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Role of vagal fibers in weight control and nutrient absorption

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In this issue of the journal, Miyato et al. present an interesting study highlighting the role of vagus nerve in visceral fat homeostasis. Using CT imaging, they assessed changes in visceral fat (VFA) and subcutaneous fat (SFA) in 77 patients who had undergone either a total gastrectomy (n=14) or a distal gastrectomy (n=63) for stage I cancer at a single institution over a 6 year period. As expected, the reduction in VFA was significantly greater after a total gastrectomy. Moreover, in the distal gastrectomy group, the 33 patients with a concomitant truncal vagotomy lost significantly more total weight as well as VFA, but not SFA. They conclude that the vagus nerve has a role in regulating weight *by modulating VFA*. These changes were independent of extent of nodal dissection, pylorus preservation, or the reconstruction technique (Billroth-I vs. Roux-en-Y) [1]. While vagal preservation may be important for patients undergoing gastrectomy for gastric cancer, these data elicit the broader implication for vagotomy as a potential therapeutic approach for weight loss. The *selective* reduction in VFA warrants special emphasis, given that VFA is considered the harbinger of adverse metabolic outcomes of obesity. Several studies have substantiated the greater correlation of adverse health events to visceral fat volume, rather than BMI or total weight [2]. Thus, as the propellant for bariatric surgery shifts towards an improvement in metabolic parameters over simple weight loss, approaches that specifically reduce VFA could offer considerable therapeutic value.

The observation that the vagus nerve regulates body weight dates back to early experiments of Dragstedt in the 1930's, during his pioneering work popularizing vagotomy for surgical treatment of peptic ulcer disease. The subsequent establishment of vagotomy for treatment of ulcers fueled an era of surgical obsession with the nerve, with various modifications that not only challenged surgeons technically, but also helped place surgeons as scientists uniquely positioned to study human disease. During these heydays of vagotomy, the procedure was in fact tried as a stand-alone procedure for obesity. In his early studies in Sweden, Kral showed that vagotomy without a drainage procedure can lead to an average weight loss of 19.6kg (approximately 40 lbs), with a wide range however (2–34 kg) [3]. Importantly, Kral went on to show improvements in glucose homeostasis in these patients, documenting the desired metabolic benefits [4]. Vagotomy for weight loss however, never gained much popularity due to concerns for motility side effects as well as greater weight loss achieved by the evolving gastric bypass operation.

With the worsening obesity and diabetic epidemics that now affects 30% and 11% of the US adult population respectively, there has been a resurgence of interest in vagal interventions

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considering their weight-reducing potential. Small studies of laparoscopic vagotomy have reported 18% excess body weight loss at 18 months, probably too low to justify this as a primary bariatric procedure. However, these results have led others to augment the outcome of restrictive only bariatric procedures such as adjustable gastric banding or vertical banded gastroplasty by including a vagotomy. These studies have in fact shown that the added vagotomy modestly improves weight loss, but the study population is still small with limited follow-up [3]. Additionally, GI dysmotility remains as major concern with either stand-alone or adjunct vagotomy. Novel approaches have therefore been tried to spare the vagus from permanent surgical division by using an implantable device to block vagal signaling with electrical pulses. In this procedure (VBLOC therapy), electrodes are placed laparoscopically on both vagal trunks at the gastroesophageal junction to electrically interrupt neural transmission. Weight loss at 6 months is however modest at 14% [5].

Our approach has been to study techniques that selectively disrupt the vagal afferent fibers, without interrupting the important efferent pathways. It is important to remember that 80% of vagal fibers are in fact afferent and convey signals related to hunger as well as satiety to the hypothalamus. Because vagotomy is associated with weight loss, the overall balance of afferent signals appears to favor hunger, with their disruption leading to a greater sense of satiety.

Our studies examining selective vagal afferent ablation in rats as an approach to treat obesity and diabetes provide an intriguing complement to the report by Miyato et al. We have found that capsaicin, a compound found in hot chili peppers that selectively destroys vagal afferent fibers, disrupts the normal circadian expression rhythm of intestinal nutrient transporters [6]. Of particular note, capsaicin treatment also produced a modest weight reduction in normal, non-obese rats maintained for 11 months (unpublished data). Importantly, there was a preferential loss of visceral fat similar to that found in humans by Miyato et al [1]. Further studies are anticipated to extend these outcomes to pathological models.

It thus appears that the vagus nerve has a critical role in weight and nutrient homeostasis, and we as surgeons, are again in a fortuitous position to lead the way in novel vagal-based therapy for the new surgical disease of the 21st century: obesity and metabolic disorders.

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