“Entero-Sensory” Detection of Foodstuffs

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The small intestine has long been thought to be only a selective barrier between external and internal environments whose the function was limited to the digestion of food and the absorption of nutrients. It is now well established that the small intestine is a highly sophisticated organ that multiply affects the body. The contribution of the gut to regulation of energy balance through the gut–brain–periphery axis is of special interest. The most recent progress in this field of has been identification of a set of intestinal chemoreceptors with high binding specificity for digestion-related luminal stimuli. This sensing system is expressed in enteroendocrine cells strategically located throughout the intestinal mucosa. During the postprandial period, stimulation of these cells induces the release of informative molecules (i.e. hormones and neuromediators) which evoke adaptive responses.

Enterochromaffin cells (EC) constitute the largest enteroendocrine cell population. Mainly located in the proximal part of the small intestine (i.e. duodenum), EC cells produce and secrete serotonin (5-hydroxytryptamine or 5-HT) and, to a lesser extent, other mediators (e.g. acetylcholine, vasoactive intestinal polypeptide, among others) with ~90 % of the total body content of 5-HT of intestinal origin [1]. This neurotransmitter has several physiological effects: via paracrine regulation and enteric nerves stimulation, intestinal 5-HT modulates digestive function during the post-prandial period by controlling electrogenic exchanges of enterocyte ion carriers, production of mucopolysaccharides by mucus cells, gastrointestinal motility,

and exocrine pancreatic secretions [1] (Fig. 1). 5-HT also affects the regulation of eating behavior [2]. 5-HT release by EC cells can be triggered by luminal stimuli [3, 4] interacting with EC cell chemoreceptors, some of which were first identified in gustatory and olfactory mucosa (Fig. 1). For instance, the bitter taste receptor T2R1 expressed in taste bud cells is also found in neoplastic human EC cells in which exposure to the prototypic bitter tastant caffeine evokes 5-HT release [3]. Similarly, olfactants, for example eugenol or thymol, which bind and activate the olfactory receptors OR73 and OR1G1 trigger EC cells secretion [4]. In brief, the small intestine is able to sense, “taste”, and “smell” changes occurring in its luminal environment during digestion of foodstuffs. Although the relative physiological importance of this “enterosensory” system is not yet fully understood, it is likely to be involved in optimization of digestive function and regulation of eating behavior and energy balance.

In this issue, Primeaux et al. [5] report that duodenal expression of genes encoding three olfactory receptors (OR 1744, OR1507, and OR124) is induced in Osborne–Mendel (OM) rats, but not S5B/P1 (S5B) rats, subjected to a high-fat diet (HFD). Because OM rats become obese whereas S5B rats are obesity-resistant when exposed to an HFD [6], this result suggests that obesity susceptibility to a HFD might be related to intestinal chemo-detection via odorant receptors. These data build on observed differences between peripheral chemoreception of OM and S5Brats. For instance, responsiveness of taste bud cells to free fatty acids differs profoundly between these two rat strains, because cells from S5B rats are more sensitive than those from OM rats [7]. Similarly, intraduodenal infusions of lipids have a greater satiating effect in S5B rats than in OM animals [8]. These data suggest that sensitivity of the gustatory papillae and the small intestine to dietary lipids is

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Fig. 1 Sensing of the luminal environment of the small intestine by enterochromaffin cells. Interaction of nutrients, bile acids (BA), tastants, or odorants with specific receptors located on the apical side of enterochromaffin cells induces a rapid rise in intracellular ionized

calcium levels (Ca^{2+}) which, in turn, induces release of serotonin (5-HT). Via paracrine regulation and activation of enteric nerves, 5-HT modulates digestive functions

different in the two strains. This difference between detection thresholds (desensitization) for lipids might contribute to fat overeating and the subsequent obesity observed for OM rats fed an HFD. A similar mechanism might also exist for other luminal chemosensors, including intestinal olfactory receptors.

Many questions remain to be answered regarding the observation of Primeaux and co-workers. For example, the relative abundance of OR 1744, OR1507, and OR124 proteins was not reported. Further, the ligands of these OR were not identified. To better understand the origin of this strain difference, further study of the genetic and endocrine disturbances induced by a greater fat mass is necessary. The literature suggests that obesity-mediated disturbances in endocrine status (e.g. changes in plasma leptin or GLP-1 levels) may affect peripheral chemoreception of specific nutrients. In mice, leptin selectively reduces sweet taste sensitivity by affecting responsiveness of taste bud sweet taste receptors to sweet compounds [9]. Sweet, sour [10], and lipids [11] detection thresholds are also substantially different in GLP-1 receptor-null mice. Hypo-sensitivity of sweet and fat receptors might lead to overconsumption of palatable energy-dense foods to achieve satiation. Although these data focus on sense of taste, hormonal dysregulation associated with obesity might also affect intestinal chemoreception, including the function of olfactory receptors.

A “functional continuum” along the oro–naso–intestinal tract, responsible for real-time analysis of the quality and quantity of ingested foods, might exist, although molecular mechanisms and physiological consequences of this integrated sensing system, especially consequences on eating behavior (preference, satiation, satiety, addiction), remain to be fully explained. A continuum being “a set of elements such that one can pass from one to another, continuously”, it can be postulated that fundamental knowledge obtained at a specific level of the continuum (e.g. regulation of OR in the duodenum as reported in Ref. [5]) might be present at other levels. Despite limitations because of the functional specificity of olfactory, lingual, and intestinal epithelia, investigation of such a model might furnish unexpected results regarding chemoreception of food components and their final effect on health.

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