Nutrient sensing in the human gastrointestinal lumen - role in appetite regulation and implications for obesity

C. Feinle-Bisset, Discipline of Medicine & NHMRC CCRE in Nutritional Physiology, University of Adelaide, Adelaide, SA 5000, Australia. (Introduced by Paul Bertrand)

The gastrointestinal (GI) tract plays an important role in the regulation of appetite and energy intake. The presence of nutrients in the small intestinal lumen is associated with the modulation of GI motor and hormone functions, and particularly the magnitude of the stimulation of pyloric pressures (associated with the slowing of gastric emptying) and the release of gut hormones have been identified as independent determinants of acute energy intake in humans.

There is evidence from both animals and humans that these GI functions can adapt to both dietary restriction and excess nutrient exposure, modifying the sensitivity to nutrient and hormonal stimuli, with potential implications for the regulation of energy intake. For example, consumption of a high-fat, high-energy diet accelerates gastric emptying and small intestinal transit of a fat-containing meal. Conversely, recent evidence from our laboratory indicates that consumption of a very-low calorie diet for 4 days markedly enhances the stimulation of pyloric pressures and plasma PYY, and the suppression of ghrelin, in response to duodenal lipid, associated with significant reductions in hunger and energy intake.

The discovery that fatty acids can be also be detected by receptors in the oral cavity of both animals and humans, is providing exciting new opportunities to evaluate mechanisms underlying, as well as factors contributing to, obesity. Since obese individuals have an increased energy/nutrient intake, it is conceivable that they may have a reduced ability to sense nutrients, both in the oral cavity and the lumen of the GI tract, associated with reduced modulation of gut functions, thus, compromising the capacity to limit their energy intake. In support, our recent studies demonstrate that habitual fat and energy intake and BMI are inversely related to the ability to taste fat in the oral cavity in healthy humans. Furthermore, obese individuals have reduced pyloric and CCK responses to intraduodenal oleic acid infusion, combined with higher oral taste thresholds for fatty acids, compared with lean individuals, and the oral and small intestinal responses to fat are related. Finally, preliminary evidence suggests that oral fat sensitivity can be modified experimentally by diet, *i.e.* both enhanced in response to a low-energy diet and reduced in response to a high-fat diet. Thus, while fat has potent effects on those GI functions that contribute to energy intake regulation, these effects are diminished by a high-fat, high-energy diet.

High-protein diets have received much attention in recent years, because they achieve significant weight loss and improve blood glucose control in obese individuals, even when ingested *ad libitum*. However, in contrast to lipid, relatively little is known about the GI mechanisms mediating the effects of protein. While a number of studies report marked stimulation of CCK, GLP-1 and PYY release after high-protein meals, the effects vary between studies, most likely due to the use of unphysiologically high amounts of proteins as well as proteins from different food sources. We have recently shown that intraduodenal infusion of whey protein resulted in a dose-related release of CCK and GLP-1, stimulation of pyloric pressures, associated with a dose-related suppression of subsequent energy intake. Moreover, due to the release of both insulin and glucagon, blood glucose was maintained in the normoglycaemic range.

When ingested orally, dietary protein appears to be much more satiating than fat or carbohydrate, and we have recently demonstrated that a high-protein meal is significantly more satiating than equally palatable high-fat or high-carbohydrate meals in both lean and obese subjects. Interestingly, while the obese had a greater energy intake in response to the high-fat and high-carbohydrate meals compared with the lean, energy intake in response to the protein-meal did not differ between lean and obese subjects, suggesting that the satiating effect of protein is maintained in the obese. Thus, in contrast to fat, it appears that prolonged exposure to a high-protein diet is not associated with adaptive responses.

Much further research is required to investigate the mechanisms underlying the effects of nutrients on energy intake regulation to determine whether these findings can be translated into efficient, novel approaches to the prevention and management of obesity.