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The Regulation Of Food Intake Via Gastrointestinal Receptors

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Obesity is a global pandemic characterized by excesive fat storage due to an balance in energy homeostasis. This metabolic imbalance is driven by increased energy in-take relative to energy expenditure. The gut vagal afferent neurons play a critical role in energy homeostasis by sensing the various chemo- and mechano-signals resulting from ingested nutrients and initiating changes in feeding behavior. However, these neurons fail to respond adequately in the context of diet-induced obesity, leading to overeating and ultimately obesity. Bariatric surgeries, which modify the anatomy of the gut, are currently the most effective but also the most invasive treatments for obesity. The mechanism(s) by which bariatric surgery modulates metabolic processes is still not fully understood. The vertical sleeve gastrectomy (VSG) procedure, a bariatric surgery where 80% of the stomach is removed, alters feeding patterns and induces sustained weight loss. Our findings demonstrate that VSG induces alterations in the signals in the gut-brain-axis, resulting in increased activation of the nucleus of the solitary tract (NTS) - a brain region critical for integrating peripheral signals and regulating food intake. Importantly, emerging data demonstrate that neurons that sense intestinal distension paid a critical role in the regulation of feeding. We hypothesized that diet induced obesity attenuates intestinal-stretch inhibition of food intake and that VSG restores it. Using non-nutritive substances such as methylcellulose and mannitol to differentiate stomach versus intestinal stretch respectively, we demonstrate that high-fat diet feeding ablates intestinal stretch-induced reductions in food intake while weight loss via dietary intervention, restores this response. More importantly, VSG restores intestinal stretch-induced food intake reduction, suggesting the reactivation of the peripheral neurons that detect intestinal stretch. Taken together, our data provide evidence that VSG alters the signals in the gut-brain-axis by creating an environment where intestinal distension is exaggerated. This effect likely contributes to the sustained weight loss and alterations in feeding patterns observed after VSG. Our findings have important implications for the development of less invasive therapies for obesity that target the gut-brain-axis and feeding behavior.

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