Concentrations of PGE2 molecule in the brain linked to both weight loss and weight gain

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A team of medical researchers at Memorial University, in Canada, has found evidence showing that concentrations of the PGE2 molecule in the

brain can lead to both weight loss and weight gain depending on the amount. In their study, reported in *Proceedings of the National Academy of Sciences*, the group tested the impact of changes in concentrations of the PGE2 molecule in the hypothalamus in rats and mice.

Prior research has shown that there is a link between increased amounts of PGE2 in the brain and weight gain. Prior research has also shown that a Western diet heavy in fats can lead to an increase in PGE2 concentrations in the brain. In this new effort, the researchers found that there is more to the story.

In their work, the research team began by noting that a type of melanin-concentrating hormone (MCH) commonly found in brain cells is known to be in involved in weight regulation. Higher levels have typically been associated with an increase in food and an associated reductions in energy expenditure. In their work, the researchers found that the neurons associated with melanin-concentrating hormone could be activated by inflammatory molecules called prostaglandins (PGE2).

In testing the impact of different PGE2 concentration levels in rats and mice, the team found that in some instances, too much PGE2 led to weight gain, but in other instances, it led to weight loss. More testing showed that a low-level increase of PGE2 led to weight gain, while a high-level increase led to weight loss. They suggest this explains why a high-fat diet leads to a weight increase—it only slightly increases levels of PGE2. Inflammatory diseases, on the other hand, which are associated with weight loss, produce more inflammation in the brain than a high-fat diet, pushing PGE2 levels much higher and thereby stifling appetite.

The team suggests that inflammation plays a bigger role in obesity than previously thought and diets that include anti-inflammatory agents should be the most effective approach to losing weight.

More information: Fang, Lisa Z. et al, Prostaglandin E2 activates melanin-concentrating hormone neurons to drive diet-induced obesity, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2302809120. www.pnas.org/cgi/doi/10.1073/pnas.2302809120