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Fundamentals of Neurogastroenterology: Physiology/Motility – Sensation

Guy Boeckxstaens,[1] Michael Camilleri,[2] Daniel Sifrim,[3] Lesley A. Houghton,[4] Sigrid Elsenbruch,[5] Greger Lindberg,[6] Fernando Azpiroz,[7] and Henry P. Parkman[8]

[1]Department of Gastroenterology, Translational Research Center for Gastrointestinal Disorders, University Hospital Leuven, KU Leuven, Leuven, Belgium; [2]Clinical Enteric Neuroscience Translational and Epidemiological Research (CENTER) Program, Mayo Clinic, Rochester, Minnesota; [3]Wingate Institute of Neurogastroenterology, Bart's and the London School of Medicine, Queen Mary, University of London, London, United Kingdom; [4]Division of Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, Florida; [5]Institute of Medical Psychology and Behavioral Immunobiology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany; [6]Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Huddinge, Stockholm, Sweden; [7]Digestive Diseases Department, University Hospital Vall D'Hebron, Autonomous University of Barcelona, Barcelona, Spain; [8]Department of Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania

The fundamental gastrointestinal functions include motility, sensation, absorption, secretion, digestion, and intestinal barrier function. Digestion of food and absorption of nutrients normally occurs without conscious perception. Symptoms of functional gastrointestinal disorders often are triggered by meal intake, suggesting abnormalities in the physiological processes are involved in the generation of symptoms. In this article, normal physiology and pathophysiology of gastrointestinal function, and the processes underlying symptom generation, are critically reviewed. The functions of each anatomic region of the digestive tract are summarized. The pathophysiology of perception, motility, mucosal barrier, and secretion in functional gastrointestinal disorders as well as effects of food, meal intake, and microbiota on gastrointestinal motility and sensation are discussed. Genetic mechanisms associated with visceral pain and motor functions in health and functional gastrointestinal disorders are reviewed. Understanding the basis for digestive tract functions is essential to understand dysfunctions in functional gastrointestinal disorders.

Keywords: Gastrointestinal Motility; Sensation; Absorption; Secretion.

The complex process of digestion of food and absorption of nutrients normally occurs without conscious perception. Symptoms reported by patients with functional gastrointestinal disorders often are triggered by meal intake, suggesting that abnormalities in the physiological processes involved in digestion are involved. Evaluation of sensory function and gastrointestinal motility aims to identify abnormalities in neuromuscular function to ultimately guide therapeutic management. In this article, more general and region-specific aspects of normal physiology and pathophysiology, and the processes underlying symptom generation, are critically discussed.

Normal Physiology: Main Components

The fundamental gastrointestinal functions include sensation, motility, digestion, absorption, and secretion.

Perception

Peripheral nerves, afferent signaling. Human beings have the capability to consciously perceive a variety of highly differentiated sensations originating from the upper and lower sections of the gut. In the upper gastrointestinal (GI) tract, specific sensations amenable to conscious awareness range from temperature, taste, hunger, fullness, satiety, nausea, and pain. In the small and large bowel, distensions and contractions cause aversive sensations such as nausea, bloating, cramping, discomfort, and pain. Only a minority of the sensory information arising from the gastrointestinal tract is perceived consciously. The majority (estimated to be >90%) of afferent sensory information from the viscera serves homeostatic functions.

The gastrointestinal tract is densely innervated to provide information on its luminal contents, processes regulating digestion and absorption, and potential threats.[1] This information was collected by intrinsic and extrinsic afferent nerves and regulates physiological responses for homeostasis and health. In brief, sensory neurons of the enteric nervous system activate local responses. Extrinsic afferent nerves transmit sensory information to the spinal cord or brainstem for further processing and integration (for brain processing, see later). In general, the extrinsic afferent innervation of the gut is conducted through the vagus nerve and the spinal afferents. The cell bodies of the vagus afferents are in the nodose ganglion, and mainly project to the nucleus of the solitary tract. Vagovagal reflexes result in stimulation of vagal efferents in the dorsal motor nucleus of the vagus nerve. Two examples of vagovagal reflexes are transient lower esophageal sphincter relaxations and meal-induced gastric accommodation.

Abbreviations used in this paper: **FGID, functional gastrointestinal disorder; GI, gastrointestinal; GNb3, Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit β-3; IBS, irritable bowel syndrome; LES, lower esophageal sphincter; LM, longitudinal muscle; MMC, migrating motor complex.**

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The spinal afferents have cell bodies in dorsal root ganglia. These afferents are thoracolumbar (with neurons in thoracolumbar dorsal root ganglia and projections via splanchnic nerves and mesenteric/colonic/hypogastric nerves) or lumbosacral (with cell bodies in lumbosacral dorsal root ganglia and projections via pelvic nerves and rectal nerves to the distal bowel) nerves, which synapse in the spinal cord and send information to the brainstem. Of note, each region of the GI tract receives dual sensory innervation reflecting functional connectivity for the distribution of extrinsic primary afferents in these pathways.

Elucidating the afferent and central mechanisms mediating the specific sensation of visceral hyperalgesia or pain is relevant in the context of the functional gastrointestinal disorders (FGIDs), especially irritable bowel syndrome (IBS) and functional dyspepsia.[2,3] The sensation of pain appears to be mediated by different afferents depending on the location of the GI tract undergoing the noxious stimulus. Pain from the rectum primarily involves pelvic pathways; more proximal intestinal sensations are mediated by thoracolumbar spinal afferents. Inflammation (or inflammatory mediators) can change both the response properties of specific classes of sensory neurons and the involvement of specific ascending pathways, which is relevant in post-inflammatory hypersensitivity and postinfectious IBS.[4]

For the sensations of hunger, satiety, fullness, and nausea, which play a prominent role in functional gastroduodenal disorders, vagal afferent pathways play a primary role. Vagal mucosal afferent pathways are activated by enteroendocrine cell mediators including cholecystokinin, ghrelin, and glucagon-like peptide-1, which regulate food intake and satiety.[1] Ghrelin is released from gastric endocrine cells and inhibits intraganglionic laminar endings located in myenteric ganglia. Abdominal vagal afferents can contribute to nausea and vomiting, at least in part through effects of 5-hydroxytryptamine released by enterochromaffin cells.[1]

Multiple or multimodal ascending and descending pathways are involved in gastrointestinal sensation through bottom-up and top-down connections between the central nervous system and the GI tract along the brain–gut axis.

Brain processing. Within the brain, the multiple facets that define the conscious experience of pain or other sensations are shaped, involving sensory–discriminative as well as affective–motivational aspects, behavioral–motor responses, and cognitive components. Multiple brain regions and interconnected networks mediate normal and disturbed responses to visceral stimulation. From the spinal cord, nociceptive ascending signals from the gut reach the brain via the anterolateral and dorsal column pathways.[5] The spinothalamic tract projects to the ventral nuclei of the thalamus and the medial thalamus and then to the primary and secondary somatosensory cortices. These structures primarily mediate the sensory–discriminatory aspects of noxious stimulation, including information regarding intensity, duration, and location. Affective–motivational aspects of pain probably are shaped via connections between the medial thalamus and the limbic system, including the anterior cingulate cortex as well as the midbrain, including the periaqueductal gray.

The spinoreticular and spinomesencephalic tracts are additional anterolateral afferent systems that conduct sensory information to various loci within the brainstem, mediating reflexive, affective, and motivational consequences of noxious stimulation. Other cortical and subcortical brain regions in normal and abnormal visceral stimulus processing include the insula, the dorsolateral and ventrolateral prefrontal cortices, and the amygdala. These regions play a role in modulation of the response to pain by emotions such as stress and cognitions such as expectations in healthy human beings, as well as in patients with chronic pain or hyperalgesia. Descending corticolimbic pain modulation via inhibitory pathways involving the brainstem modulates afferent visceral signaling. Disturbed endogenous pain modulation probably plays a role in abnormal brain responsiveness to visceral pain stimuli in FGIDs.[6,7]

Motility

The major functions of human digestive tract motility are to accomplish propulsion along the gut, to mix gut contents with digestive secretions and expose them to the absorptive surface, to facilitate temporary storage in certain regions of the gut, to prevent retrograde movement of contents from one region to another, and to dispose of residues.

Anatomic and functional considerations. In each region of the gastrointestinal tract, the muscle layers of the gut wall and their innervation are adapted and organized to produce the specific motor patterns that serve the motor functions. The entire gastrointestinal tract interacts with the central nervous system and communication between various parts of the gut is facilitated by the longitudinal transmission of myogenic and neurogenic signals through the intrinsic neurons, as well as by reflex arcs through autonomic neurons. The aspects of gut motility that appear most relevant to the FGIDs are contractile activity and tone, compliance, and transit.

Contractile activity and tone. Phasic (short-duration) contractions originate from electrical spikes on the plateau phase of the slow-wave activity, and thus the frequency of the phasic contractions in the stomach and small intestine is dictated by the slow wave frequency. The slow-wave frequency varies along the length of the gastrointestinal tract; the maximum contractile frequency varies similarly. The maximum contractile frequency in the stomach is approximately 3 per minute, whereas in the small intestine the frequency decreases gradually from approximately 12 per minute in the duodenum to 7 per minute in the terminal ileum. A mixture of slow-wave frequencies is found in the colon and ranges from 1 to 12 per minute where the correlation between electrical and contractile activities is less clear. Whether the gut phasic contractions accomplish mainly mixing or propulsion depends on their temporal (eg, frequency, duration) and spatial (eg, spread of propagation) characteristics.[8]

A more prolonged state of contraction, referred to as *tone*, is not regulated by slow waves and may be recognized clearly in the proximal stomach (accommodation response to a meal) and the colon (response to feeding), as well as in