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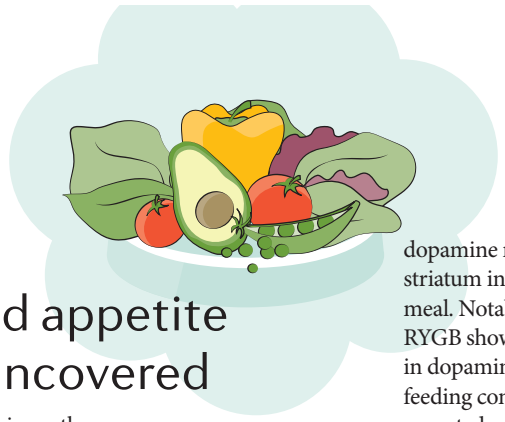


OBESITY

Mechanisms behind reduced appetite for fat after gastric bypass uncovered

New research in rats shows that decreased preference for dietary fat after Roux-en-Y gastric bypass (RYGB) stems from increased dopamine release in the dorsal striatum, mediated by greater intestinal synthesis of oleoylethanolamide (OEA) — a lipid satiety molecule and PPARα ligand — and subsequent vagus nerve signalling.

Bariatric surgery remains the only effective long-term treatment to induce and maintain weight loss in individuals who are obese. RYGB is one of the most commonly used procedures, increasing satiety and decreasing hunger in recipients; evidence suggests RYGB decreases preference for highly palatable foods, but the mechanisms underlying this shift are poorly understood.

"Previous work had shown that dorsal striatal dopamine release is reduced in obesity, and that this is linked to reduced intestinal synthesis of OEA," explains author Wiebke Fenske. "Our hypothesis was that RYGB increases meal-stimulated dorsal striatal dopamine release, via increased intestinal OEA synthesis, to reduce fat appetite".

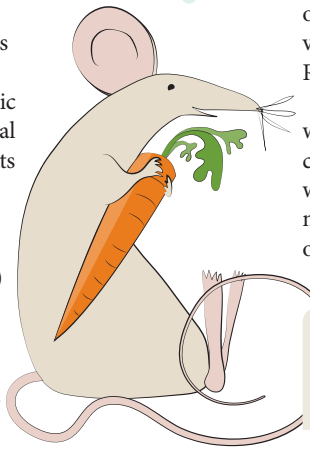
In an established obese rat model of RYGB, the researchers confirmed that fat preference was markedly reduced in animals receiving the surgery compared with those receiving a sham operation. As previously reported, OEA synthesis in the proximal duodenum was decreased in rats exposed to chronic high-fat diet. However, postprandial OEA synthesis in RYGB-treated rats was substantially increased in the common channel compared with the corresponding intestine sections (duodenum and jejunum) in sham-treated animals.

Because OEA is known to increase dorsal striatal dopamine release, the investigators measured whether RYGB surgery altered dopamine release in the dorsal striatum in response to a high-fat meal. Notably, animals receiving RYGB showed a twofold increase in dopamine release at 60 min after feeding compared with sham-operated rats; however, in RYGB-treated animals, vagotomy blocked this increased dopamine efflux.

"Our most significant finding was made when we blocked dopamine signalling in the dorsal striatum," notes author Ute Krügel. "We found that the dramatically suppressed fat appetite in RYGB rats was almost completely reversed." Intestinal administration of a PPARα antagonist or complete subdiaphragmatic truncal vagotomy also blocked the effects of RYGB on fat preference.

"The translational aspect of this work is obviously of great importance," comments Fenske. "Ultimately, we hope that this work will help to manage the devastating consequences of obesity more effectively."

Hugh Thomas



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ORIGINAL ARTICLE Hankir, M. K. *et al.* Gastric bypass surgery recruits a gut PPAR-α-striatal D1R pathway to reduce fat appetite in obese rats. *Cell. Metab.* http://dx.doi.org/10.1016/jcmet.2016.12.006 (2017)