

Chapter 6—Summary

The papers in this chapter have examined the influence of the central nervous system (CNS) and other body systems on visceral sensitivity and adaptation, with particular reference to functional disorders such as irritable bowel syndrome (IBS). Recent studies suggest that hypersensitivity of the gut may result from moderate stimulation of intrinsic sensory neurones which leads to enhanced excitability of these neurones over several hours, that is, sustained slow postsynaptic excitation (SSPE). This phenomenon may explain long term changes in the responsiveness of enteric neurones and resultant hypersensitivity observed in conditions such as IBS. There is evidence from both human and animal studies that IBS-like changes can be induced by repeated stimulation of intrinsic sensory neurones. A probable mechanism behind SSPE is phosphorylation of ion channels or their regulator proteins and these channel alterations may be responsible for “memorising” changes in the sensitivity of the neurones. Such changes can be either adaptive for digestive purposes or pathological, as in IBS. Inflammatory mediators also have a profound effect on enteric neurones and smooth muscle and can induce phenotypic changes in the gut intrinsic nervous system which result in altered production or release of neurotransmitters, as well as altering the number of postsynaptic receptors for them. Conversely, intrinsic and extrinsic enteric neurones seem to be involved in the regulation of the inflammatory process and may indirectly affect local neuroimmune reactions. Activation of the gut immune system is thought to trigger both the immediate and persistent changes in the enteric nervous system (ENS) which may be responsible for chronic bowel dysfunction such as that observed in IBS. Prostaglandins are also released during inflammatory processes, although there is some evidence which suggests that they may have a physiological role in the absence of inflammation. These ubiquitous substances may be derived intracellularly via the enzyme cyclooxygenase 2 and may activate or modulate autonomic, endocrine, and behavioural responses to visceral sensory input.

Under normal circumstances, afferent input to the CNS from the viscera is not consciously perceived unless the body is required to react in some way, for example to empty

the bladder or defecate. Recent experiments have been conducted in normal subjects and IBS patients to assess differences in their perception of visceral stimuli. The discomfort threshold to rectal distension was assessed before and after delivery of a noxious conditioning stimulus to the sigmoid colon. These experiments showed no significant change in perception of rectal distension following the conditioning stimulus in normal subjects, whereas IBS patients frequently showed a decrease in their discomfort threshold. The opposite was true for inflammatory bowel disease patients who showed a blunted response. Brain imaging studies show that there is greater activation of certain areas of the brain associated with antinociception in normal individuals than in IBS patients, suggesting that IBS patients may have a “defect” in their response. Further studies are required to assess what role this plays in the viscerosensory abnormalities observed in IBS patients. It may be that the antinociceptive mechanisms come into play only following noxious stimuli. Psychosocial factors also have a role in the perception of symptoms and there are many studies which indicate a deleterious effect of anxiety and depression on symptom perception, although there is no unique diagnostic profile for symptom development. Patients with functional gastrointestinal disorders do, however, seem to have been exposed to more chronic “stressors” (for example, divorce, lawsuit, etc) than normal individuals. Psychotherapy combined with medical treatment has been shown to improve the prognosis in IBS patients. It is suggested, however, that patients who meet the DSM criteria for a psychiatric diagnosis should be treated as a separate group and not included in studies assessing the benefits of psychotherapy in functional gastrointestinal disorders.

In conclusion, this chapter has explored the roles of different systems which interact with the ENS to produce some form of integrated response or adaptation to visceral stimuli, for example, mechanical, immunological, or psychosocial. Research indicating abnormalities in the various systems has also been discussed as a possible explanation for some common functional gastrointestinal disorders.