Psychosomatic Aspects of the Brain Function in Response to Visceral Stimulation

Toyohiro Hamaguchi, O.T.R., Ph. D.\textsuperscript{1,2}, Shin Fukudo, M.D., Ph. D.\textsuperscript{1}

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Abstract
Psychosocial factors, such as stress, abuse history, psychiatric disturbance, coping style, and learned illness behaviors, play an important role in functional gastrointestinal disorders in terms of symptom experience and clinical outcome. These psychosocial factors are influenced by and influence gastrointestinal disorders symptoms in a bidirectional manner as mediated through the brain-gut axis.

Recent Studies of brain imaging suggest pathways involved in visceral pain perception overlap with limbic pathways. These data may explain how psychological factors interact with irritable bowel syndrome. However, only limited information has been provided on the influence of gastrointestinal tract stimulation on the brain. We reviewed several brain regions including somatosensory, insula, anterior cingulate, and prefrontal cortices in response to visceral stimulations.

Introduction
Gastrointestinal sensory disorders are commonly referred to as gastrointestinal motility disorders or functional gastrointestinal disorders. Sensory and autonomic control of gastrointestinal motility are thought to be modulated by the central nervous system (CNS). Visceral discomfort reaches awareness via neural connections termed the brain-gut interactions. Pathophysiology of that upregulate afferent sensory signal intensity anywhere in this system could induce hypersensitivity, pain, and discomfort. These include stimulus amplification in the intestinal tract prior to the primary afferent nerve itself.

Recent studies of brain imaging suggest the pathways involved in visceral pain perception overlap with limbic pathways\textsuperscript{1-5}. These data may explain how psychological factors interact with gastrointestinal disorders. Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic abdominal pain and abnormal bowel habituation\textsuperscript{6,7}. Symptoms of IBS are often aggravated by stress, which alters colonic motility and visceral perception\textsuperscript{8,9}. The functional interaction between brain and gut is considered to be a major pathophysiology of IBS\textsuperscript{1,8,10}.

According to other recent studies, the

\textsuperscript{1} Department of Occupational Therapy, Niigata University of Health and Welfare, School of Health Sciences, 1398, Shimami, Niigata 950-3198, Japan
\textsuperscript{2} Department of Behavioral Medicine, Tohoku University Graduate School of Medicine, 2-1 Seiryo, Aoba, Sendai 980-8575, Japan.
Phone +81-22-717-8214, FAX +81-22-717-8214
Address for Correspondence:
Toyohiro Hamaguchi, O.T.R., Ph.D., Department of Occupational Therapy, Niigata University of Health and Welfare, School of Health Sciences, 1398, Shimami, Niigata 950-3198, Japan.
Phone +81-25-257-4447, FAX +81-25-257-4447
E-mail hamaguchi@nuhw.ac.jp
processing and modulation of visceral perception may be related to activity of the thalamus, insula cortex, anterior cingulate cortex (ACC), somatosensory cortex, especially the prefrontal cortex (PFC)
. It seem that activation of the hippocampus and the amygdala relates to memory of the pleasant or unpleasant stimulus likely the learning and/or conditioning. However, the brain areas related to initial programming for formation of visceral perception provoked by the visceral stimulation is still unknown. Here we reviewed the functional module of the brain in response to visceral stimulations.

**Activation of the primary and association sensory cortices in responses to visceral stimulation and somatosensory stimulation.**

Rectal stimulation resulted in bilateral activation of the inferior primary somatosensory, secondary somatosensory, sensory association, insula, periorbital, anterior cingulate and prefrontal cortices. Hobday et al. showed that rectal stimulation activates the inferior part of the somatosensory cortices (SI) which also activated by esophageal perception and swallowing. In contrast, anal canal stimulation activates the middle part of SI, which is just superior to the area for hand sensation. These studies suggest that the different processes of the perception of visceral and somatic system are represented differently in the cerebral cortex, that is, visceral and somatic perceptions are represented in the inferior and middle parts of the SI, respectively. Anal and rectal sensation resulted in a similar pattern of cortical activation, including areas involved with spatial discrimination, attention and affect. In monkeys, single neuron recordings from the cortex have demonstrated viscerosomatic convergence within the SI, but with the viscera only being represented within the inferior part of the SI. The differences in sensory perception from different regions can be explained by their different representation in the primary somatosensory cortex.

SI and secondary somatosensory cortex (SII) receive the direct projections from ventral posterior thalamic nuclei, it has usually been assumed that SI and SII were involved in parallel processing of tactile sensory information derived from this thalamic source of input. The SII receives afferents from the SII and also directly from the thalamus. There is evidence to suggest that for somatic sensation the functionally more important afferents are those from SI and that SII is involved in the serial secondary processing of sensory information after primary processing has occurred in SI. Magnetencephalography studies following esophageal stimulation showed only SII activation, suggesting that for visceral perception SII may be functionally more important than SI.

**Activity of the Insular cortex to visceral stimulation**

The insula as limbic sensory cortex, which is based on its association with visceral and autonomic function, its multimodal features and, particularly, its strong interconnections with hypothalamus, amygdala, cingulate and orbitofrontal cortices. Temperature sensation is regarded as a submodality of touch, but Craig et al. reported involvement of insular cortex rather than parietal somatosensory cortices. On the other hand, the insula activation in response to rectal distention was reported by Hobday et al., this could be due to processing of the affective aspects of rectal sensation, or as a result of visceral sensory-motor responses.

The insula cortex forms part of the limbic system, with efferent connections to both the cingulate and prefrontal cortices and afferent connections from thalamus. Lesions of the insula result in loss of the affective response but preservation of the spatial discriminative aspects of pain. Direct electrical stimulation of the insula at surgery results in visceral motor as well as
sensory responses which include abdominal pain and nausea. It is unknown, however, whether these visceral perceptions are a direct result of insula stimulation, or secondary to changes in visceral motor function.

Descending projections from insular cortex terminate in lamina I as well as in the same brainstem pre-autonomic and homeostatic sites noted above. Stimulation or lesions of insular cortex affect cardiorespiratory, gastrointestinal, sympathetic and thermoregulatory activity. In primates, the thalamic projection to the dorsal margin of the insula is contiguous anteriorly with the region that receives general (vagal) and special (gustatory) visceral input by way of the thalamic nucleus. The common source of ascending input to insular cortex in all mammals is the parabrachial nucleus, the brainstem homeostatic site that integrates both vagal and lamina I inputs; accordingly, the primordial role of insular cortex can be regarded as modulation of multimodal input to goal-directed, homeostatic motor processing in the hypothalamus, amygdala and other sites. Consonant with the enormous encephalization in primates, especially humans, primate enterocceptive sensory inputs, with a direct gustatory projection from the solitary nucleus to thalamus and a topographic, dedicated lamina I projection to thalamus. These pathways seem to provide a highly resolved enterocceptive representation of the body’s condition in humans, including the specific sensations of temperature, pain and visceral perception from the body.

**ACC and visceral perception**

The ACC universally activates in human studies of pain, both somatic and visceral. The ACC is also involved in autonomic responses. ACC stimulation by electrodes leads to autonomic responses that include cardiovascular and gastrointestinal motor responses. ACC stimulation is associated with nausea, vomiting, and bowel evacuation very similar to stress responses in animals. These responses are also typical of functional gastrointestinal symptoms, specifically IBS. In humans, surgical lesions of the ACC reduce the suffering associated with chronic pain (the affective portion of pain) without eliminating the detection of pain. By positron emission tomography (PET) scanning, ACC activity has also been linked to self-induced sadness. Hypnosis to increase the unpleasantness of painful thermal stimulation also increases ACC activation, measured by PET.

The ACC forms part of the limbic system and has also been shown in PET studies to be activated by sad emotions, and to be activated during depression. Esophageal stimulation have caused ACC activation during non-painful visceral perception. The ACC representation of non-painful visceral stimuli could explain the greater autonomic reflexes and affective responses seen in response to visceral, compared with somatic stimulation. ACC activation has also been demonstrated with the anticipation of visceral and somatic pain. This suggests a role for the ACC in generating an affective response to a stimulus. In addition, the ACC has connections with the motor cortex, and it has been suggested that plays an important role in selecting appropriate behavioral response to stimulus.

The ACC is a brain center critically involved in pain and the affective responses to pain. It has direct neural connections to a variety of brain centers such as the limbic system (anterior thalamus and amygdala), autonomic effector areas (dorsal vagal motor nucleus, amygdala, and hypothalamus), and centers of arousal and pain modulation (periaqueductal gray and locus caeruleus). Given the association of the ACC with pain, affect, and gut motor function, its relevance to IBS is great.
PFC activation to visceral perception and emotion

The PFC is involved with cognition and memory, and receives inputs from the sensory association cortex. The PFC is thought to serve higher executive functions in pain perception. We reported that distention of the descending colon induces visceral perception and emotion and that these changes significantly correlate with activation of specific regions in the brain including the limbic system and the association cortex, especially the PFC (Figure 1).

The PFC has recently been considered to be projected area of visceral perception and signals from visceral organs are projected to the PFC through the lateral thalamic nucleus group11,46. An alternative interpretation is that the dorsolateral PFC redirects attention away from pain, as it has been implicated in general attentional processes47,48. PFC mechanisms may play a role in triggering opioid release in the midbrain. In addition, it has been suggested that the PFC is responsible for evaluating given stimulations against previous experience and accumulated memory and may be the final point where the exact meaning of each stimulation (comfort or discomfort) is determined49,50. Visceral stimuli possibly cause associated learning of the visceral perception through activation of the PFC.

Conclusions

CNS processing of afferent (sensory) information may be abnormal in patients with IBS, causing overexpression of visceral afferent stimuli. Previous studies of visceral and somatic pain using PET or fMRI to measure regional cerebral blood flow have suggested that the ACC, PFC, insular cortex, and thalamus are important in pain perception. Studies of visceral pain have generally suggested that these same brain centers are important in sensation. However, there are many unknown points of processing and modulation of visceral perception, accompanying emotions, and about its pathophysiology. We need some ideas basis for the volitional modulation of feelings, emotion and efferent activity affecting the taste of body that clearly emphasizes the role of the body in human

![Figure 1. Parametric maps showing brain activation in 15 healthy volunteers during colonic distention. Regions of activation (gray areas) were superimposed on Talairach-Tournoux stereotaxic atlas of the human brain. Regions of the brain that were activated during colonic distention with 40 mmHg comprised the putamen, thalamus, cerebellum, caudate body, superior frontal gyrus, anterior cingulate gyrus, postcentral gyrus (Broadmann Area: BA 40), and inferior parietal gyrus (BA 40).]
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