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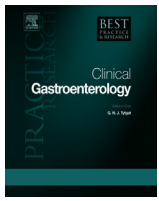

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# The stomach–brain axis

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A B S T R A C T

The stomach has distinct functions in relation to the ingestion and handling of solids and liquids. These functions include storage of the food before it is gradually emptied into the duodenum, mechanical crushing of larger food particles to increase the surface area, secretion of an acidic enzyme rich gastric juice and mixing the ingested food with the gastric juice. In addition, the stomach 'senses' the composition of the gastric content and this information is passed via the vagal nerve to the lateral hypothalamus and the limbic system, most likely as palatability signals that influence eating behaviour. Other sensory qualities related to the stimulation of gastric tension receptors are satiety and fullness. Receptors that respond to macronutrient content or gastric wall tension influence appetite and meal related hormone responses.

The ingestion of food – in contrast to an infusion of nutrients into the stomach – has distinct effects on the activation of specific brain regions. Brain areas such as thalamus, amygdala, putamen and praecuneus are activated by the ingestion of food. Gastric nutrient infusion evokes greater activation in the hippocampus and anterior cingulate. The brain integrates these interrelated neural and hormonal signals arising from the stomach as well as visual, olfactory and anticipatory stimuli that ultimately influence eating and other behavioural patterns. Furthermore, there is now good evidence from experimental studies that gastric afferents

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influence mood, and animal studies point towards the possibility that gastric dysfunction may be a risk factor for mood disorders such as anxiety and depression. The stomach is also not only colonised by *Helicobacter pylori* but a large array of bacteria. While there is sufficient evidence to suggest that *H. pylori* may alter caloric intake and mood, the role of other gastric microbiome for the brain function is unknown. To address this appropriate targeted gastric microbiome studies would be required instead of widely utilised opportunistic stool microbiome studies.

In summary, it is now well established that there are important links between the brain and the stomach that have significant effects on gastric function. However, the stomach also influences the brain. Disturbances in the crosstalk between the stomach and the brain may manifest as functional GI disorders while disturbances in the stomach–brain communication may also result in an altered regulation of satiety and as a consequence may affect eating behaviour and mood. These observations may enable the identification of novel therapies targeted at the gastroduodenum that positively alter brain function and treat or prevent conditions such as obesity or functional gastrointestinal disorders.

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## Introduction

The gastric phase of digestion is complex. The ingestion of food stimulates gastric acid secretion and changes the motility of the stomach. The high acidity of the gastric juice helps to kill potentially harmful bacterial contamination of the ingested food. The acidity of the gastric juice also activates pepsin that helps to digest ingested peptides. At the same time the fundic smooth muscles of the stomach initially relax via a vago-vagal reflex to allow to store the ingested nutrients in the proximal stomach while the distal stomach 'grinds' the gastric content and slowly delivers the chime into the duodenum where it is sensed and duodenogastric reflexes are stimulated that alter gastric function.

Following this initial relaxation (accommodation), the tone of the proximal stomach gradually increases and the ingested food is moved towards the distal stomach. The distal part is able to crush the soft food particles (antral mill) and controls the delivery of food into the duodenum. Thus, while the stomach appears to be a simple hollow dilated muscular organ between the oesophagus and the small bowel it serves important functions. Besides the exposure to the acidic gastric juice it ensures that the ingested nutrients are delivered into the duodenum at a rate that does not exceed the digestive capacity of the intestine [1–3].

Thus, well-coordinated gastric motor function is considered critical for the gastric phase of the digestion of food. This complex process is regulated by different and most likely redundant feedback mechanisms: The nutrient stimuli (volume and chemical properties of intraluminal nutrients) are sensed by mechosensory and chemosensory receptors. These receptors trigger either enteric (intrinsic) or vagal and sympathetic (extrinsic) pathways to regulate and control motor and secretory function sensed by specific receptors in the gut wall and initiate reflexes via either the intrinsic (enteric) nervous system or extrinsic (vagal and sympathetic) pathways, to control and coordinate gastric contractile activity [4].

### *Connections between the brain and the stomach: Gastric sensory functions and the cephalic phase of digestion*

The digestive tract – and not only the stomach – senses the gastrointestinal content including nutrients ingested with meals in various ways. Volume or wall tension [5,6], osmolality, acidity, and macronutrient composition represent the dominant sensory modalities [7,8]. This sensory information is partly mediated via the enteric nervous system [9] to facilitate secretion, absorption, and motility

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