



Painful Functional Bowel Disorders: Psychological Factors

Painful functional bowel syndromes such as irritable bowel syndrome and functional dyspepsia (FD) are characterized by unexplained persistent or recurrent pain in the abdomen. These syndromes are common across the world, affecting up to 15–20% of the population [3,10,12,15]. A number of mechanisms have been suggested to explain this syndrome, with two major themes dominating the clinical literature [10]. First, visceral hypersensitivity to mechanical distension is found in a significant subset of patients and appears to correlate with postprandial pain [14,18,22]. Second, psychological and psychiatric problems are very common and are widely held to have a pathogenic role, given that patients with FD are more anxious and depressed than healthy controls [3,12,15,21]. In a clinical study that included structured psychiatric interviews, the investigators found that 87% of patients with FD, compared to 25% of patients with organic dyspepsia, had a psychiatric diagnosis [15]. Psychological factors related to FD patients included major depressive disorders, anxiety disorders, and somatization [10,12].

Psychological Factors as Drivers of Gastrointestinal Symptoms

Anybody who has experienced “butterflies in the stomach” or stress-related changes in bowel habits can attest to the fact that the brain can influence gut function and sensation. Several clinical studies have suggested that psychosocial comorbidity is a major contributor to the severity of functional dyspepsia and its impact on quality of life [19]. These findings are reinforced by a considerable volume of experimental research that links stress and depression to altered gastrointestinal sensory and motor function [1,5,6,9,17]. Together, these findings have led to the widespread belief that the physical symptoms of FD reflect either somatization or stress-induced disturbance of upper-gastrointestinal physiology. Indeed, successful management of patients with functional bowel disorders requires careful attention to these psychosocial factors, often in consultation with mental health professionals.

Gastrointestinal Problems as Drivers of Psychological Symptoms

Despite the studies reviewed above, it is still unclear whether the association between functional bowel disorders and psychological symptoms represents a cause or effect. This question will require rigorously conducted longitudinal studies that document the onset of psychosocial dysfunction in relationship to visceral symptoms. Indeed, recent studies indicate that the relationship may be bidirectional—symptoms in the gut can lead to psychological issues, and vice versa. For example, investigators in Australia followed a cohort of patients prospectively for 12 years and found that among people free of a functional gastrointestinal disorder (FGID) at baseline, higher levels of anxiety at baseline represented a significant independent predictor of developing new-onset FGIDs 12 years later. Conversely, among people who did not have elevated levels of anxiety and depression at baseline, those with a FGID at baseline had significantly higher levels of anxiety and depression at follow-up [7]. These results are reinforced by experimental findings that suggest that minor, transient irritation of the gut in neonatal animals can lead to features of depression and anxiety that persist into adulthood [11].

The Brain-Gut Axis and Underlying Biological and Neural Circuits

The biological basis of these phenomena is only just beginning to be understood. The gut and brain communicate with each other by multiple means, including hormonal and neural mechanisms. An important example of hormonal involvement is CRF (corticotropin-releasing factor), a hormone secreted by the hypothalamus. Experimental alterations in secretion of CRF and expression of its receptor, CRF1, have been implicated in the pathophysiology of stress-related phenomena as well as anxiety, depression, and changes in gastrointestinal motility and visceral sensation [16,20]. A variety of CRF-receptor antagonists have also demonstrated the ability to block increased colonic activity and painful sensations induced by acute or chronic stress [13].

The gut also relays information to various important nuclei in the brain via ascending fibers in the vagus nerve, with potentially far-reaching consequences. The central amygdala, for instance, transforms noxious and stressful signals into behavioral and autonomic responses that include anxiety and depression. A recent report showed that a probiotic (*Lactobacillus rhamnosus*) can reduce stress-induced corticosterone and anxiety- and depression-related behavior in mice, but this beneficial effect can be prevented by vagotomy [2,8]. Electrical modulation of the vagus nerve has been approved by the U.S. Food and Drug Administration for the treatment of depression [4]. Thus, the vagus nerve can modulate emotional responses to gastrointestinal stimulation.

Facts and Fallacies

It is clear that psychological morbidity is common in patients with functional visceral pain conditions, and an understanding of this issue is crucial to the optimal management of these disorders. What is not clear is how much of this comorbidity is cause and effect. Nevertheless, recognition of this association has led to many unintended consequences, including the stigmatization of this syndrome as being “all in the head,” dismissal of patients’ suffering, and a lack of an organized approach to drug development. Much remains to be learned about the complex relationship between the “big brain” in the head and the “little brain” in the gut and how pathology in one can lead to changes in the other. Research in this area could significantly alter our clinical approach and treatment of these disorders.

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