

SUMMARY 3

Role of visceral sensitivity in functional disorders

Irritable bowel syndrome: pathophysiology

The pathophysiology of functional digestive disorders is incompletely understood, despite significant advances in the recognition of aetiological factors and pathological mechanisms. Abnormal motility patterns observed in irritable bowel syndrome (IBS) are neither constant nor specific, and few data from the literature have shown a link between these patterns and pain episodes. Using current methodology, hypersensitivity of afferent fibres is a frequent but not a constant finding among patients with IBS.

Hypervigilance to abdominal events and stress both sensitise healthy volunteers to distension. Recently developed functional imaging techniques have shown differences in cortical activation induced by rectal distension between patients and controls and between male and female patients with IBS. However, further studies are needed to confirm these observations and to define the exact roles of the peripheral and central components of visceral hypersensitivity. Meanwhile, recent advances in our knowledge of the neurotransmitters and receptors involved in processing visceral sensation provides a major opening for the development of new treatments for functional gastrointestinal disorders.

Sensation and intestinal gas dynamics in functional gastrointestinal disorders

Gas is the element that has the highest probability of being a trigger for intestinal distension and afferent sensory stimulation. Using an intrajejunal gas challenge test, patients with IBS and functional bloating exhibit diminished ability to mobilise and expel gas, thus developing abdominal distension and discomfort. This behaviour is in contrast with that observed in most healthy individuals who promptly dispose of the gas and do not develop any abdominal symptoms. This finding supports the presence of a motor abnormality in patients with functional bowel disorders and also suggests a role for retained intestinal gas in the production of symptoms. Coexisting visceral hypersensitivity amplifies the discomfort produced by abnormal gas retention, and may also be responsible for symptoms in those patients in whom gas is retained below the normal threshold for discomfort. Interventions that normalise gas flow dynamics, adjust bowel capacitance, and decrease visceral perception may serve to alleviate abdominal pain and bloating.

IBS: the role of the psyche in modulating sensation

Stress is associated with bowel disturbance in approximately 50% of normal subjects and in 70–80% of patients with IBS. Up to 60% of patients with IBS have psychological disturbances, including major depression and anxiety. These patients are more likely to seek consultation than IBS patients without psychosocial disturbance. However, the majority of patients with IBS do not seek medical advice which means that the presenting population represents only about 5% of the total and predominantly includes those who have psychosocial disturbances.

Patients adopt various coping strategies for pain. Those who “catastrophise” pain have a morbid view of their condition, with poor ability to cope and poor outcome. Approximately 30% of patients with IBS behave in a similar manner to those with depression but they do not see themselves as being depressed. Patients with severe pain have higher healthcare utilisation and are the most likely to be depressed.

IBS: pain perception

Three areas in the brain are thought to be involved in pain perception. The anterior cingulate cortex is the probable brain modulating centre. The rostral area deals with the emotive aspect of pain and becomes activated when patients are told that a procedure is going to be unpleasant. It is possible that this part of the cortex becomes overactive in patients with IBS. The third centre, the perigenual area, is associated with affective disturbance and is also the centre that is most rich in beta endorphin activity, suggesting that it plays a role in downregulating pain.

Both inhibiting and disinhibiting pathways descending from the brain may significantly affect peripheral inputs and result in pain in

circumstances that would not normally be painful. What we need to understand is how changes in the balance between the facilitating and inhibiting processes alter the outcome to therapy.

Non-invasive measurement of gastric accommodation

The barostat is the most widely used method for measuring changes in intragastric pressure, volume, and sensation. It is the only technique that allows simultaneous measurement of gastric accommodation and sensation. However, the procedure itself alters the intragastric distribution of a meal and possibly exaggerates relaxation of the gastric fundus, making it difficult to measure accommodation in response to ingested foods.

Conventional two dimensional ultrasound is used to measure antral and fundal diameter and area. This cheap and readily available technique is non-invasive and does not expose the patient to radiation. However, the results are highly user dependent and the procedure has technical limitations. It also fails to differentiate between food and gastric secretion, or between solid and liquid contents. Three dimensional ultrasound provides much improved definition and facilitates volume assessment of the entire stomach. However, the procedure is technically demanding and is not widely available.

Single photon emission computed tomography is a non-invasive technique which allows assessment of the entire stomach and its contents. It also enables gastric accommodation to be studied. The main limitation is the high radiation exposure which restricts repetitive measurement making it unsuitable for clinical trial use.

Magnetic resonance imaging (MRI) is probably the only technique that allows the simultaneous measurement of gastric accommodation, gastric motility, and emptying. Measurement of gastric contents and air can also be assessed. However, the procedure is technically difficult, and the equipment expensive. Despite these constraints, MRI will probably pave the way for the future of neurogastroenterology by enabling the measurement of gastric emptying and secretion, and of gastroduodenal and pyloric motility.

Non-invasive techniques have the advantage of being less uncomfortable for the patient but the information provided does not necessarily replace that of the invasive techniques and for now, the barostat remains the standard for gastric accommodation measurements.

In addition to MRI, drug modelling and gastric accommodation studies are also possible goals for the future.

Functional dyspepsia: pathophysiology

The pathophysiological mechanisms responsible for functional dyspepsia include alterations in motility and visceral sensation, abnormal acid secretion, and *Helicobacter pylori* infection. Approximately 50% of patients with functional dyspepsia have motor disorders. These include impaired fundic relaxation, antral dilation and/or hypomotility, delayed gastric emptying, or small bowel dysmotility. These motor disturbances are possibly related to abnormal autonomic control, especially in patients with delayed gastric emptying and small bowel transit. In terms of sensory disorders, patients typically present with gastric hypersensitivity resulting from abnormal afferent function, or with gastro-gastric or duodenogastric reflex hyporeactivity in which normal relaxation of the proximal stomach is impaired due to either afferent or efferent dysfunction.

The role of *H pylori* in functional dyspepsia is difficult to define and the literature yields inconsistent and often confusing results. The general consensus is that *H pylori* infection is not associated with impaired gastric emptying and that the abnormalities seen in *H pylori* positive patients coexist independent of their *H pylori* status. However, meta-analysis of seven controlled studies reported a non-significant odds ratio in favour of *H pylori* eradication therapy in patients with functional dyspepsia.

Further studies are needed to establish a clear causal relation between physiological dysfunction and specific symptoms of functional dyspepsia. Future therapeutic strategies should be aimed at reducing nociception as well as enhancing the accommodation response.