What happens in the vagus, . . .?

Nicholas T. Bello and Timothy H. Moran

Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland

THE VAGAL AFFERENTS THAT INNERVATE the gastrointestinal (GI) tract play a major role in conveying meal-related signals to the central nervous system. Functional alterations of these sensory neurons have been implicated in obesity (17) and eating disorders (9). In the past, chemical or surgical deafferentation methods have been used to examine the specific contribution of these GI afferents to the negative control of food intake. The findings from these “loss of function” experiments, although somewhat contingent on the method of deafferentation, have yielded insight into the roles of this heterogeneous population of afferent fibers. The excitotoxin capsaicin, for example, which selectively destroys unmyelinated afferent fibers (12), has been shown to increase the initial consumption of an unfamiliar high-fat diet, an effect that attenuates with repeated diet exposure (4). In contrast, surgical subdiaphragmatic vagal deafferentation has been demonstrated to increase both meal size and decrease meal number, an effect that was not dependent on the novelty of the diet (18).

To further examine how signals conveyed by vagal afferents contribute to meal-related feeding controls, Chi and Powley (6) in this issue of the American Journal of Physiology-Regulatory, Integrative and Comparative Physiology have employed a genetic method that results in a reduction of GI afferent innervation, the neurotrophin-4 (NT-4) knockout mouse. NT-4 is a neurotrophic factor closely related to brain-derived neurotrophic factor and nerve growth factor, which have been shown to be critical for neuronal development and regulation of neuronal plasticity (14, 16). In addition to being a specific chemoattractant for dorsal root ganglion neurons (14), NT-4 has been demonstrated to be a potent stimulator of neurite outgrowth of adult mouse nodose ganglion in vitro, suggesting it may be involved in trophic support following regeneration or synaptic reorganization (19). NT-4 knockout mice have significant reductions in the number of nodose ganglion neurons [to 45% of levels in wild-type (WT) mice] and reductions in afferent vagal terminals both in the duodenum (10% of WT) and ileum (9% of WT) without any alteration in motor neurons (10). Previously, it has been shown that NT-4 knockout mice fed a standard diet exhibit disruptions in short-term meal-related feedback controls (i.e., increases in meal duration and size), while the long-term maintenance of body weight and calories remains intact (i.e., no differences from WT controls) (10).

The current study by Chi and Powley (6) examined the contribution of vagal afferent information to the negative feedback actions of two representative macronutrients, fat and carbohydrates, using NT-4 knockout mice. To temporally relate food consumption with the gastric presence of the nutrient, the mice were exposed to yoked infusion paradigms in which the mice were exposed to yoked infusion paradigms in which late food consumption with the gastric presence of the nutrient, carbohydrates, using NT-4 knockout mice. To temporally reorganize the overall amount of food intake. In the present work (6),...
increases in intake on fat infusion days did not result in significant increases in the body weights of the NT-4 knockout mice. Since, the fat infusions did not occur on consecutive days but every 2–3 days, the lack of weight gain is likely due to adjustments in caloric intake by the NT-4 knockout mice on the noninfusion days. Data from experiments examining the ability of jejunal fat infusions to affect food intake suggest the possibility that vagal afferent feedback can, in fact, play a role in longer-term controls of food intake and body weight. Jejunal infusion of linoleic acid, a LCFFA, produces suppressions of food intake beyond their caloric value resulting in decreases in body weight (7). This suppressive effect of jejunal-infused linoleic acid on food intake has been shown to be attenuated by deafferentation of the celiac branch of the vagus (8), suggesting that alteration in vagal afferent signaling can result in longer-term changes in food intake sufficient for affecting body weight. Future investigation into whether consecutive days of gastric fat infusions would lead to long-term body weight changes in NT-4 mice would be helpful in addressing whether short-term meal alterations, as a result of decreased GI vagal innervation, can translate into long-term body weight changes, a finding that would have important implication for the current obesity epidemic.

REFERENCES