Gut feelings: visceral hypersensitivity and functional gastrointestinal disorders
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CHAPTER 3
HYPERSENSITIVITY TO RECTAL DISTENSION IN PATIENTS WITH IRRITABLE BOWEL SYNDROME IS NOT ASSOCIATED WITH SPECIFIC SYMPTOMS

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Chapter 3

ABSTRACT

BACKGROUND AND AIMS: Visceral hypersensitivity is a consistent abnormality in a substantial subpopulation of patients with irritable bowel syndrome (IBS). Although controversial, these patients may have a different pathogenesis compared to IBS patients with normal gut sensitivity, and may therefore present with different symptom patterns. The aim of this study was to detect possible associations between symptoms and the presence of hypersensitivity to rectal distension.

METHODS: Ninety-two IBS patients and 17 healthy volunteers (HV) underwent a rectal barostat study. The association between specific IBS symptoms and the presence of hypersensitivity was examined using Area under the Receiver Operating Characteristic (A-ROC) curves.

RESULTS: IBS patients had significantly lower thresholds for discomfort/pain than HV (25 ± 11 and 35 ± 12 mm Hg above MDP, respectively). Forty-one patients (45%) showed hypersensitivity to rectal distension. Hypersensitivity was more prevalent in female (56%) than in male patients (30%, \( P = 0.02 \)). Proportions of patients with predominant bowel habits were similar in hypersensitive and normosensitive subgroups (diarrhoea predominant: 39% and 41%, respectively; alternating type: 27% and 28%, respectively; constipation predominant: 34% and 31%, respectively). Severe abdominal pain was more frequent in hypersensitive, compared to normosensitive patients (88% versus 67%, \( P = 0.02 \)), but none of the individual IBS symptoms could accurately predict the presence of hypersensitivity, as assessed by A-ROC curve analysis.

CONCLUSIONS: Hypersensitive and normosensitive IBS patients present with comparable, heterogeneous symptomatology. Therefore, selection based on clinical parameters is unlikely to discriminate individual IBS patients with visceral hypersensitivity from those with normal visceral sensitivity.

ABBREVIATIONS: IBS: Irritable bowel syndrome; HV: healthy volunteers; MDP: minimal distending pressure; GSRS: Gastrointestinal Symptom Rating Scale; A-ROC: Area under the Receiver Operating Characteristic; IBS-C: constipation predominant IBS; IBS-A: alternating type IBS; IBS-D, diarrhoea predominant IBS.
INTRODUCTION

The irritable bowel syndrome (IBS) is defined as a functional bowel disorder characterised by chronic abdominal pain or discomfort, associated with altered defecation and changes in bowel habit, in the absence of any detectable organic cause.1 Because reliable biological markers are not available, the diagnosis is based on symptom-based criteria such as the Rome criteria.1

IBS is a multifactorial disorder, of which the aetiology is largely unknown. Proposed mechanisms contributing to development of IBS symptoms include abnormal motility and associated alterations in gut transit, psychological factors including mental stress, food allergens and postinfectious neuroimmune modulation of gut functions (see Camilleri for review2). However at present, the most widely accepted mechanism underlying the origin of symptoms in IBS is enhanced visceral sensitivity or visceral hypersensitivity.3,4 Hypersensitivity of the gut may lead to alterations in gut motility by altering regulatory reflex pathways and secretory functions, which in turn may lead to functional disturbances. In addition, normal, physiologic stimuli may be perceived with increased intensity or may even cause pain. The evidence that patients with IBS exhibit enhanced visceral sensitivity is illustrated by studies evaluating the sensory responses to mechanical distension of the colon and recto-sigmoid.5-8 As a group, patients with IBS report pain at distension levels that are normally not perceived as painful. Furthermore, the magnitude of the sensory responses to colorectal distension is increased compared to healthy controls. Hypersensitivity to rectal distension has been shown to discriminate IBS from other causes of abdominal pain with reasonable accuracy (sensitivity: 96%; specificity: 72%).8

However, although visceral hypersensitivity has been proposed to represent a biological marker for IBS,6-8 specific hypersensitivity to colorectal distension has only been reported in 20% to 80% of IBS patients across studies.9 In the remainder of patients, colorectal sensitivity appears to be normal. It has previously been suggested that IBS patients with visceral hypersensitivity and IBS patients with normal sensitivity may represent different subpopulations with distinct pathophysiologies.3,6,10 These subpopulations may therefore present with different symptom patterns, related to the presence or absence of a hyperreactive gut. Moreover, these subpopulations may show differential responses to certain pharmacological interventions. In particular, hypersensitive IBS patients could benefit from drugs that are aimed to reduce visceral sensitivity. So far, these issues have not been well addressed in clinical studies. For example, the κ-opioid agonist fedotozine has been shown to normalise the sensory responses to colonic distension in selected IBS patients with visceral hypersensitivity. However, no such selection was made for patients that underwent clinical evaluation of the compound, possibly explaining its disappointing efficacy.11 We previously showed that the antidepressant fluoxetine may reduce abdominal pain in hypersensitive, but not in normosensitive IBS patients.12 These differential clinical benefits may apply to several other compounds with proposed viscerosensory effects.13 Therefore, future clinical efficacy studies with drug classes that are aimed at reducing visceral...
sensitivity in IBS may need to take into account the presence or absence of visceral hypersensitivity in individual patients. At present, these individuals can only be identified by measuring the sensory responses to gut distension. However, this method is relatively invasive, time-consuming and costly and requires instruments such as the barostat that are generally not available to the average gastroenterologist. Ideally, these subgroups should be distinguishable on clinical parameters. A similar study in patients with functional dyspepsia (a condition with a largely overlapping pathophysiology) indeed confirmed that the presence of hypersensitivity to gastric distension was associated with specific dyspeptic symptoms.

The present study aimed to identify possible associations between specific IBS symptoms and the presence of hypersensitivity to rectal distension. Such associations may further support the concept that individuals with visceral hypersensitivity may represent a distinct subpopulation of IBS patients. In addition, positive associations between symptoms and visceral hypersensitivity could help to classify or select patients for large-scale evaluations of future interventions aimed at reducing visceral hypersensitivity in IBS.

PATIENTS AND METHODS

STUDY SUBJECTS

Healthy volunteers

In order to obtain normal values, 17 healthy volunteers (8 women (47%); age, 19 - 62 years; mean age, 39 ± 17 years) were recruited by public advertisement. Each healthy volunteer needed to be free of gastrointestinal symptoms, without previous gastrointestinal surgery and not taking any medication.

Patients

The patient data in this study were obtained from 92 consecutive patients between 1999 and 2003. The patients were referred to our laboratory from the outpatient clinics of the departments of Gastroenterology and Internal Medicine at the Academic Medical Centre, a tertiary referral centre. Ninety-two IBS patients (52 women (57%); age, 18 - 65 years; mean age, 39 ± 12 years) were evaluated. All patients fulfilled the Rome II criteria for IBS. In addition to careful history taking, all patients underwent a minimal work-up to exclude organic disease. This included a normal physical examination, a negative sigmoidoscopy or colonoscopy, normal thyroid stimulating hormone levels and blood counts and negative stool examinations. Patients had to be free of any concomitant disease, including overt psychiatric disorders. Concomitant medication likely to interfere with gastrointestinal tract function or visceral perception other than fibres or bulking agents was discontinued at least seven days before the study. Patients who previously underwent abdominal surgery, except for uncomplicated appendectomy or laparoscopic cholecystectomy, were excluded.
SYMPTOM QUESTIONNAIRES

Gastrointestinal symptoms
The intensity of individual gastrointestinal symptoms of abdominal bloating, flatulence, decreased bowel movements, increased bowel movements, soft stools, hard stools, urgency and the feeling of incomplete evacuation was scored on a self-rated scale, derived from the validated Gastrointestinal Symptom Rating Scale (GSRS), in which the intensities of the symptoms are scored on a 7-graded Likert scale, with descriptive anchors (0 = no symptoms at all; 1 = minimal symptoms; 2 = mild symptoms; 3 = moderate symptoms; 4 = rather serious symptoms; 5 = serious symptoms; and 6 = very severe symptoms).

Abdominal pain
A five-point score was used to evaluate abdominal pain. Patients had to answer the following question: ‘Please consider how much abdominal pain you experienced in the past 4 weeks’. Possible answers were: 1 = none; 2 = mild; 3 = moderate; 4 = severe; 5 = very severe.

BAROSTAT STUDIES
To assess the sensitivity to rectal distension, we used an electronic barostat that automatically corrected for the compressibility of air (Synetics Visceral Stimulator, Stockholm, Sweden). Before the distension studies, subjects received a tap water enema, followed by a 60-minute rest. Subsequently, a 500-ml polyethylene bag (maximal diameter 9 cm), tightly wrapped on the distal end of a double lumen polyvinyl tube (Salem Sump tube 14 Ch.; Sherwood Medical St Louis, USA) was introduced in the rectum. The catheter was then connected to the barostat device and the subject was placed in the left lateral decubitus position. The bag was unfolded by inflating it with 200 ml of air and positioned in the distal rectum by gently pulling the catheter back. After a 15-minute adaptation period, minimal distending pressure (MDP) was determined as the minimum pressure at which the intrabag volume was >30 ml. This pressure level equals the intra-abdominal pressure. The distension protocol consisted of a series of phasic, semirandomly ascending isobaric distensions, of 3 mm Hg increment above MDP (3, 6, 12, 9, 18, 15, 24, 21, 30 mm Hg, etc.). The inflation rate was 38 ml/s and each distension step lasted 2 minutes, separated by 1-minute intervals at baseline (MDP). Sensations were scored halfway (at 1 minute) along each distension step. We used a 6-point scale with verbal descriptors (0 = no sensation; 1 = first sensation; 2 = first sense of urge; 3 = normal urge to defecate; 4 = severe urge to defecate; 5 = discomfort/pain). Sensation scores were automatically logged onto the data file at each score point. If the subject reported discomfort or pain, the bag was instantaneously deflated. In addition, the bag was automatically deflated at pressures above 60 mm Hg or volumes above 500 ml.
STATISTICAL ANALYSIS
Primary endpoints were the thresholds for first sensation, urge and discomfort/pain during rectal distension. The discomfort/pain thresholds obtained from the healthy volunteers were used to define the normal range (between the 5th and 95th percentile) for sensitivity to rectal distension. In previous studies, hypersensitivity has been defined as a threshold below the 95% confidence interval of a normal control group.\textsuperscript{6,7} However, this definition is largely influenced by the sample size and test distribution. Therefore, we used the lower limit of the normal range of discomfort/pain thresholds (5th percentile) as a cut-off to distinguish patients with hypersensitivity to rectal distension from patients with normal rectal sensitivity. The association between specific IBS symptoms and the presence of hypersensitivity was examined using Area under the Receiver Operating Characteristic (A-ROC) curves.\textsuperscript{18,19} The A-ROC curve summarises the accuracy of a specific symptom to distinguish hypersensitive from normosensitive patients. The A-ROC curve is obtained by plotting the true positive proportion (hypersensitive patients with the symptom present, y-axis) to the 1 minus true negative proportion (normosensitive patients with the symptom absent, x-axis) at each possible cut-off (0-7 points or 1-5 points for GSRS and pain scores, respectively) defining the presence of a particular symptom. The area under a ROC curve represents the probability that a random pair of patients will be correctly classified as hypersensitive or normosensitive by the concerning symptom. A value of 0.50 is obtained when the symptom does no better than chance, whereas a value of 1.0 means perfect accuracy or discrimination. Estimates of A-ROC curves for each symptom were expressed with their 95% confidence limits.\textsuperscript{20} All other data are given as mean ± SD. Continuous data were compared using Student's \textit{t}-test and categorical data using Chi-square tests. Differences were considered significant at the 5% level. Statistical evaluations were performed using commercially available software (SPSS 11.0; SPSS Inc. Chicago IL, USA).

RESULTS

CLINICAL CHARACTERISTICS OF IBS PATIENTS
No significant differences were seen between patients and healthy volunteers for age and gender. Based on their predominant bowel habit, 37 IBS patients (40%) were considered as diarrhoea predominant (IBS-D), 25 (27%) as constipation predominant IBS (IBS-C) and 30 (33%) as alternating IBS (IBS-A). The mean duration of symptoms at intake was 8 ± 8 years (range 1-30 years). Table 1 shows the prevalence and severity of individual IBS symptoms in the overall number of patients.
Symptoms & rectal sensitivity

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Absent</th>
<th>Present a)</th>
<th>Severe b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal bloating</td>
<td>11 (12)</td>
<td>81 (88)</td>
<td>35 (38)</td>
</tr>
<tr>
<td>Flatulence</td>
<td>6 (7)</td>
<td>86 (93)</td>
<td>36 (39)</td>
</tr>
<tr>
<td>Decreased bowel movements</td>
<td>50 (54)</td>
<td>42 (46)</td>
<td>11 (12)</td>
</tr>
<tr>
<td>Increased bowel movements</td>
<td>29 (31)</td>
<td>63 (69)</td>
<td>17 (19)</td>
</tr>
<tr>
<td>Hard stools</td>
<td>17 (18)</td>
<td>75 (82)</td>
<td>22 (24)</td>
</tr>
<tr>
<td>Soft stools</td>
<td>44 (48)</td>
<td>48 (52)</td>
<td>7 (8)</td>
</tr>
<tr>
<td>Urgency</td>
<td>28 (31)</td>
<td>64 (69)</td>
<td>20 (22)</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>11 (12)</td>
<td>81 (88)</td>
<td>22 (24)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0 (0)</td>
<td>92 (100)</td>
<td>70 (76)</td>
</tr>
</tbody>
</table>

TABLE 1. Prevalence and severity of IBS symptoms in 92 IBS patients. Data are presented as absolute numbers and (row percentages). a) Present; scores of ≥ 2 on a 0-6 (GSRS) or a 1-5 (Pain) scale. b) Severe: scores of ≥ 5 or ≥ 4, on a 0-6 (GSRS) or a 1-5 (Pain) scale, respectively.

SENSITIVITY TO RECTAL DISTENSION IN HEALTHY VOLUNTEERS
In healthy volunteers, the mean MDP was 6 ± 3 mm Hg. Thresholds for first sensation, urge and discomfort/pain were 5 ± 4, 13 ± 5 and 35 ± 12 mm Hg above MDP, respectively. The individual thresholds for discomfort/pain are shown in Figure 1. The normal range for the threshold for discomfort/pain (between the 5th and 95th percentile) was 18 to 57 mm Hg above MDP.

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Individual thresholds for discomfort/pain in healthy volunteers (HV) and patients with IBS. Solid horizontal lines represent mean values; the dotted lines represent the normal range of normal values obtained in HV. *P < 0.01 versus HV.
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SENSITIVITY TO RECTAL DISTENSION IN IBS PATIENTS

All IBS patients

In IBS patients, MDP was 6 ± 3 mm Hg. Overall, thresholds for first sensation, urge and discomfort/pain were 4 ± 3, 10 ± 7 and 25 ± 11 mm Hg above MDP, respectively. The individual thresholds at which IBS patients reported discomfort/pain are shown in figure 1. Although the thresholds for first sensation and urge were not significantly different from those in healthy volunteers, thresholds for discomfort/pain were significantly lower (P= 0.001, see Table 2).

Hypersensitive versus normosensitive IBS patients

Using the 5th percentile cut-off of the normal values obtained in healthy volunteers (i.e. a maximum threshold for discomfort/pain of 18 mm Hg above MDP) 41 patients (45%) showed hypersensitivity to rectal distension. The prevalence of hypersensitivity was significantly higher in female, compared to male patients (56% and 30%, respectively, P= 0.014). Mean age was not significantly different between the subgroups (36 ± 11 and 40 ± 13 years for hypersensitive and normosensitive patients, respectively). The sensory thresholds of hypersensitive versus normosensitive patients are summarised in Table 2. In hypersensitive patients, thresholds for first sensation, urge and discomfort/pain were significantly lower, compared to both healthy volunteers and normosensitive patients, whereas the sensory thresholds in normosensitive patients were comparable to those in healthy volunteers (Table 2).

<table>
<thead>
<tr>
<th>HV</th>
<th>IBS</th>
<th>All</th>
<th>Hypersensitive</th>
<th>Normosensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First sensation</td>
<td>5 ± 4</td>
<td>4 ± 3</td>
<td>3 ± 2&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>5 ± 3</td>
</tr>
<tr>
<td>Urge to defecate</td>
<td>13 ± 5</td>
<td>10 ± 7</td>
<td>7 ± 2&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>13 ± 8</td>
</tr>
<tr>
<td>Discomfort/Pain</td>
<td>35 ± 12</td>
<td>25 ± 11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15 ± 4&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>32 ± 9</td>
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<tr>
<td>n = 17</td>
<td>n = 92</td>
<td>n = 41</td>
<td>n = 51</td>
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</tr>
</tbody>
</table>

TABLE 2. Sensory thresholds in IBS and IBS subpopulations compared to healthy volunteers.

Data are expressed as mean ± SD. Hypersensitive patients were defined by a threshold for discomfort/pain below the 5th percentile of healthy volunteers; <sup>a</sup>P< 0.05 versus healthy volunteers; <sup>b</sup>P< 0.001 versus healthy volunteers; <sup>c</sup>P< 0.001 versus normosensitive.
SYMPTOM PREVALENCE IN HYPERSENSITIVE VERSUS NORMOSENSITIVE IBS PATIENTS

**Dominant bowel habit**

Bowel habit predominance was not associated with the presence or absence of hypersensitivity to rectal distension. In total, 16/41 (39%) of the hypersensitive patients were considered as having IBS-D, 11/41 (27%) IBS-A, and 14/41 (34%) IBS-C, versus 21/51 (41%), 14/51 (28%), and 16/51 (31%) of the normosensitive patients, respectively (figure 2).

![Figure 2](image)

**FIGURE 2.** Prevalence of IBS subgroups based on predominant bowel habit in normosensitive (NS) versus hypersensitive (HS) patients. IBS-C, constipation predominant; IBS-A, alternating constipation and diarrhoea; IBS-D, diarrhoea predominant.

**Individual IBS symptoms**

We evaluated the prevalence of individual IBS symptoms in normosensitive and hypersensitive patients defined by two different cut-offs, i.e. symptoms of at least mild intensity (GSRS or pain scores of ≥ 2) and at least severe intensity (GSRS scores of ≥ 5 or pain scores ≥ 4). Abdominal pain of at least mild intensity was present in all patients (figure 3A). The prevalence of individual GSRS symptoms of at least mild severity was comparable between hypersensitive and normosensitive patients (figure 3A). Likewise, the observed prevalence for individual GSRS symptoms that were rated at least severe was not statistically different between hypersensitive and normosensitive patients (figure 3B). In contrast, severe pain scores (≥ 4) were more prevalent in hypersensitive, compared to normosensitive IBS patients (88% versus 67%, P= 0.018, Chi-square).
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**Figure 3.** Prevalence of individual IBS symptoms in normosensitive (NS) versus hypersensitive (HS) patients. (B, bloating; F, flatulence; dB, decreased bowel movements; iB, increased bowel movements; LS, loose stools; HS, hard stools; U, urgency; IE, incomplete evacuation; P, pain). A: Percentage of patients reporting at least mild symptom intensity (i.e., scores of ≥ 2 on a 0-6 (GSRS) or a 1-5 (Pain) scale); B: Percentage of patients reporting at least severe symptom intensity (i.e., scores of ≥ 5 or ≥ 4, on a 0-6 (GSRS) or a 1-5 (Pain) scale, respectively. *P < 0.05 by Chi-square.

**DISCRIMINATIVE VALUE OF SPECIFIC SYMPTOMS TO DISTINGUISH HYPERSENSITIVE FROM NORMOSENSITIVE IBS PATIENTS.**

The association between specific IBS symptoms and the presence of hypersensitivity was examined using Area under the Receiver Operating Characteristic (A-ROC) curves. As described above, the A-ROC curve represents the accuracy or discrimination of a particular symptom to correctly classify a patient as hypersensitive or normosensitive at each possible cut-off. As shown in Table 3, the A-ROC values of the individual symptoms were all close to the non-discriminative value of 0.5. The highest accuracy to detect hypersensitive individuals was obtained by the abdominal pain scores (A-ROC value: 0.61). However, the lower limit of the 95% confidence interval was still smaller than 0.5, indicating that the discriminative value is still limited.
Symptoms & rectal sensitivity

A-ROC (95% confidence interval)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>A-ROC (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloating</td>
<td>0.53 (0.41-0.65)</td>
</tr>
<tr>
<td>Flatulence</td>
<td>0.52 (0.40-0.64)</td>
</tr>
<tr>
<td>Decreased bowel movements</td>
<td>0.55 (0.43-0.67)</td>
</tr>
<tr>
<td>Increased bowel movements</td>
<td>0.51 (0.39-0.63)</td>
</tr>
<tr>
<td>Loose stools</td>
<td>0.54 (0.42-0.65)</td>
</tr>
<tr>
<td>Hard stools</td>
<td>0.53 (0.41-0.65)</td>
</tr>
<tr>
<td>Urgency</td>
<td>0.53 (0.41-0.65)</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>0.57 (0.45-0.69)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0.61 (0.49-0.72)</td>
</tr>
</tbody>
</table>

**TABLE 3: Accuracy of specific IBS symptoms to correctly classify hypersensitive or normosensitive individuals**

A-ROC: Area under the Receiver Operating Characteristic (Interpretation: 0.5 = no better than chance; 1.0 = perfect accuracy)

**DISCUSSION**

This study aimed to explore the possible associations between specific IBS symptoms and the presence of visceral hypersensitivity in patients with IBS. Our data confirm that hypersensitivity to rectal distension can be demonstrated in about one-half of patients with IBS. Visceral hypersensitivity was more prevalent in female, compared to male patients. The two subpopulations of IBS patients, defined by the presence or absence of visceral hypersensitivity, were comparable in terms of age and bowel habit predominance. Severe abdominal pain was more prevalent in hypersensitive patients, whereas the prevalence of individual gastrointestinal symptoms was similar in both groups. However, none of the specific IBS symptoms (including pain) could accurately distinguish hypersensitive from normosensitive subjects. Therefore, selection based on clinical parameters is unlikely to discriminate individual IBS patients with visceral hypersensitivity from those with normal visceral sensitivity.

Visceral hypersensitivity is considered one of the major pathophysiological mechanisms underlying the generation of symptoms in IBS. As a group, patients with IBS show increased sensory responses to rectal distension, a phenomenon that is able to discriminate IBS from other causes of abdominal pain. Decreased discomfort/pain thresholds to colorectal distension have been a consistent finding in 20% to 80% of IBS patients across studies. Similarly, in the present study hypersensitivity was found in 45% of patients. Thus, although substantial, visceral hypersensitivity may only play a role in a subset of IBS patients. As previously
suggested, these patients may represent a distinct subpopulation based on the underlying pathophysiology, requiring a different therapeutic approach, such as restoring normal visceral sensitivity. Several candidate drugs with proposed viscerosensory effects have been identified as possible new treatments for IBS. However, their clinical efficacy has not been well established. In order to confirm the concept that pure visceranalgesics (e.g. the x-opioid receptor agonist fedotozine) could be efficacious in IBS, it is likely that we need to select only those patients that exhibit visceral hypersensitivity. So far, this issue has not been addressed in clinical trials, partly because this would require large-scale rectal sensitivity testing, which is expensive, time-consuming and often bothersome for patients. Our previous observation that fluoxetine reduced abdominal pain in hypersensitive, but not in normosensitive IBS patients may however further provide a rationale for such an approach in future studies.

In the view of the above mentioned, it would be favourable if IBS patients exhibiting visceral hypersensitivity could be selected based on clinical parameters. One possible parameter may be bowel habit. Earlier studies have indeed suggested that rectal sensory characteristics may differ between IBS-C and IBS-D subgroups, the former experiencing decreased sensations of urge during rectal distension. However in the present study, differences in bowel habit were not associated with the presence or absence of hypersensitivity to rectal distension. Alternatively, individual symptoms have been suggested to correlate with a specific underlying pathophysiological mechanism in patients with functional bowel disorders. For example, in IBS, the feeling of incomplete evacuation and urgency have been reported to be possibly related to visceral hypersensitivity. However, comparable to previous studies, we were unable to demonstrate such correlation. In contrast, we showed that severe pain was significantly more prevalent in hypersensitive patients. Similar finding have been reported in functional dyspepsia, where the presence of visceral hypersensitivity was associated with epigastric pain. Furthermore, it was also shown that patients with pain predominant IBS were more susceptible to rectal sensitisation in response to repetitive sigmoid distension, compared with non-pain predominant IBS patients. These findings suggest that there may be an association between pain and visceral hypersensitivity. To evaluate the possible predictive value of this symptom, we performed an A-ROC curve analysis. This revealed that the rather weak association was unable to select individual IBS patients with hypersensitivity. The same was true for all other symptoms studied, illustrating that IBS patients with visceral hypersensitivity cannot be identified solely based on clinical symptoms.

The fact that hypersensitive and normosensitive IBS present with comparable, heterogeneous symptom patterns does not exclude that hypersensitive patients may have a different underlying pathophysiology, and that restoring normal sensitivity could benefit these patients. Patient selection based on other criteria, such as bowel habit and gender, has already been shown to be of great importance for the outcome of clinical trials evaluating the efficacy of several contemporary compounds for IBS, for example alosetron and tegaserod. Hence, future trials with visceronalgesic drugs in IBS require more rigid patient selection criteria and
only include patients with visceral hypersensitivity. Interestingly, visceral hypersensitivity was more prevalent in female, compared to male IBS patients. Selection of IBS patients based on female sex is therefore likely to increase the overall number of individuals exhibiting visceral hypersensitivity. Although speculative, this may in part explain the gender differences in response to treatment seen in IBS patients. Nevertheless, until clear criteria or alternative methods have been established to select hypersensitive individual patients, evaluation of perceptual thresholds to gut distension is still required.

In conclusion, despite their substantial demonstrable differences in gut sensitivity, hypersensitive and normosensitive IBS patients present with comparable, heterogeneous symptom patterns. Therefore, selection based on clinical parameters is unlikely to discriminate individual IBS patients with visceral hypersensitivity from those with normal visceral sensitivity.

REFERENCES


