Brain-Gut Interaction and Psychological Factors
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Abstract
Functional bowel disorders are commonly referred to as gastrointestinal motility disorders or gastrointestinal sensory disorders. Autonomic control of gastrointestinal motility and sensory are thought to be modulated by central nerves system.

Visceral pain sensitivity has been called a biological marker for Irritable bowel syndrome (IBS). Recently developed symptom-based criteria provide the tools necessary to make a diagnosis and treatments.

Psychological factors influence pain thresholds in patients with IBS. Consistent with the observations in both patients and doctors that psychosocial disturbances seem to precede the onset or exacerbation of gut symptoms, researches have consistently found high levels of emotional distress in a proportion of patients with IBS and other functional gastrointestinal disorders. The precise underlying pathophysiology of IBS remains unknown. This article is a review of the psychological influences on visceral perception for background of IBS.

Introduction
Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic abdominal pain and abnormal bowel habituation 1, 2, 3, 4. Symptoms of IBS are often aggravated by stress, which alters colonic motility and visceral perception 3, 5, 6. In addition, the functional relation between the brain and gut is considered to be a major pathophysiology of IBS 5, 7, 8.

IBS patients have a higher proportion of abnormal personality patterns, greater illness behaviors, and lower positive stressful life event scores than IBS nonpatients and normals 3. Psychological factors influence pain thresholds in patients with IBS 9. Mental activity may modulate gut perception and overrides the effects of somatic stimulation on gut perception 6.

Advances in functional neuroimaging on IBS have provided an understanding of how the central nervous system responds to and modulates visceral afferent signals 10-14. A study using positron emission tomography (PET) has shown that rectal distention activates the anterior cingulate cortex (ACC) in healthy subjects but not in IBS patients 8. Another study using functional magnetic resonance imaging (fMRI)
has indicated that IBS patients show more activated ACC in response to rectal distention than normal subjects\(^7\).

In this review of experimental studies that delineate the underlying mechanisms of the stress response, we focused on brain-gut pathways and psychological factors in modulating visceral sensitivity induced by IBS.

**Relationship between Awaking and Gastrointestinal Motility**

IBS patients sometimes complain of sleep disturbance, depression, and various autonomic symptoms. Using an electroencephalogram (EEG) to evaluate brain activity while at rest and during mental arithmetic stress with pharmacologic neostigmine administered to IBS patients, inspection of the EEG showed significantly greater EEG abnormality in the IBS patients than in the healthy controls\(^15\).

Continuous 72-h recordings of duodenojejunal contractile activity were obtained that patients with IBS defecation was significantly prolonged with a greater number of voluntary abdominal contractions than in healthy controls\(^16\). Prolonged ambulant monitoring of proximal bowel motor activity were defined the striking difference in motility between the sleeping and waking state and shown that abnormalities associated with IBS\(^16\). In patients with IBS, if waking level is high, the abnormalities in gastrointestinal motility will be more induced, and if waking level is low, like a sleeping, the abnormalities in motility of the gut cannot arise easily.

**The Mental Abnormalities in IBS**

The association of psychosocial disturbances with more severe IBS is well recognized. IBS patients have a higher proportion of abnormal personality patterns, greater illness behaviors, and lower positive stressful life event scores than IBS nonpatients and normals\(^3\).

Blomhoff et al\(^17\) compared IBS patients with and without comorbid phobic anxiety to see if the comorbid disorder influenced brain information processing of auditory stimuli, and looked for possible consequences with respect to visceral sensitivity thresholds and disease severity. At the frontal midline electrode IBS patients had significantly enhanced N100 amplitude to stimuli, persisting after adjustment for age, current emotions, and personality traits\(^17\). In the frontal brain region, IBS patients seem to have a hyperreactivity to auditory stimuli compared with controls\(^17\).

Previous studies indicated that aberrant brain functioning might be an element of the IBS. It may elucidate a mechanism for brain-gut interaction by which psychosocial stress may influence visceral pain perception in non-psychiatric subjects with an intestinal motility disorder and also the efficacy of psychiatric treatment on IBS symptoms\(^18\).

**Brain Responses to Hypervigilance**

Patients with IBS show evidence of altered perceptual responses to visceral stimuli, consistent with altered processing of visceral afferent information by the brain\(^7,19\). Mertz et al\(^7\) reported that brain responses to anticipated and delivered rectal balloon distention were assessed. Using the PET, in 12 nonconstipated IBS patients and 12 healthy control subjects, regional cerebral blood flow (rCBF) responses to moderate rectal distention (45 mm Hg) and anticipated but undelivered distention were assessed before and after a series of repetitive noxious (60 mm Hg) sigmoid distentions. Compared with control subjects, patients with IBS showed lateralized activation of right prefrontal cortex; reduced activation of perigenual cortex, temporal lobe, and brain stem, but enhanced activation of rostral anterior cingulate and posterior cingulate cortices\(^7\). Patients with IBS show altered brain responses to rectal stimuli, regardless of whether these stimuli are actually delivered or simply
anticipated. These alterations are consistent with reported alterations in autonomic and perceptual responses and may be related to altered central noradrenergic modulation.

Paying attention to the gut may magnify perception of abdominal symptoms, but the actual influence of attention by anticipatory knowledge and distraction on gut perception remains poorly defined. Recent evidence demonstrating multiple regions of human cerebral cortex activated by pain has prompted speculation about their individual contributions to this complex experience. In pain affect, hypnotic suggestions were used to alter selectively the unpleasantness of noxious stimuli, without changing the perceived intensity. PET revealed significant changes in pain-evoked activity within ACC, consistent with the encoding of perceived unpleasantness, whereas primary somatosensory cortex activation was unaltered. These findings provide direct experimental evidence in humans linking frontal-lobe limbic activity with pain affect, as originally suggested by early clinical lesion studies.

The relationship between the central processes of classical conditioning and conditioned responses of the gastrointestinal function is incompletely understood in humans. We tested the hypothesis that the rectosigmoid motility becomes conditioned with anticipatory painful somatosensory stimulus and that characteristic brain areas become activated during anticipation. In nine right-handed healthy male subjects, a loud buzzer (CS, conditional stimulus) was paired with painful transcutaneous electrical nerve stimulation to the right hand (unconditional stimulus). Rectosigmoid muscle tone measured by the barostat as the intrabag volume, phasic contractions of the bowel measured as the number of phasic volume events (PVEs), and rCBF assessed by PET, were measured before and after conditioning. Following conditional trials, the bag volume after CS alone did not show significant changes between before and after the stimulus, but the number of PVEs after 2-minute interval of the CS alone was significantly greater than that before the stimulus. The PET data showed the conditioning elicited significant cerebral activation of the prefrontal, anterior cingulate, parietal and insula cortices. Rectosigmoid motility can be conditioned with increase in phasic contractions in humans.

The experience of pain arises from both physiological and psychological factors, including one’s beliefs and expectations. Thus, placebo treatments that have no intrinsic pharmacological effects may produce analgesia by altering expectations. However, controversy exists regarding whether placebos alter sensory pain transmission, pain affect, or simply produce compliance with the suggestions of investigators. Wager et al. reported that placebo analgesia was related to decreased brain activity in pain-sensitive brain regions, including the thalamus, insula, and anterior cingulate cortex, and was associated with increased activity during anticipation of pain in the prefrontal cortex, providing evidence that placebos alter the experience of pain.

Gastrointestinal Symptoms and Psychological Status in Humans

Perception thresholds to gastrointestinal distention can be affected by stress, psychological factors may play an important role in visceral perception. The cerebral evoked potential (CEP), which originates from the processing of afferent neural pathways, may reflect such higher-level processing of painful stimuli. Topographic study suggests that early peaks of CEP originate from deep central brain structures, whereas later peaks originate from the cortex. Kanazawa et al. reported that patients with functional dyspepsia have shorter peak latency of the late CEP component by esophageal electrical stimulation (ES), suggesting that patients with dyspepsia may
have an altered central processing of visceral perception\textsuperscript{26}. Kanazawa et al.\textsuperscript{27} reported that significant negative correlation between the late peak latency of CEP (N2) and the score of hypochondriasis in Minnesota Multiphasic Personality Inventory (MMPI) among healthy subjects and patients with functional dyspepsia in the univariate analysis with linear regression. These studies suggested that neurotic personality traits might be related to central processing of visceral perception, and cognitive patterns associated with some personality variables might promote visceral hypersensitivity via cortical processing\textsuperscript{27}.

**Psychotherapy for IBS**

Although the standard treatments for the IBS are medical, growing evidence indicates the substantial therapeutic value of psychological therapy\textsuperscript{28}. Twenty-four IBS outpatients were randomly assigned to the combination of standardized multicomponent behavioral therapy plus standard medical treatment (SMBT) or standard medical treatment alone (SMT). SMBT included IBS information and education, progressive muscle relaxation, training in illness-related cognitive coping strategies, problem-solving, and assertiveness training in 10 sessions over 10 wk\textsuperscript{28}. Pre- and post-treatment evaluations showed significantly greater IBS symptom reduction as measured by daily symptom diaries for the SMBT group than for the SMT group. Overall well-being significantly improved in the SMBT group but remained unchanged in the SMT group. Subjects in the SMBT group, unlike those in the SMT group, felt significantly more in control of their health, and quality of life was significantly improved in the SMBT group but remained unchanged in the SMT group\textsuperscript{28}. Even if the psychotherapy to IBS was successful, visceral hypersensitivity did not improve. The effect of the psychotherapy may have been effective in pathophysiology of the descending signal from the brain by psychological stress.

Cognitive-behavioral therapy (CBT) has received increased attention in light of this recent shift in the conceptualization of IBS. Toner reviewed to provide a critical review of controlled trials on CBT for IBS, and to discuss ways of further developing CBT interventions that are more clinically relevant and meaningful to health care providers and individuals with a diagnosis of IBS\textsuperscript{29}. A theme from a CBT intervention will be presented to illustrate how CBT interventions can be incorporated within a larger social context. A review of CBT for IBS lends some limited support for improvement in some IBS symptoms and associated psychosocial distress\textsuperscript{29}.

**Conclusions**

We conclude that the psychological factors previously attributed to the IBS are associated with patient status underlying the central nervous system. These factors may interact with physiologic disturbances in the bowel to determine how the illness is experienced and acted upon. Future studies will need to further develop more relevant treatment protocols that more fully integrate the patient’s perspective and challenge to clarify about brain-gut interaction.

**References**

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