

## Gut-focused hypnotherapy normalizes disordered rectal sensitivity in patients with irritable bowel syndrome

R. LEA\*, L. A. HOUGHTON\*, E. L. CALVERT\*, S. LARDER\*, W. M. GONSALKORALE†, V. WHELAN†, J. RANGLES†, P. COOPER†, P. CRUICKSHANKS†, V. MILLER† & P. J. WHORWELL\*†

\*Academic Department of Medicine and †Hypnotherapy Unit, University Hospital of South Manchester, Manchester, UK

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### SUMMARY

**Background:** We have previously shown that hypnotherapy alters rectal sensitivity in some patients with irritable bowel syndrome. However, this previous study used incremental volume distension of a latex balloon, which might be susceptible to subject response bias and might compromise the assessment of compliance. In addition, the study group was symptomatically rather than physiologically defined.

**Aim:** To assess the effect of hypnotherapy on rectal sensitivity in hypersensitive, hyposensitive and normally sensitive irritable bowel syndrome patients using a distension technique (barostat) that addresses these technical issues.

**Methods:** Twenty-three irritable bowel syndrome (Rome I) patients (aged 24–72 years) were assessed before and

after 12 weeks of hypnotherapy in terms of rectal sensitivity, symptomatology, anxiety and depression. Normal values for sensitivity were established in 17 healthy volunteers (aged 20–55 years).

**Results:** Compared with controls, 10 patients were hypersensitive, seven hyposensitive and six normally sensitive before treatment. Following hypnotherapy, the mean pain sensory threshold increased in the hypersensitive group ( $P = 0.04$ ) and decreased in the hyposensitive group, although the latter failed to reach statistical significance ( $P = 0.19$ ). Normal sensory perception was unchanged. Sensory improvement in the hypersensitive patients tended to correlate with a reduction in abdominal pain ( $r = 0.714$ ,  $P = 0.07$ ).

**Conclusion:** Hypnotherapy improves abnormal sensory perception in irritable bowel syndrome, leaving normal sensation unchanged.

### INTRODUCTION

Despite much research over the past 20–30 years, our understanding of the pathophysiology of irritable bowel syndrome and how best to treat this often debilitating disorder remain unclear. Early studies focused on motor abnormalities of the small and large bowel, but these were often conflicting and no clear relationship between

the presence of symptoms and the occurrence of an abnormality has been established.<sup>1, 2</sup> Probably the most consistent motor disorder recorded is exaggerated phasic contractile activity of the jejunum<sup>3, 4</sup> and colon<sup>5, 6</sup> following meal ingestion. However, the observation that abdominal pain can occur in association with normal motor events<sup>7</sup> supports more recent suggestions that some patients with irritable bowel syndrome appear to be more viscerally sensitive than healthy controls to intra-luminal events, such as distension, occurring within the gastrointestinal tract.<sup>8–15</sup> Previous studies have shown, for example, that approximately 55–86% of patients with diarrhoea-predominant

Correspondence to: Dr L. A. Houghton, Academic Department of Medicine, University Hospital of South Manchester, Nell Lane, West Didsbury, Manchester M20 2LR, UK.  
E-mail: lahoughton@man.ac.uk

irritable bowel syndrome<sup>11–14</sup> and 7–68% of patients with constipation-predominant irritable bowel syndrome<sup>11, 13–16</sup> are rectally sensitive to balloon distension. In addition, two studies have shown that between 6 and 19% of patients with constipation-predominant irritable bowel syndrome can also be hyposensitive or insensitive to rectal phasic distension.<sup>14, 16</sup>

In contrast with most clinical trials assessing the efficacy of currently available conventional medications,<sup>17</sup> hypnotherapy has been shown to be a highly effective treatment for refractory irritable bowel syndrome.<sup>18–23</sup> The classical symptoms of irritable bowel syndrome, such as pain, bloating and bowel habit, are significantly improved,<sup>18–23</sup> as are extra-intestinal symptoms,<sup>20, 21</sup> quality of life<sup>20, 21</sup> and economic functioning of the individual.<sup>20</sup> The exact mechanism by which hypnotherapy exerts its benefit is unknown, but it has been shown to improve psychological symptoms, such as anxiety and depression,<sup>20, 21</sup> and to modulate colonic motility.<sup>24</sup> In the past, we have shown that hypnotherapy increases the sensory thresholds for gas and urgency, but not for pain/discomfort to rectal distension, in patients with diarrhoea-predominant irritable bowel syndrome.<sup>25</sup> In addition, we found that there was a tendency for rectal sensitivity to increase in patients with constipation-predominant irritable bowel syndrome.<sup>25</sup> However, these studies were undertaken without the advantages of a barostat, which uses a computer-driven pump to deliver fixed pressure (rather than volume) inflations in an unpredictable manner to the subject (e.g. tracking),<sup>26</sup> reducing the previous problems of inaccurate compliance assessment and response bias. Another feature of our previous study was that patients were divided symptomatically into diarrhoea- and constipation-predominant irritable bowel syndrome sub-groups based on the assumption that this would be likely to reflect their sensitivity status. However, recent studies have reported a similar prevalence of hypersensitivity in patients with diarrhoea- and constipation-predominant irritable bowel syndrome,<sup>11, 13–16</sup> and hyposensitivity is only present in a relatively small proportion of constipation-predominant irritable bowel syndrome patients.<sup>14, 16</sup>

The aim of this study was to re-assess the effect of hypnotherapy on rectal sensitivity using a distension technique (ascending method of limits followed by tracking) that is less susceptible to subject response bias, together with a flaccid bag coupled to a barostat for fixed pressure rather than volume distension. Any

relationship to symptomatic improvement was also assessed.

## MATERIALS AND METHODS

### *Subjects*

Twenty-three patients with irritable bowel syndrome (aged 24–72 years; mean, 45.0 years; 16 female), diagnosed according to Rome I criteria,<sup>27</sup> were recruited to the study. In addition, 17 healthy volunteers (aged 20–55 years; mean, 37.6 years; nine female) were recruited. All had normal laboratory investigations and, in the case of the patients, normal colonoscopy or barium enema if aged over 40 years, together with no evidence of co-existent disease.

Subjects who drank greater than the recommended maximum alcohol limit (males, 21 units/week; females, 14 units/week) and smoked more than five cigarettes per day were excluded from the study. Medication known to alter gastrointestinal function, alcohol- or caffeine-containing drinks and cigarette smoking were prohibited for 48 h prior to the study. The study was approved by the South Manchester Medical Research Ethics Committee and all patients gave written informed consent.

### *Protocol*

Sensory and motor responses to distension of the rectum were assessed within 2 weeks both before and after a 12-week course of hypnotherapy in patients with irritable bowel syndrome.

On each occasion, the subject attended the Clinical Investigations Unit after an overnight fast. Following a Fleet enema (Laboratorios Casen-Fleet SA, Zaragoza, Spain), a catheter (customized rectal barostat catheter, Part no. C7-2CB-R (22F); MUI Scientific, Mississauga, Ont., Canada), to which was attached a polyethylene bag (Pillow Type Rectal Barostat Balloon, Part no. CT-BP600R; length, 22 cm; diameter, 15 cm; capacity, 600 mL; MUI Scientific, Mississauga, Ont., Canada), was inserted into the rectum and positioned such that the centre of the bag was 11 cm from the anal verge. The bag was then unfolded by transiently inflating it with 150 mL of air and then deflating it completely (conditioning distension). After a 1-h recovery period, the catheter was connected to a computer-driven volume displacement device (G & J Electronics Inc.,

Toronto, Ont., Canada) and the pressure in the bag was increased in increments of 2 mmHg until respiratory excursions were observed or, if respiratory variations were not obvious, set at 12 mmHg (basal operating pressure). This pressure was then maintained for 15 min whilst monitoring the intra-bag volume continuously to give a measure of rectal tone.

The bag was then serially inflated from the basal operating pressure in increments of 4 mmHg until moderate pain was experienced (see below) or a maximum pressure of 48 mmHg was reached (ascending method of limits). Each inflation was maintained for 2 min, and separated by 2 min, during which the pressure in the bag was returned to the basal operating pressure. Sixty seconds after commencement of each inflation, the patients were prompted to indicate on a standard pro forma whether they were experiencing pain/discomfort on the following scale: 0, no pain/discomfort; 1, mild but not sustained pain/discomfort; 2, mild and sustained pain/discomfort; 3, moderate pain; 4, intense pain.

When the subject first experienced moderate pain (score, 3), the volume displacement device was programmed to terminate the ascending method of limits sequence and to start tracking around this pressure until a total of 15 inflation trials had occurred. The sensory threshold was calculated as the average pressure over the series of tracking inflations rated as at least moderately painful. This procedure is designed to make the distension sequence unpredictable to the subject and to minimize response bias.<sup>26</sup> At any time, both the patient and investigator could discontinue the inflation for any reason by pressing the 'panic button'.

Symptomatology, in particular the severity of abdominal pain/discomfort, bloating and dissatisfaction with bowel habit (visual analogue scale), and anxiety and depression levels (Hospital Anxiety and Depression Scale<sup>28</sup>) were assessed before and after hypnotherapy.<sup>20, 21</sup>

### *Hypnotherapy*

Patients received hypnotherapy for 12 weeks at weekly intervals for approximately 1 h per session. Hypnotherapy was based on the techniques previously described,<sup>18-21</sup> and involved hypnotic induction using progressive relaxation and other procedures to deepen the hypnotic state. This was followed by suggestions,

imagery and other techniques appropriate to the individual, such as inducing warmth through the patient's hands on the abdomen, directed towards the control and normalization of gut function, in addition to relevant ego-strengthening interventions. Patients were asked to practise these hypnotic skills on a daily basis with the help of an audio-tape, as well as to use them as necessary to relieve symptoms. At each session, interventions were reinforced or modified according to the patient's needs.

### *Normal sensory reference range*

A normal 95% reference range for the sensory threshold to moderate pain (score, 3) was obtained by carrying out the same procedure in 17 healthy volunteers.

### *Data analysis*

The following measurements were derived: (i) the sensory threshold for pain, calculated as the average pressure over the series of tracking inflations rated as at least moderate pain (score, 3); (ii) rectal tone, calculated from the average bag volume whilst maintaining the pressure at basal operating pressure for 15 min;<sup>29</sup> (iii) static compliance ( $C_{stat}$ ), calculated as the volume/pressure relationship at 20 mmHg;<sup>30</sup> and (iv) dynamic compliance ( $C_{dyn}$ ), calculated from the slope of the compliance curve.<sup>30, 31</sup>

In addition, each patient was classified as having a normally sensitive, hypersensitive or hyposensitive rectum. This was based on the 95% reference range for the sensory threshold to moderate pain (score, 3) obtained from the healthy volunteers. Patients having a rectal sensory threshold below the 2.5th percentile limit were defined as hypersensitive, those with a sensory threshold above the 97.5th percentile limit were defined as hyposensitive and those with a sensory threshold within these limits were defined as normally sensitive.

### *Statistical analysis*

The effect of hypnotherapy on symptomatic and physiological parameters was assessed using the paired *t*-test (parametric data), Wilcoxon test (non-parametric data) or McNemars test (categorical data). Differences between patient sub-groups were evaluated using analysis of variance (ANOVA) or chi-squared test, whilst correlations were determined using Pearson's (parametric

data) or Spearman's rank (non-parametric data) tests. Results are expressed as the mean and 95% confidence intervals (parametric data) or median and interquartile range (non-parametric data).

**RESULTS**

*Rectal sensation*

The healthy volunteers had a mean pressure threshold for moderate pain of 31.25 mmHg, with 2.5th and 97.5th percentile limits of 24.52 and 37.99 mmHg, respectively.

Consequently, 10 of the 23 patients (44%) studied were found to be hypersensitive, seven (30%) hyposensitive and six (26%) normally sensitive to distension before hypnotherapy.

Following hypnotherapy, the pressure threshold for moderate pain increased significantly in patients who were hypersensitive ( $P = 0.04$ ) and tended to decrease

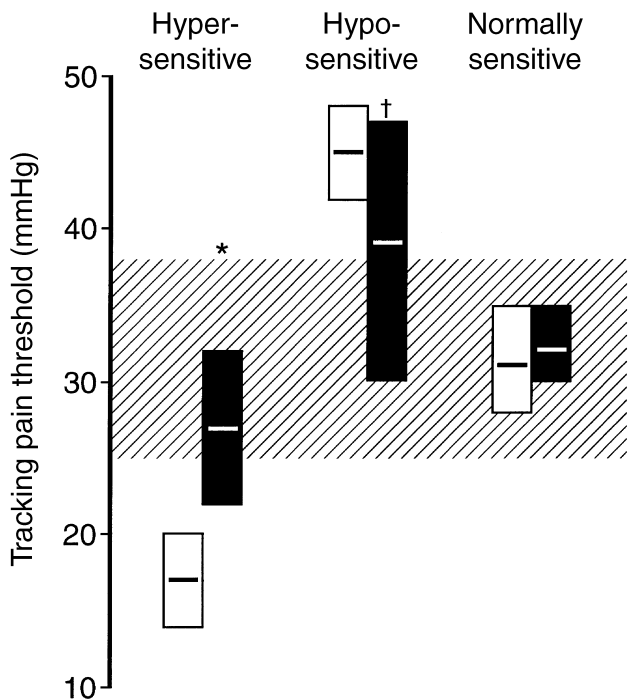


Figure 1. Tracking pain thresholds (mmHg) before (open bars) and after (filled bars) hypnotherapy in hypersensitive, hyposensitive and normally sensitive patients with irritable bowel syndrome. Results are expressed as the mean and 95% confidence interval. The shaded area shows the 2.5th and 97.5th percentile limits for the tracking pain threshold of normal healthy volunteers. \* $P = 0.04$  and † $P = 0.19$  compared with before hypnotherapy.

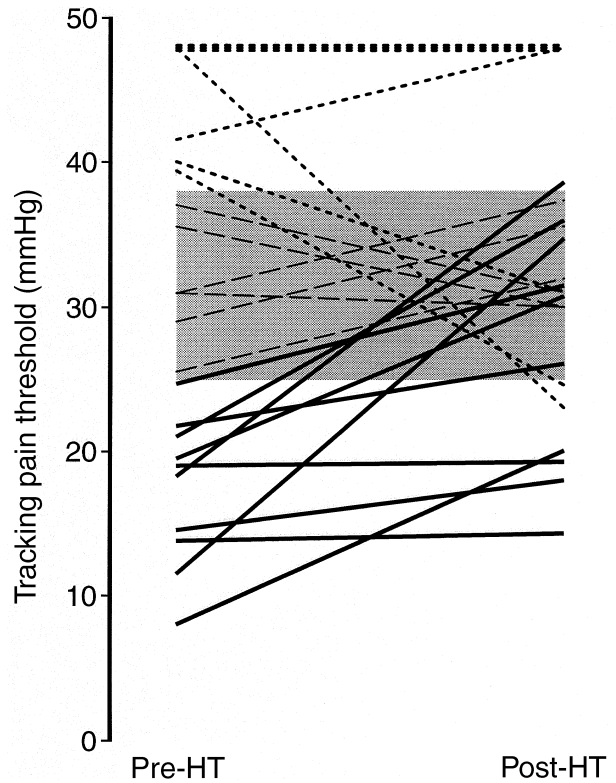


Figure 2. Tracking pain thresholds (mmHg) pre- and post-hypnotherapy (HT) in hypersensitive (full line), hyposensitive (---) and normally sensitive (· · ·) patients with irritable bowel syndrome. The shaded area represents the 2.5th and 97.5th percentile limits for the tracking pain threshold of normal healthy volunteers. Following hypnotherapy, the mean pain threshold increased in patients who were hypersensitive ( $P = 0.04$ ) and tended to decrease in patients who were hyposensitive ( $P = 0.19$ ) prior to hypnotherapy.

in patients who were hyposensitive ( $P = 0.19$ ) prior to treatment (Figures 1 and 2). Sensory thresholds were not significantly affected in those patients whose pain threshold was within normal limits prior to treatment (Figures 1 and 2).

*Rectal compliance and tone*

Prior to treatment, there was no statistical difference in dynamic ( $C_{dyn}$ ) or static ( $C_{stat}$ ) compliance, or tone, between the patient sub-groups. Following hypnotherapy, neither dynamic ( $C_{dyn}$ ) or static ( $C_{stat}$ ) compliance, nor tone, changed with hypnotherapy in rectally hypersensitive or hyposensitive patients (Table 1). However,  $C_{stat}$ , but not  $C_{dyn}$  or tone, tended to increase following hypnotherapy in patients who had normal rectal sensitivity prior to treatment (Table 1).

Table 1. Effect of hypnotherapy on rectal compliance, tension and tone

	Pre-hypnotherapy	Post-hypnotherapy	P
Hypersensitive			
C <sub>stat</sub>	2.35 (1.78, 2.92)	3.71 (0, 7.65)	0.91
C <sub>dyn</sub>	4.81 (1.99, 7.63)	5.07 (2.78, 7.36)	0.82
Tone*	19.04 (17.40, 54.28)	5.00 (2.56, 30.27)	0.46
Hyposensitive			
C <sub>stat</sub>	4.22 (2.45, 5.99)	4.48 (2.39, 6.56)	0.76
C <sub>dyn</sub>	7.44 (5.06, 9.82)	7.65 (4.68, 10.62)	0.79
Tone*	1.92 (-0.8, 26.52)	34.20 (21.14, 45.56)	0.50
Normally sensitive			
C <sub>stat</sub>	4.03 (1.47, 6.59)	6.56 (3.93, 9.19)	0.09
C <sub>dyn</sub>	7.53 (4.19, 10.87)	9.01 (6.53, 11.49)	0.13
Tone*	21.86 (-2.71, 86.84)	32.84 (3.81, 68.83)	0.46

C<sub>stat</sub>, static compliance in mL/mmHg; C<sub>dyn</sub>, dynamic compliance in mL/mmHg; tone in mL. Results expressed as mean (95% confidence interval) or \*median (interquartile range).

### Symptomatology and relationship to sensitivity

Table 2 shows the presenting predominant bowel habit and age and gender characteristics of the hypersensitive, hyposensitive and normally sensitive patients prior to rectal distension. Nine of the 10 (90%) patients who were rectally sensitive prior to hypnotherapy had diarrhoea-predominant irritable bowel syndrome, whilst there was an even distribution of patients with diarrhoea- and constipation-predominant irritable bowel syndrome in the other two groups. There was no statistical difference amongst the sub-groups in terms of age and gender (Table 2).

Prior to treatment, there was no statistical difference in the severity of pain, bloating and dissatisfaction with bowel habit between the patient sub-groups. Following hypnotherapy, pain, bloating and dissatisfaction with bowel habit all statistically improved in the hypersensitive and normally sensitive patients ( $P < 0.05$ ), but only dissatisfaction with bowel habit significantly

improved in the hyposensitive patients ( $P = 0.02$ ) (Figure 3). No one sub-group improved significantly more than another and, when the sub-groups were combined, hypnotherapy was shown to be generally effective at relieving symptoms in patients with irritable bowel syndrome ( $P = 0.002$ ).

Similarly, there was no statistical difference in the basal levels of anxiety and depression between the patient sub-groups, and both improved following hypnotherapy in all three sub-groups (Table 3). No one sub-group improved significantly more than another.

Finally, the degree of improvement in the pain sensory threshold tended to correlate with the degree of improve-

Table 2. Presenting characteristics in rectally hypersensitive, hyposensitive and normally sensitive irritable bowel syndrome patients

	Hypersensitive	Hyposensitive	Normally sensitive
Number	10	7	6
Diarrhoea	9	3	3
Constipation	0	3	3
Alternating	1	1	0
Age, mean (range) (years)	48 (24–72)	47 (32–71)	38 (26–49)
Female/male	7/3	6/1	3/3

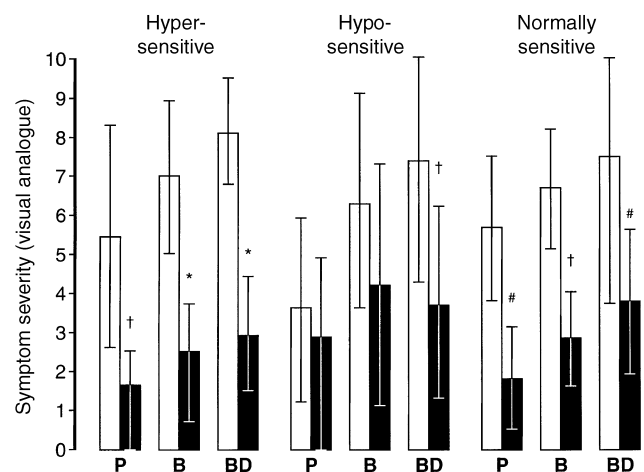


Figure 3. Abdominal pain (P), bloating (B) and bowel habit dissatisfaction (BD) before (open bars) and after (filled bars) hypnotherapy. Results are expressed as the mean and 95% confidence interval. \* $P = 0.002$ , † $P = 0.02$  and # $P < 0.05$  compared with before hypnotherapy.

Table 3. Effect of hypnotherapy on anxiety and depression

	Pre-hypnotherapy	Post-hypnotherapy	P
Hypersensitive			
Anxiety	12 (10, 15)	5 (3, 11)	0.06
Depression	6 (4, 8)	0 (0, 6)	0.03
Hyposensitive			
Anxiety	10 (7, 11)	7 (4, 7)	0.03
Depression	7 (3, 10)	4 (1, 8)	0.04
Normally sensitive			
Anxiety	8 (8, 14)	6 (5, 8)	0.07
Depression	8 (5, 13)	3 (2, 8)	0.07

Results expressed as median (interquartile range).

ment in the severity of abdominal pain ( $r = 0.714$ ;  $P = 0.07$ ) and depression ( $r = 0.780$ ;  $P = 0.07$ ) in patients who were rectally sensitive prior to treatment, but not in the other two sub-groups. There was no correlation with the degree of improvement in anxiety. Furthermore, the degree of improvement in abdominal pain severity did not correlate with the degree of improvement in either anxiety or depression in any of the three sub-groups.

## DISCUSSION

This study extends our previous observations by showing that hypnotherapy normalizes rectal sensory thresholds for pain in patients with irritable bowel syndrome exhibiting either hypersensitivity or hyposensitivity. In addition, the increase in sensory threshold induced by hypnotherapy in hypersensitive patients tends to be positively correlated with a concomitant reduction in abdominal pain. Of particular note was the observation that hypnotherapy does not appear to affect normal rectal sensation, a quality that would be most desirable for any new pharmacological intervention coming on to the market for irritable bowel syndrome.

The patients recruited to this study were at the beginning of a waiting list to receive a course of hypnotherapy from our National Health Service-supported Hypnotherapy Unit,<sup>21</sup> and represent a mixture from tertiary, secondary and primary care settings. However, as hypnotherapy is often the treatment of choice for patients refractory to conventional medication, these patients probably have more severe irritable bowel syndrome than that seen in similar hospital out-patients. This could explain the slightly high proportion of patients in this study (74%) who had abnormal

visceral sensitivity, although the percentage showing hypersensitivity (44%) was well within that reported by other studies (33% to >60%).<sup>11, 14</sup> The percentage of patients with hyposensitivity, however, was slightly higher than that reported by Prior *et al.* (10%),<sup>14</sup> but this may be related to the different distension techniques employed and the population of patients studied (Rome I criteria were not used). Hyposensitivity, however, has received very little attention from researchers, so that the true extent of this abnormality in the irritable bowel syndrome population is unknown.

One possible criticism that could be directed at our results is that they represent a regression to the mean phenomenon (i.e. high values tend to decrease and low values tend to increase on repeated testing). This seems doubtful, however, as some patients did not show a change in their sensory threshold and, in others, it moved away from the mean sensory threshold for healthy volunteers of 31 mmHg following hypnotherapy. Previous studies, in which rectal sensitivity was assessed at four different times throughout the menstrual cycle in healthy volunteers, have shown that it is reproducible during repeated testing.<sup>32</sup>

The mechanism by which hypnotherapy normalizes sensory perception cannot be elucidated from the present study. However, it is unlikely to be due to alterations in psychological vigilance, as the effect of this on the subject's response to the distension procedure was minimal in the present study because of the use of a tracking distension protocol, which makes the pressure inflations unpredictable to the subject. Many studies have examined the possible role played by psychological factors, such as anxiety and depression, in disordered sensitivity and, in general, have been unable to show any direct relationship.<sup>33, 34</sup> Our data, which show comparable pre-study anxiety/depression levels and similar changes induced by hypnotherapy in patients with and without pre-study sensory abnormalities (together with the fact that there was no correlation between the reduction in anxiety and improvement in sensory threshold for either of the disordered sensitivity sub-groups), support this view. However, there was a tendency for the reduction in depression levels to be positively correlated with an improvement in sensory threshold in the hypersensitive group. The significance of this single finding is unclear, given that no similar correlation was observed for the hyposensitive group, and in the light of recent observations showing that the antidepressant,

fluoxetine, was unable to modify rectal sensitivity in a group of irritable bowel syndrome patients.<sup>35</sup> Larger studies using more specific and sensitive psychological assessment are required. Changes in rectal compliance (change in  $dV/dP$  or  $C_{dyn}$ ), tension (change in  $C_{stat}$  without change in  $C_{dyn}$ ) and tone also cannot explain the improvements seen in rectal sensitivity. Given the mode of application of hypnotherapy, the central nervous system must at least be initially involved in this alteration of pain processing, and recent positron emission tomography studies of the brain during hypnosis lend some support to this view.<sup>36</sup> It has been shown that, when hypnosis is used to increase or decrease the perception of a somatic thermal stimulus, associated increases and decreases in the activity of the anterior cingulate cortex, an area of the brain important in pain processing, are demonstrated.<sup>36</sup> Using functional magnetic resonance imaging, this particular area of the brain has also been implicated in the abnormal processing of visceral stimulation in patients with irritable bowel syndrome,<sup>37</sup> suggesting that hypnotherapy might be modulating the activity of the anterior cingulate cortex in patients undergoing this form of treatment for their disorder.

As in previous studies,<sup>18–23</sup> hypnotherapy significantly improved the cardinal symptoms of abdominal pain, bloating and dissatisfaction with bowel habit in the group as a whole, and, in the hypersensitive group, there was a trend towards a correlation between the reduction in sensitivity and improvement in pain. This suggests that hypersensitivity may have a role in the pathogenesis of pain in such patients, which is an important finding, as it has, in the past, always been difficult to demonstrate any relationship between the putative physiological abnormalities observed in irritable bowel syndrome and symptomatology. Patients who were normally sensitive prior to treatment also showed an improvement in their symptoms with hypnotherapy. Although hypnotherapy did not modulate rectal sensitivity in this group of patients, this does not exclude possible changes in visceral sensitivity elsewhere in the gut, as previous studies have shown that irritable bowel syndrome patients can have disordered sensitivity at other sites within the gastrointestinal tract without the rectum necessarily being involved.<sup>12, 16</sup> For example, these patients may have had increased sensitivity in the jejunum, a region of the gastrointestinal tract in which patients more often appear to be hypersensitive to distension in comparison with the rectum (75% vs.

55%),<sup>12, 16</sup> and thus symptomatic improvement may have been associated with a normalization of this, rather than the rectal sensitivity. Interestingly, however, this group of normally sensitive patients showed a tendency for the static compliance to increase following hypnotherapy, which might have had some beneficial effect on their symptoms. Previous studies have shown that relaxation of the stomach pharmacologically may be associated with a reduction in symptomatology in patients with functional dyspepsia,<sup>38</sup> but may not always be related to a reduction in visceral sensitivity.<sup>29</sup> Finally, those patients who were hyposensitive prior to treatment showed a significant improvement in their dissatisfaction with bowel habit only, and not in abdominal pain or bloating. The reason for this is unknown, but does not appear to be a result of these patients being more symptomatic and/or anxious or depressed before treatment. The number of patients studied, however, was small, and larger studies are required to confirm both the symptomatic and sensitivity findings in this group.

In summary, in contrast with pharmacological interventions, hypnotherapy has the potential to normalize a range of often opposing physiological abnormalities in gastrointestinal function seen in patients with irritable bowel syndrome, which may explain why it is helpful irrespective of the sub-group being treated.

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