 2019 and February 2020. The term

"crossover" refers to a study design in which subjects undergo two or more treatments (drugs, procedures, etc.) at different times, and the sequence of treatments is randomized for each subject.

Women were excluded from this study because the menstrual cycle influences appetite control and hormone release. The participants exercised for 30 minutes, either fasting or after ingesting a bolus of carbohydrate. They were then given an ad libitum meal, and the researchers assessed calorie intake, subjective feelings of appetite, and bloodborne metabolites and hormones.

Both the carbohydrate and the exercise raised blood levels of hunger-reducing hormone GLP-1 and lowered levels of ghrelin, a hormone that increases hunger.

"Metabolites appeared to be more responsive to exercise than to carbohydrate ingestion, producing an exercise-dependent set of hormones/metabolites with the potential to suppress appetite despite the increase in energy expenditure induced by exercise," Brunetta and Lund conclude.

Obesity, which heightens the risk of heart disease, diabetes and high blood pressure, is set to affect 1 billion people worldwide by 2030, according to the World Obesity Atlas, produced by the World Obesity Federation, which expects the proportion of Brazil's adult population living with obesity to reach 30% by then.

Research line

Brunetta is a member of a team led by Marcelo Mori, a professor at UNICAMP's Institute of Biology. Mori and his team were the first to show, in July 2020, that SARS-CoV-2 could infect human fat cells and to suggest that adipose tissue could serve as a reservoir for the virus.

Brunetta has spent years on research involving obesity and metabolism. Since 2019, he has focused on hormones, metabolites and other substances secreted by adipose tissue. "Because Frampton and his group were trying to understand how secreted substances control metabolism, it clearly related to what I was doing. We now know organs release many more substances than hormones and these substances are very active," he said.

Initially considered an energy reserve, adipose tissue is now understood to be an important endocrine organ. It communicates with other organs by secreting microRNAs (miRNAs) and cell-signaling proteins called adipokines. An article co-authored by Brunetta and published as a preprint in *bioRxiv* discusses adequate bioenergetic adaptation of brown adipose tissue.

More information: Henver S. Brunetta et al, Chasing the hunger-suppressive signals of human exercise, *The Journal of Physiology* (2023). DOI: 10.1113/JP285096

James Frampton et al, The metabolic interplay between dietary carbohydrate and exercise and its role in acute appetite regulation in males: a randomized controlled study, *The Journal of Physiology* (2023). DOI: 10.1113/JP284294

Henver S. Brunetta et al, IF1 controls UCP1-dependent mitochondrial bioenergetics in brown adipocytes, *bioRxiv* (2023). DOI: 10.1101/2023.07.27.550888

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