The autonomic nervous system in functional bowel disorders

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Summary
Communications along the brain-gut axis involve neural pathways as well as immune and endocrine mechanisms. The two branches of the autonomic nervous system are integrated anatomically and functionally with visceral sensory pathways, and are responsible for the homeostatic regulation of gut function. The autonomic nervous system is also a major mediator of the visceral response to central influences such as psychological stress and other central factors.

As presently defined, functional disorders represent a constellation of symptoms, some of which suggest the presence of altered perception while other symptoms point to disordered gastrointestinal function as the cause of the symptoms. There have been a growing number of reports demonstrating disordered autonomic function in subgroups of functional bowel patients. While a number of different methods were used to assess autonomic function, they generally point to decreased vagal (parasympathetic) outflow or increased sympathetic activity in conditions usually associated with slow or decreased gastrointestinal motility. Other studies found either increased cholinergic activity or decreased sympathetic activity in patients with symptoms compatible with increased motor activity. Under certain conditions, altered autonomic balance (including low vagal tone and increased sympathetic activity) may also alter visceral perception.

Autonomic dysfunction could also represent the physiological pathway accounting for many of the extraintestinal symptoms seen in irritable bowel syndrome (IBS) patients, and for some of the frequent gastrointestinal complaints reported by patients with disorders such as chronic fatigue and fibromyalgia.

Introduction
In recent years, we have undergone a substantial shift in our conceptual definitions of what constitutes functional bowel disorders and IBS. In general, we now view these conditions as a group of disorders or clinical entities characterised by the presence of, to a varying degree, chronic pain, discomfort, and disordered gastrointestinal function. While this type of clinical definition corresponds to how these patients present, it has proved difficult to apply in the search for the pathophysiological factor(s) potentially involved in these conditions. While much remains to be done in that regard, it is increasingly accepted that these conditions are multifactorial, and that the symptoms experienced by two individual patients, although somewhat similar, may in fact result from a number of different aetiologies.

Abnormalities of motor and secretory function as well as altered enteric neural function can be identified in many patients with functional disorders (fig 1). However, most patients have no demonstrable motor dysfunction and the abnormalities that have been identified vary from study to study, each of these abnormalities being present in small and very specific groups of patients which do not represent the majority of those seen in clinical practice. The concept of these conditions being primarily motility or enteric nervous disorders is now also generally viewed as failing to account for many of the other characteristics that are present in these patients, in particular the discomfort and pain often reported in the presence of apparently normal gastrointestinal function.

In many patients with functional bowel disorders, the presence of altered visceral perception to various visceral stimuli, such as distension, has been identified. This issue of altered visceral perception in IBS is extensively discussed elsewhere. It remains important to point out that while a primary disorder of visceral sensory perception provides a plausible explanation for many of the symptoms reported in functional bowel disorders, it remains a largely unproved

Figure 1 Putative pathogenesis of dyspepsia. ANS, autonomic nervous system; HP, Helicobacter pylori.

Abbreviations used in this paper: IBS, irritable bowel syndrome.
Autonomic nervous system in functional bowel disorders

In assessing the role of the autonomic nervous system in functional bowel disorders (fig 2), it is essential to remember the homeostatic nature of autonomic function. While many local gastrointestinal stimuli will elicit a reflex response and reflexes whose involvement is essentially limited to the immediate region that was primarily stimulated, when more intense or potentially noxious stimuli occur, other systems, including the central nervous system, are also involved in addition to the gastrointestinal tract. Transmission of information to the central nervous system allows for elaboration of an integrated homeostatic response that may include a behavioural as well as a physiological response. In this type of response, both visceral and autonomic nervous pathways are essential.

Assessing autonomic function
A number of methods have been developed to assess specific aspects of autonomic nervous function. Some of the older approaches, which were very cumbersome and involved rather complex measurements, have been largely abandoned. In recent years, the development of techniques based on the autonomic modulation of heart rate function have largely replaced other methods because of their simplicity and validity as markers of vagal as well as sympathetic function. The use of techniques such as power spectral analysis of heart rate variability now provide a simple and accurate measure of the respective outflow of the vagal and sympathetic branches of the autonomic nervous system.

Functional bowel disorders: brain-gut, gut-brain, or both?
In assessing the role of the autonomic nervous system in conditions such as functional bowel disorders, it is crucial to consider the brain-gut and gut-brain pathways. Firstly, the condition (IBS) involves central as well as peripheral sites: pain is ultimately a cortical event while events such as diarrhoea and mucus production imply that there is also dysfunction of the gut per se. Therefore, functional disorders must to some extent involve the brain as well as the gut. Secondly, if visceral factors such as an infectious event in the gut affect the cortical response to visceral stimuli, and if conversely, psychological events can alter the function of the gut, gut-brain and brain-gut communication must be one of the important modulators involved. Therefore, it seems logical that the autonomic nervous system, which is the primary pathway involved in brain-gut communication, plays an important role in functional bowel disorders (fig 2).

The autonomic nervous system could be simply a conduit through which the central nervous system controls visceral function or it may be that primary alterations in visceral autonomic function are one of the pathophysiological factors involved in these conditions. In the following sections we will examine the possible role of the autonomic nervous system in functional disorders and some of the therapeutic opportunities that modulation of autonomic function may provide in the management of functional disorders.

Figure 2  Autonomic nervous system alternate view.
with non-cardiac chest pain, we have found the opposite; those patients with increased visceral sensitivity to oesophageal acid infusion had higher resting sympathetic tone and decreased vagal activity, suggesting that the abnormalities may differ according to the gut region involved (foregut v hindgut).1

However, it is difficult from these associations to ascribe a definite causative role to any type of autonomic dysfunction in functional disorders until studies aimed at restoring a more normal basal autonomic balance are also shown to change the altered visceral perception and function that is present in these patients. Central and emotional factors, which are well known to be associated with functional gut symptoms, are also capable of altering autonomic balance. It would be naïve not to consider that in a large number of cases where central as well as autonomic factors are involved it is the effects of the former that may lead to the occurrence of the latter and of gastrointestinal symptoms (fig 3).

Conclusions
There is increasing agreement that autonomic abnormalities can often be associated with functional disorders of the gut. We still have to gain a better understanding of the mechanisms responsible for the symptoms and of their fate with restoration of autonomic function. Until then the exact role of altered autonomic function in the pathogenesis of functional disorders will remain as poorly defined as that of the other putative mechanisms involved in these disorders. Once more, the urgent need for studies focusing on the mechanisms of disease rather than its clinical manifestation, and on pathophysiology rather than symptomatology, is apparent.