Visceral Hypersensitivity in Irritable Bowel Syndrome: A Summary Review

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We examined published reports from 1970 to the present to evaluate the theory that abnormal visceral sensitivity characterizes the irritable bowel syndrome. Evidence to support claims that abnormal visceral sensitivity defines the irritable bowel syndrome falls short because of cognitive deficits in gastrointestinal neurobiology, limitations in experimental design and execution, and the interpretation of results.

KEY WORDS: Irritable bowel syndrome; visceral sensitivity; visceral nociceptors; constipation; diarrhea.

Physicians generally seem to accept the idea that an enhanced or inappropriate visceral perception identifies irritable bowel syndrome (IBS), generates its symptoms, and even defines it (1–7). We examined the clinical evidence for these conclusions, combing MEDLINE for relevant publications in English from 1970 through 2004, where patients with IBS were compared to appropriate control subjects. From all included articles, data were extracted on (a) criteria used for diagnosis of IBS, (b) characteristics of the study samples, (c) baseline similarity of patient and control group, (d) methodological characteristics, and (e) statistical analysis. It turned out that the variability of the criteria used to make the diagnosis of IBS, the major variation in the testing methodology, and the differing sensations observed preclude a standard meta-analytic approach to aggregate the reported data.

RESULTS

Defining Patients and Methods of Testing. An objective definition of IBS has been the goal of a fruitless century-long search (8). This goal underlies the current enthusiasm to demonstrate visceral hypersensitivity in IBS. Many studies we reviewed defined IBS by one or another of the various versions of the Rome criteria (Delphic symptom-lists created by authorities) successively revised from 1989 through 1999. Note that more than two-thirds of patients who fulfilled the original Rome criteria (9) would not have been diagnosed if the 1999 Rome criteria (10) had been applied (11). The 1999 version (10) requires (in addition to a sensation of bloating and one or more features of an abnormal bowel habit) the absence of a structural or biochemical explanation for the symptoms and the presence of abdominal discomfort or pain of at least 12 weeks’ duration (not necessarily consecutive). The pain must have two of three features: (a) relief with defecation, (b) onset associated with a change in stool frequency, and (c) onset associated with a change in stool form or appearance.

Other studies used other criteria. None acknowledged the inescapable uncertainty involved in selecting patients for study on the basis of poorly quantified sensations, impressions, and other such strictly subjective criteria. All definitions of IBS include a clause requiring the exclusion of defined diseases capable of inducing the symptoms. None of the studies we reviewed listed the specific diagnoses they excluded in defining their patient cohorts or the specific tests they required to be normal in order to exclude such diagnoses. Also, none specified adequately the possible confounding illnesses that would exclude volunteers from control groups.

Patient and control groups were small, and the latter, in part, used in multiple studies (2, 12–16). Further, control
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cohorts were sometimes strongly biased to one gender or to a narrow age range. Neither the patient groups nor the control groups from different studies could be combined usefully because of conflicting or incomplete defining criteria.

Most studies measured visceral sensitivity by observing various sensations evoked by the experimental distension of a part of the gastrointestinal tract with a balloon inflated with air. Many failed to take into account the basic mechanical properties and behaviors of the gastrointestinal tract (17), and many ignored obvious truths (such as the likelihood that the distension of a rectal balloon stimulates neuroreceptive elements in other organs in the lesser pelvis such as the genitourinary organs).

Early investigators, distending balloons in the gut with handheld syringes, observed that the threshold for evoked sensations varied with the rate of expansion of the segment. For this reason, later investigators used computer-regulated pumps to control inflation rates. The idea emerged that relatively slow distensions may more resemble physiological events, while relatively rapid distensions are more likely to be perceived as aversive.

Sensory thresholds assessed by these techniques depend on distension protocols that differ widely among the reports reviewed. Balloon inflations followed either a slow continuous path (ramp distension), a stepped course (staircase distension), or brief rapid distensions of either progressive or randomly varied magnitude separated by periods of deflation (phasic distension). Some studies sought thresholds for two or more sensations (fullness, discomfort, pain, urge to defecate), while others assessed only one.

Anticipation might modify responses. Some studies attempted to reduce the perceptual bias related to anticipation by making the sensation intensity unpredictable. They used protocols in which distensions of increasing amplitude first revealed the level that produces the first perception (the threshold), with subsequent confirmatory distensions made at magnitudes randomly above and below that threshold.

Sensitivity of Sigmoid Colon and Rectum in IBS. Some investigators found that the uncontrolled distension of a balloon in the sigmoid colon causes pain at lower volumes in patients with undefined IBS than in control subjects (18–20), but others could not confirm that conclusion (21). Measurements of pressures in balloons (rather than of balloon volumes) associated with such distensions of the sigmoid colon also yielded conflicting conclusions about hypersensitivity in IBS patients (22, 23).

Later studies in the rectal sensitivity of patients with IBS used more sophisticated protocols for distension and sought different sensations. With both controlled pressure ramp and phasic rectal distensions of predictable magnitude, conflicting conclusions were reached about hypersensitivity for discomfort, stool sensation, and the urge to defecate. With slow ramp distensions, patients with IBS did not differ in their colorectal sensory thresholds from healthy subjects (2, 3, 12, 24). With rapid phasic distensions (often aversive) of predictable magnitude, by contrast, IBS patients were reported to feel discomfort or pain either at lower (2, 6, 12, 25–27) or the same (3, 26) distension levels than control subjects. The idea arose that some persons may express alterations in rectal perception more in terms of discomfort and others more in terms of intensity of sensation and that an altered quality in rectal perception may mark IBS (2, 3, 6). However, IBS patients who were more sensitive to phasic distensions of predictable magnitude than healthy subjects did not differ from the latter in sensitivity to distensions of unpredictable magnitude (25, 26, 28–31). Thus, a heightened sensitivity to stimuli of predictable magnitude in IBS patients may indicate hypervigilance rather than hypersensitivity, as supported by the evidence for a crucial effect of attention on sensory thresholds for a variety of stimuli (27, 32–36).

A few studies with transmucosal electrical stimulation in the rectosigmoid area (thought to excite mucosal pain fibers directly) suggested that hypersensitivity in IBS is related to alterations in the nervous system rather than in biomechanical parameters such as tension and strain of the gut wall (22, 23).

Some investigators concluded that lower sensory thresholds to rectal distension in IBS were stress-induced (37, 38) or reflected, rather than an increased sensitivity, a perceptual bias representing a psychological marker for the disorder (26).

The conception that noxious repetitive distension of the sigmoid colon might affect rectal sensitivity by sensitizing visceral afferents or increasing central neuronal excitability (39) received some attention, inconclusively (28–30, 40, 41).

Sensitivity in Gut Segments Rostral to the Colon in IBS. The idea that hypersensitivity in the ileum and jejunum might characterize IBS patients led to investigations with distension of those regions. Some studies supported the idea (42–44) but others did not (45). Sensory thresholds to transmucosal electrical stimulation of the jejunum were as high in IBS patients as in healthy subjects (43). Suggestions of a more general gastrointestinal hypersensitivity in IBS also came from inconclusive studies with balloon distension of the duodenum (46), stomach (47), and esophagus (48, 49).

Rectal Sensitivity in Diarrhea- and Constipation-Predominant IBS. In patients with disordered defecation, the fear of incontinence might well create