Visceral afferent mechanisms and their implications for functional disorders of the gastrointestinal tract

Until now, the development of effective therapies for the treatment of functional disorders such as irritable bowel syndrome (IBS) has been thwarted by a general lack of knowledge about how events in the intestine are detected by visceral afferent neurones.

There are considerable gaps in our knowledge of the anatomy as well as the function and modulation of visceral afferent projections, in particular about what causes visceral hypersensitivity or abnormal sensory perception of stimuli in the gut. The field is advancing rapidly and it is rare that bench researchers and clinicians come together to compare and discuss the implications of their results. This supplement consists of a series of specialised papers by some of the best experts in this field, arising from a workshop that took place in 2002 under the auspices of AstraZeneca. The workshop was aimed at reviewing the current status of knowledge relating to the way in which the visceral nerves end in the wall of the digestive tract and how they are activated, with particular attention to the underlying molecular mechanisms.

A brief review of the anatomical aspects of vagal, spinal, and sacral (pelvic and pudendal) visceral afferent nerve endings is followed by a discussion of mechanisms whereby they can be activated both mechanically and chemically. Activation of the various pathways and initiation of afferent nerve impulses is then explored at the molecular level, with emphasis on how thresholds for excitation may be modulated. Sensitisation and desensitisation of visceral afferents is of particular relevance in diseases such as IBS, so functionally relevant types of visceral afferent plasticity are described and their implications discussed. The interface between the intestinal environment and the nervous system constitutes an important sensory organ whereby the intestinal contents can influence afferent nerve fibres in the lamina propria of the intestinal mucosa. Various cell types, including enteroendocrine cells and enterocytes, are examined, and their potential to act as sensors or transmitters of information relating to luminal factors such as microbial fauna is discussed.

On the basis of our current understanding of visceral hyperalgesia, the final paper concentrates on putative targets for therapeutic intervention in functional and inflammatory bowel conditions.

We would like to take this opportunity to thank all the participants, and in particular to express our gratitude to Karin Wiburger and Lynn Campbell for their excellent organisation. We would also like to recognise the superb professional help of Madeline Frame in the preparation of this supplement.

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