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Review article

Brain imaging of visceral functions in healthy volunteers and IBS patients

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Abstract

From experience, most people know about a link between psychological processes and gastrointestinal sensory and motor functions. Cognitive processes (e.g., attention) as well as affective processes (e.g., fear) play a role in gastrointestinal sensations in healthy controls and patients with irritable bowel syndrome (IBS) alike. However, the exact nature of this relationship has not been completely understood yet. Brain imaging techniques allow for the study of brain–gut interactions in vivo. Accordingly, positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been widely used to study neural mechanisms underlying visceral sensations. This article will summarize the results of functional brain imaging studies in healthy controls and selected studies assessing the influence of psychological processes on gastrointestinal functions. Subsequently, this article will deal with those brain areas activated by visceral stimulation in IBS patients. Special attention will be paid to recently published studies concerning psychological factors and novel research questions.
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Keywords: Irritable bowel syndrome; Brain imaging; Emotions, Pain

Introduction

About 10 years ago, functional brain imaging was used for the first time to study brain-gut interactions. In the following years, positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been used widely to study neural mechanisms underlying visceral sensations in healthy volunteers as well as in patients with irritable bowel syndrome (IBS) [1]. PET and fMRI allow for the identification and localization of in-vivo activity with high anatomical precision. Aziz et al. [2] have been one of the first to describe cortical activation patterns caused by visceral stimulation (nonpainful and painful oesophageal stimulation) with PET.

In the following, a short summary of psychophysiological processes that may cause or influence IBS is given; for more details, see the articles by Musial et al. and Riedl et al. in this issue.

From experience, most people know about a link between emotions and gastrointestinal sensory and motor functions. Stress, anxiety or worry, for example, can lead to abdominal symptoms, such as chronic abdominal pain or changes in gastrointestinal motility and stool habits [3]. IBS patients often report of abdominal discomfort, cramps, or pain—abdominal pain is the predominant reason why such patients seek medical attention [4–6]. However, the only abnormality found is visceral hypersensitivity, which means that such patients feel pain after gut stimulation at lower intensities than healthy volunteers [7,8]. Up to 60% of IBS patients show lower pain thresholds in studies with rectal distension [9,10]. This type of hypersensitivity has been described for the whole gastrointestinal tract and, consequently, does not seem to be a local phenomenon [11]. In IBS patients, a high

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Table 1
Localization of cortical activity in healthy controls during rectal stimulation

					Brain activations						
Author	Year	Ref.	Modality	*N*	ACC	IC	PFC	Tha	SI/II	PCC	Brainstem
Silverman et al.	1997	[28]	PET	6	X	(X)	(X)	(X)	nr	nr	nr
Baciu et al.	1999	[16]	fMRI	8	X	X	X	nr	X	X	nr
Mertz et al.	2000	[15]	PET	16	X	X	X	X	nr	nr	nr
Naliboff et al.	2001	[24]	PET	12	X	X	X	X	nr	X	X
Hobday et al.	2001	[26]	fMRI	8	X	X	X	nr	X	nr	nr
Lotze et al.	2001	[27]	fMRI	8	X	X	X	(X)	SII	nr	nr
Yuan et al.	2003	[47]	fMRI	11	X	X	X	X	nr	nr	nr
Verne et al.	2003	[53]	fMRI	9	X	X	X	X	X	X	nr
Wilder-Smith et al.	2004	[9]	fMRI	10	X	X	X	X	X	X	nr
Andresen et al.	2005	[46]	fMRI	8	X	X	X	X	X	nr	nr

Tha, Thalamus; PCC, posterior cingulate cortex; (), nonsignificant activation of some extend; na, no activation; nr, not reported.

incidence (50–80%) of psychological disorders can be found, such as heightened anxiety, depression, somatisation, dysthymia, and panic disorders [4]. Additionally, other nongastrointestinal functional diseases are common, such as fibromyalgia or chronic fatigue syndrome [12]. About 50–90% of IBS patients in gastroenterology clinics have at least one psychiatric disorder [11]. Furthermore, stressful life events have been shown to be associated with the rise of symptoms in IBS patients [13]. However, the exact interrelation between psychological factors on the one hand and visceral gastrointestinal functions on the other has not been completely understood yet. Some novel studies examine the connection between affective processes (e.g., fear and anxiety) and cognitive processes (e.g., attention) with the perception of visceral signals from the gut. In addition, disease attribution may also have an influence on visceral perception in IBS patients [10].

This article will give an overview of brain imaging studies of gastrointestinal functions in healthy people and in IBS patients. Its main focus will be on the circuit between psychological factors and gastrointestinal sensory functions. Special attention will be paid to recently published studies.

Brain imaging studies

Brain imaging studies use different methods to examine the role of the autonomic nervous system in healthy subjects and patients with IBS. For visceral stimulation, balloon distension [14–16], electrical stimulation [17], or acid infusion in the oesophagus [18] have been used. Furthermore, different parts of the gastrointestinal system were stimulated, such as the oesophagus [19,20], the gastric fundus [14,21,22], and the gastric antrum [23], as well as the sigmoid colon and rectum [15,24–27]. Also, different intensities of stimulation (nonpainful vs. painful) have been applied. Additionally, the impact of anticipated distension has been examined [24,28,29]. Some studies focused on gender differences in perception and cortical response to visceral stimulation [30–35].

The enormous differences in study designs described above make it difficult to compare study results.

Brain imaging studies in healthy volunteers

Brain imaging studies in healthy volunteers during rectal stimulation have quite consistently shown brain activations in the cingulate cortex, the insula, the prefrontal cortex (PFC), the primary and secondary somatosensory cortex (SI/II), and the thalamus (see Table 1).

In healthy people, various forms of emotional arousal (e.g., anxiety, fear or “stress”) have been found to have an influence on gastric [36,37] and rectal sensorimotor functions [38,39]. This “communication” between gut and brain is not only caused by the autonomic nervous system described above but also by neuroendocrine (hypothalamo-pituitary-adrenal axis) and neuroimmune pathways [40]. It is well known that psychological factors can influence pain perception and gastrointestinal functions [8]. Geeraerts et al. [37] showed that experimentally induced anxiety leads to lower gastric compliance and accommodation, as well as higher abdominal symptoms such as the feeling of fullness and bloating. Phillips et al. [20] studied the importance of the emotional context for cerebral activation during nonpainful oesophageal stimulation in eight healthy subjects using fMRI. They found higher activation in the anterior cingulate cortex (ACC) and the right insula cortex while volunteers viewed fearful faces (negative emotional condition), compared with volunteers viewing neutral faces (neutral emotional condition). In a second experiment, they found higher activations in the left ACC and the bilateral anterior insular cortex (IC) during high intensity fearful visual stimulus, compared with low intensity of fear expression. The high intensity emotional condition was associated with significantly greater oesophageal discomfort and anxiety. Yaguez et al. [41] explored the importance of anticipation in visceral pain with fMRI. They used a classic conditioning paradigm in which neutral (visual) stimuli (conditioned stimuli) were paired with painful oesophageal distension or air puff to the wrist (unconditioned stimuli) or nothing.

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