Towards an integrated psychoneurophysiological approach of irritable bowel syndrome

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SHORT AND LONG TERM BENEFIT OF RELAXATION TRAINING FOR IRRITABLE BOWEL SYNDROME

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ABSTRACT

Background: Psychotherapy is effective in treating Irritable Bowel Syndrome (IBS), but the effect of relaxation training (RT), a brief psychological group intervention, is not known.

Aim: To determine the efficacy of RT in a large cohort of IBS-patients.

Methods: Ninety-eight IBS-patients were included in this randomized controlled trial. Forty-six patients received standard medical care (CON) and 52 received four 90-minute sessions of RT in small groups in addition to standard medical care. IBS symptom severity, medical consumption and quality of life were assessed at baseline in patients and in 38 healthy controls and evaluated in patients at 3, 6 and 12 months after intervention.

Results: IBS symptom severity was significantly reduced in the RT group compared to CON at 3, 6 and 12 months after treatment (time by treatment interaction, P=0.002). The number needed to treat for long term improvement was 5. Quality of life was improved (General Health, P=0.017; Health Change, P=0.05). Frequency of doctor visits was reduced (P=0.039).

Conclusion: Relaxation training is a brief group intervention that significantly improves symptom severity, general health perception and medical consumption in IBS patients immediately after, as well as 6 and 12 months after intervention.

INTRODUCTION

Irritable Bowel Syndrome (IBS), a frequently occurring functional bowel disorder, is characterized by recurrent abdominal discomfort or pain accompanied by altered bowel habits[1]. IBS has considerable economic impact[2], accounting for total annual direct costs of £ 45.6 million on average in the United Kingdom[3]. In the Netherlands, health care utilization and absence from work in IBS patients is approximately twice that of the general population[4].

Since curative treatment is currently not available[5], therapeutic interventions are directed against predominating symptoms. These interventions include antispasmodics, laxatives or antidiarrhoeals in addition to patient education, reassurance, and dietary advice[6]. Novel therapies focus on serotonergic and psychotropic agents, but therapeutic gain is at best restricted to subgroups of patients[7-10]. In addition to pharmacotherapy, efficacy of psychological interventions such as cognitive behavioural therapy, dynamic psychotherapy and hypnotherapy has been demonstrated in a number of studies[11-15]. Most of these interventions, however, require multiple sessions in individual patients and are therefore time-consuming and expensive.

Relaxation training (RT) is a brief psychological intervention that can not only be provided to individuals, but also to groups of patients. Most forms of psychotherapy incorporate a relaxation technique, but sound data on the efficacy of RT as solitary treatment for IBS are lacking[16]. Two studies on the efficacy of RT in IBS provided promising results but had methodological limitations (small patient number, high drop-out rate)[17-18]. We conducted a randomized controlled trial to determine short and long-term efficacy of group RT, when added to standard medical care (CON), in a large cohort of IBS patients.

MATERIALS AND METHODS

Patients

Between March 2001 and July 2002, IBS patients between 18 and 65 years of age were invited to participate. To obtain a representative sample from the IBS population, patients were recruited both through the outpatient Department of Gastroenterology and Hepatology of the Leiden University Medical Centre (LUMC) and through advertisement in a local newspaper. All eligible patients were screened by one of the investigators (PvdV) to confirm that each participant met Rome II criteria for IBS[1]. Exclusion criteria were presence of any organic disease (particularly inflammatory bowel disease and thyroid disease), previous abdominal surgery (except cholecystectomy and appendectomy), pregnancy and dependence on analgesics. Use

of antispasmodics, laxatives, bulking agents and occasional use of analgesics was permitted. The Mini International Neuropsychiatric Interview (Dutch version 5.0.0)[19] was used to exclude patients with psychotic disorder, substance use disorder or risk of suicide. Thirty-eight age and sex-matched healthy volunteers were included for baseline comparisons. Informed consent was obtained from each participant. The study protocol was approved by the LUMC ethics committee.

Study design

Randomization

This study was designed and conducted as a randomized controlled trial. To guarantee participation of 5 patients per RT group, block wise randomization was carried out in 10 patients using sealed envelopes by a co-worker who was not involved in the study. The day and time of treatment was decided on the agenda of the trainers, not of the patients. Patients randomized to RT, who were unable to attend all scheduled sessions, were asked to participate in the subsequent RT group. If this was not possible, they were replaced by a patient from the control group (CON) who was not yet informed about the randomization results. This procedure was also performed by the same co-worker (Fig 1).

Patient characteristics

Baseline demographics, clinical characteristics and quality of life were assessed in patients and in healthy volunteers. To further characterize the patient group, levels of anxiety, depression, somatic symptoms and psychoneuroticism were measured in patients and healthy controls using the Symptom Checklist 90[20]. The presence of dysfunctional IBS related cognitions was assessed by the Cognitive Scale for Functional Bowel Disorders[21].

Intervention

During the screening visit, all patients received information on gut function in IBS. The physician provided a positive diagnosis for IBS with explanation and a rationale for the specific symptoms. In the control treatment arm patients were instructed to have, upon request and for the duration of the study, free access to specialized gastroenterological care including symptom-oriented pharmacotherapy. No attempt was made to control for contact time between therapist and patient in the control versus the RT arm. The primary aim was to make the control condition credible, plausible and acceptable for the patient. Patients in the RT group were also allowed free access to specialized gastroenterological care and pharmacotherapy.

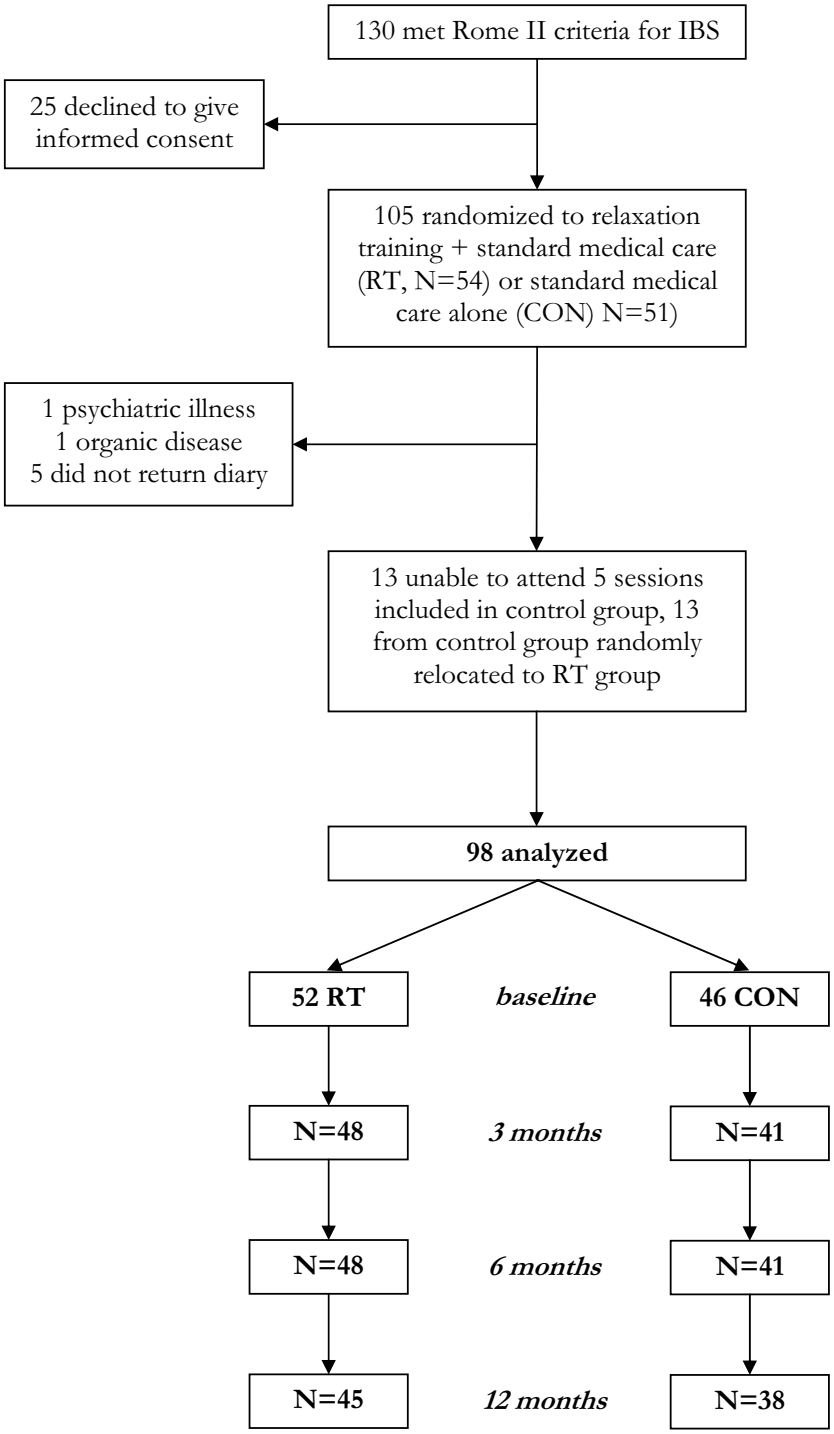

Figure 1. Patient flow during randomisation and number of patients during each phase of the study

A treatment group of 5 or 6 patients was guided by one of three experienced therapists and one of two trainees. Two of three therapists were professional cognitive behavioural therapists and one had nearly finished training. They co-operated with the trainees, who were postgraduate psychologists. Before RT commenced, trainers met each patient individually for 45 minutes to get acquainted to one another and to explain the treatment rationale. Briefly, the therapists explained to patients that abdominal pain involuntarily induces muscle tension. Chronic muscle tension not only maintains abdominal pain, but can also lead to other IBS-associated symptoms, such as borborygmi, indigestion and bloating. By applying relaxation techniques, patients should be able to counteract chronic muscle tension and subsequently experience symptom relief.

RT consisted of weekly 90-min sessions for 4 weeks and one booster session after 3 months. Exercises were audiotaped to facilitate home practice. Training was given according to a written treatment protocol (available on request). Training sessions focused on 1) recognition of muscle tension (progressive relaxation technique), 2) relaxation of muscles (suggestive relaxation technique) combined with breathing retraining, as most IBS patients show evidence of breathing pattern disorders, 3) teaching the patient to elicit a quick relaxation response by prompt recognition of muscle tension and subsequent relaxation, and 4) implementation into daily life. In the booster session, patients shared their experiences and were encouraged to continue using relaxation techniques. All sessions were videotaped and reviewed to monitor therapists' adherence to the treatment protocol. Before randomization, all patients were informed through the consent form that they would be randomized to either RT or standard medical care (CON). On request, patients were notified that, when randomized to standard treatment alone, it would be possible to receive RT after ending of the trial, but only if the efficacy of RT for IBS had been demonstrated.

Outcome measures

Patients used a symptom diary card to rate the severity of abdominal discomfort, abdominal pain, constipation, diarrhoea, bloating, as well as overall symptom severity, daily for 14 days, on a 5-point Likert scale (0 = no symptoms, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe symptoms). The primary outcome measure was the IBS composite score, computed as the sum of the 14-day mean scores for abdominal pain, discomfort, constipation, diarrhoea and bloating (score range 0-20). Secondary outcome measures were: the number of symptom-free days (i.e. overall symptom rating is zero) (score range 0-14); overall symptom rating (i.e., the severity of all symptoms rated together rather than each symptom separately; score range 0-4); quality of life (SF-36)[22]; and medical consumption defined by 1) the number of doctor visits in the previous 3 months and 2) the number of analgesics and laxatives/

antidiarrhoeals used in the previous 14 days. All outcome measures were evaluated at baseline and 3, 6 and 12 months after RT.

Missing data

In case certain questions in the SCL-90 were not answered, subscales of anxiety, depression, somatic symptoms or psychoneuroticism could not be calculated and were regarded as missing. In these cases subscale scores were calculated as ((observed score x the number of scale items) / (the number of scale items - number of missing items)). The same approach was used for missing items on subscales of the SF-36 and the Cognitive Scale for Functional Bowel Disorders. The statistical package dealt with missing subscale scores for all primary and secondary outcome parameters by inserting the mean score of the other patients for that parameter.

Statistical analysis

We aimed to enrol fifty patients per treatment arm, based on: 1) 20 % difference in improvement in IBS composite score (RT versus CON) one year after therapy, which we considered clinically relevant; 2) power of 0.80 and standard deviation of the relative improvement of 47%, based on previous studies by our group, and 3) 20% dropout rate.

Patients' baseline scores were compared to scores in healthy volunteers by one-way analysis of variance (ANOVA). Treatment efficacy with respect to primary and secondary outcome measures was assessed by a mixed model analysis (SPSS for Windows, 11.0). Patients who had missing data were not excluded from the analysis (see above). Confounders of baseline IBS composite scores, time, treatment condition (i.e., relaxation training *versus* standard treatment) and time by treatment interaction were all analyzed as separate contributors to the model. Patient numbers were used as indicator for repeated measurements.

Responders to therapy were identified using Jacobson and Truax' criteria for 'clinical significant change' on the IBS composite score[23]. This change, defined as the extent to which treatment puts an individual outside the range of the patient population or within the range of the non-patient population, was determined by calculation of a reliable change index (RC). This is the difference between pre- and post-test scores divided by the standard error of the difference. An RC larger than 1.96 indicates true change in post-test versus pre-test scores. Differences in responder versus non-responder distributions between groups were calculated by chi-square analysis. Binary logistic regression was used to determine which of the following demographical, clinical and psychological variables could predict therapy success: age, sex, recruitment strategy (outpatient clinic or advertisement), IBS subgroup (diarrhoea, constipation, alternating type), treatment (relaxation or standard medical

care), general health (SF-36), anxiety (SCL-90), depression (SCL-90), somatisation (SCL-90), psychoneuroticism (SCL-90), dysfunctional cognitions (Cognitive Scale for Functional Bowel Disorders), frequency of doctor visits, frequency of analgesic use.

We assessed the efficacy of RT by an intention-to-treat analysis. Data are expressed as mean ± SEM. The level of significance is set at $P<0.05$.

RESULTS

Patients' characteristics

We screened 130 patients of whom 105 provided informed consent. Fifty-four patients were randomized to RT and 51 patients to CON (Fig 1). Seven patients were excluded from the analysis: 1 patient had conversion disorder (diagnosed during the individual session with the therapist), 1 patient had ulcerative colitis (diagnosed after randomization), and 5 patients did not return any of the symptom diaries. Ninety-eight patients were included in the final analysis (RT group, 52; CON group, 46). Sixty-eight patients were recruited through advertisement and 30 through the outpatient department. Some patients did not return 1 or 2 symptom diaries during follow-up, despite regular reminders by telephone to do so (n=9 at 3 months, n=9 at 6 months, n=15 at 12 months, Fig 1). These patients were included in the final analysis (see Missing data). Thirteen patients who were randomized to RT were unable to attend treatment sessions (mostly due to other obligations such as work) and were included in the CON group. These patients were replaced by 13 patients in the CON group (see above).

Table 1 lists baseline demographical and clinical characteristics of both treatment groups and healthy controls. IBS patients had higher symptom scores, impaired quality of life on 6 out of 8 SF-36 subscales, more IBS related dysfunctional cognitions and higher medical consumption. Levels of anxiety and depression did not differ. Baseline IBS composite scores were higher in patients recruited through the outpatient clinic versus patients recruited through advertisement (5.50 ± 0.4 versus 3.85 ± 0.3, P=0.002).

Intention-to-treat analysis

Primary outcome: IBS composite score

IBS composite scores showed a significantly larger reduction in patients who received RT compared to patients who received standard medical care (CON) (time by treatment interaction, P=0.002; Fig 2). Although baseline composite scores were higher in hospital-recruited patients compared to advertisement-recruited patients, the time-by-treatment interaction remained significant after correction for recruitment (P=0.002).

Table 1. Baseline demographical and clinical characteristics of IBS patients and healthy volunteers

Characteristic	Relaxation (n=52)	Control (n=46)	Healthy controls (n=38)
Demographics			
Age (yr)	42.9 ± 1.9	41.7 ± 2.1	39.7 ± 2.4
Female sex (%)	75	72	63
Ethnicity (% Caucasian)	96	89	95
Employment (%)	64	61	-*
Married (%)	84†	70	61
Children (%)	61	52	58
Alcohol use (%)	70	78	94
Current smoking (%)	20	39†	13
Recruitment (% advertisement)	69	70	100
Bowel habit (%)			
Diarrhoea	36	30	0
Constipation	25	48	0
Alternating	31	15	0
Normal or not specified	8	7	100
IBS symptoms			
IBS symptom severity score (0-20)	4.32 ± 0.3	4.41 ± 0.4	0.43 ± 0.1 †
N of symptom free days (0-14)	2.31 ± 0.4	3.02 ± 0.6	0.89 ± 0.3 †
Overall symptom rating (0-4)	1.29 ± 0.1	1.32 ± 0.1	0.13 ± 0.0 †
Psychological profile			
Anxiety (10-50)‡	13.2 ± 0.6	13.8 ± 0.7	12.2 ± 0.6
Depression (16-80)‡	21.6 ± 0.8	23.6 ± 1.2	20.7 ± 1.4
Somatic symptoms (12-60)‡	17.8 ± 0.7	19.0 ± 0.9	15.0 ± 0.6 †
Psychoneuroticism (90-450)‡	119.8 ± 3.8	128.0 ± 5.4	113.3 ± 5.1
Dysfunctional cognitions (31-217)§	108.1 ± 5.1	111.9 ± 5.1	85.6 ± 6.3 †
Quality of life (0-100) **			
Physical functioning	84.2 ± 2.6	79.3 ± 3.3	94.1 ± 1.7 †
Role limitations-physical	58.2 ± 6.0	63.3 ± 6.0	87.2 ± 4.7 †
Bodily pain	63.2 ± 2.6	60.5 ± 3.1	90.3 ± 2.6 †
Mental health	77.3 ± 2.1	73.0 ± 2.6	78.5 ± 2.2
Role limitations-emotional	85.6 ± 4.4	77.0 ± 5.6	91.0 ± 4.4
Social functioning	78.8 ± 2.7	67.1 ± 3.9	90.9 ± 2.4 †
Vitality	61.3 ± 2.2	55.8 ± 2.7	70.8 ± 2.6 †
General health	61.3 ± 2.7	61.6 ± 2.7	75.1 ± 2.4 †
Health change	52.9 ± 3.0	49.5 ± 3.3	53.5 ± 2.5
Medical consumption			
Doctor visits (n/3 months)	1.6 ± 0.1	1.7 ± 0.1	0.7 ± 0.1 †
Analgesics (n/14 days)	2.4 ± 0.7	2.1 ± 0.5	0.6 ± 0.2
Laxative/antidiarrhoeal (n/14 days)	5.4 ± 1.3	4.7 ± 1.2	0.0 ± 0.0 †

Data are presented as mean ± standard error. Numbers in parentheses indicate the range of possible scores for a particular item, with the lower number indicating the best possible score and the higher number indicating the worst possible score. * unknown; † $P<0.01$ versus patient subgroups; ‡ measured using SCL-90 subscales § measured using the Cognitive Scale for Functional Bowel Disorders; ** measured using the SF-36.

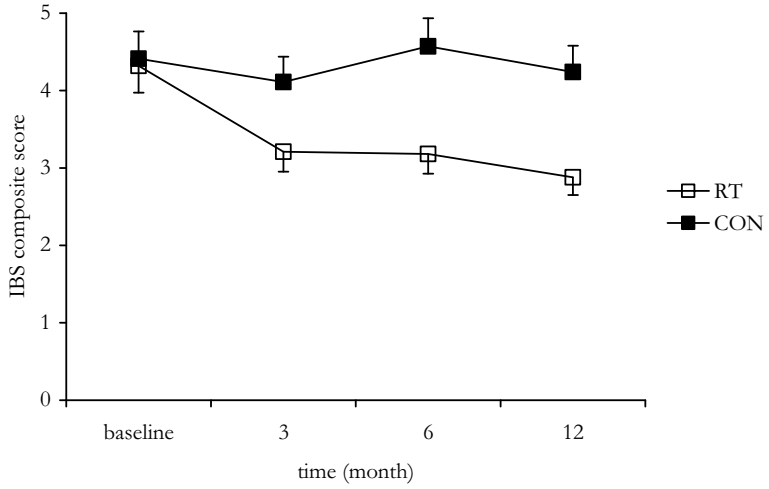

Figure 2. Symptom severity score after 3, 6 and 12 months follow-up in the RT and CON group (time by treatment interaction, P=0.002).

Secondary outcome measures

The number of days without any symptoms (i.e. overall symptom rating was zero) increased significantly more in RT versus CON (time-by-treatment interaction, P=0.027) (Fig 3). Overall symptom rating showed a significantly greater improve-

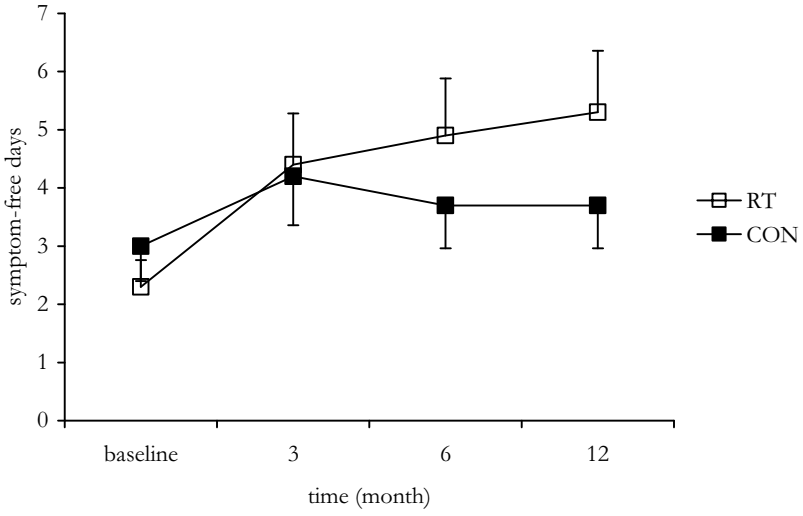

Figure 3. Number of symptom-free days (per 14 days) after 3, 6 and 12 months follow-up in the RT and CON group (time by treatment interaction, P=0.027).

ment in patients who received RT compared to CON (time-by-treatment interaction, P=0.021; data not shown).

Patients in the RT group showed significantly more improvement on the SF-36 General Health (P=0.017) (Fig 4A) and Health Change subscales (P=0.05, Fig 4B). None of the other domains showed significant differences between both groups

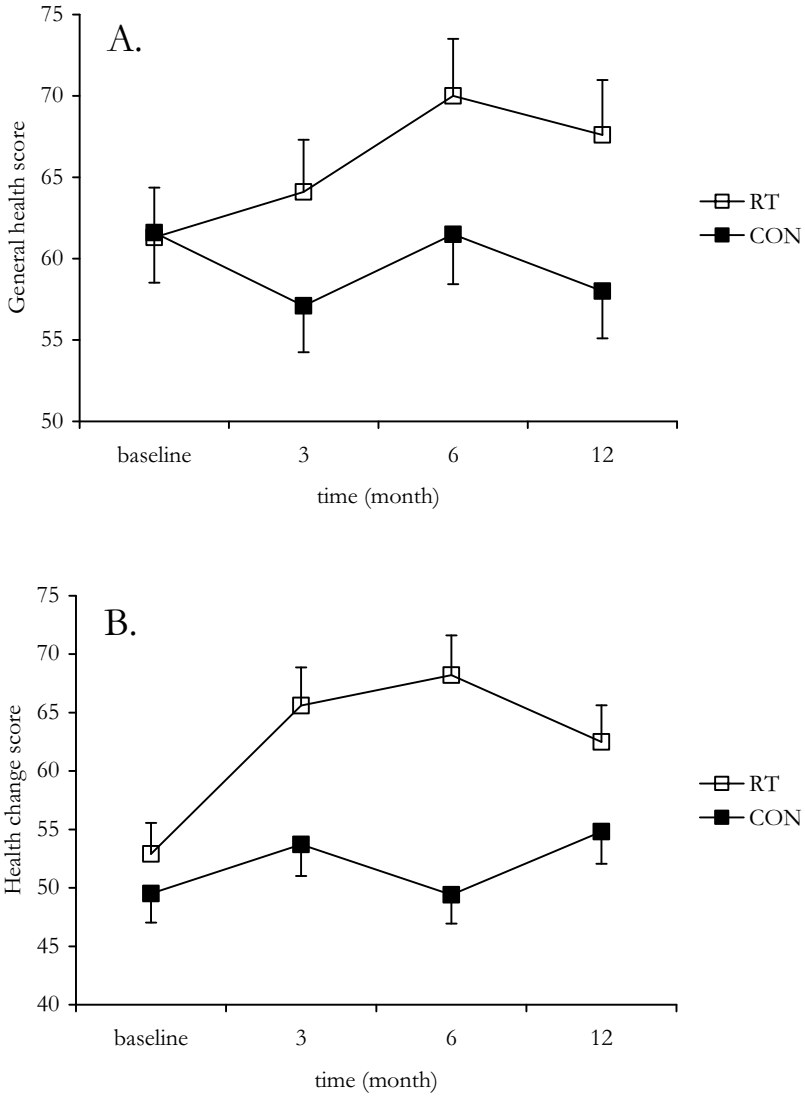

Figure 4. (A.) General Health score (SF-36) after 3, 6 and 12 months follow-up in the RT and CON group (time by treatment interaction, P=0.017). (B.) Health Change score (SF-36) after 3, 6 and 12 months follow-up in the RT and CON group (time by treatment interaction, P=0.05).

Table 2. Medical consumption

	Month of study				
Measure	baseline	3	6	12	P-value*
Doctor visits†					
relaxation	1.6 ± 0.1	2.0 ± 0.2	1.6 ± 0.2	1.4 ± 0.2	0.039
standard medical care	1.7 ± 0.1	1.9 ± 0.3	1.4 ± 0.2	2.0 ± 0.3	
Analgesics ‡					
relaxation	2.4 ± 0.7	2.0 ± 0.7	2.5 ± 0.9	2.7 ± 0.9	0.464
standard medical care	2.1 ± 0.5	1.6 ± 0.5	1.2 ± 0.4	1.9 ± 0.5	
Laxatives/antidiarrhoeals ‡					
relaxation	5.4 ± 1.3	3.7 ± 1.1	2.6 ± 0.9	3.2 ± 1.0	0.496
standard medical care	4.7 ± 1.2	3.4 ± 0.9	2.5 ± 0.8	4.0 ± 1.2	

Data are presented as mean ± standard error. * P-value for time by treatment interaction; † number of doctor visits per 3 months; ‡ number of tablets per 14 days.

(data not shown). Table 2 shows that time by treatment interaction was significant for the number of doctor visits (P=0.039), indicating that patients in the RT group visited their physician less frequently than patients in the CON group. This difference was most pronounced at 12 months post-treatment. No differences were found between the RT and CON groups regarding use of medication.

Response to therapy

According to the Jacobson and Truax' criteria, 8 treated patients (17%) versus 1 control (2%) were significantly improved at 3 months after therapy (P=0.026); 8 treated patients (17%) versus 0 controls were significantly improved at 6 months (P=0.007) and 10 treated patients (23%) versus 1 control (3%) were significantly improved one year after therapy (P=0.009). The number needed to treat (NNT) for long-term improvement was 5 (95% confidence interval (CI) 3.0-15.2). Responders at 1-year follow-up showed similar levels of baseline anxiety (13.4 ± 5.1, range 10-50) as non-responders (12.4 ± 2.6; P=0.41). Binary logistic regression revealed that of all tested demographical, clinical and psychological variables, only treatment condition predicted therapy success (P=0.04). Within the RT group, pre-treatment symptom severity was significantly higher in 12-month responders compared to non-responders (6.90 ± 0.8 versus 3.61 ± 0.3, P<0.001).

DISCUSSION

This is the first randomized controlled trial that has assessed the long-term effect of group-based relaxation training on symptoms and quality of life in a large cohort of

IBS patients. This study shows that RT leads to significant symptom improvement, comparable to symptom reduction obtained with more comprehensive psychotherapies[11-13,18,26]. For example, Creed et al. found that 15 months after psychodynamic interpersonal therapy, which consisted of 8 individual sessions, typical IBS pain scores showed approximately 20% reduction[11]. Boyce et al. found that after 1 year, bowel symptom severity was reduced by 21% in IBS patients who received RT (8 individual sessions) and by 19% in patients who received cognitive behavioural therapy (8 individual sessions)[18]. In both trials, symptom reduction was similar between the treatment group and the group receiving routine clinical care. Our results show that 12 months after five group sessions of RT, IBS composite scores had dropped 34% in the RT group and 12% in the CON group, i.e. a difference of 22%.

Our study extends preliminary data and provides evidence for the efficacy of relaxation training in treating IBS. The first explorative study on this topic suggested that symptom reduction 4 weeks after RT was greater in patients who received treatment (n=8) compared to control patients who only monitored symptoms (n=8)[17]. In our study, symptom improvement increased over time in patients who received RT and was most pronounced after 12 months follow-up, the endpoint of this study. It is unlikely that this increase resulted from symptom fluctuation (a key feature of IBS), because symptom severity remained unchanged in the CON group. In our opinion, routine use of relaxation techniques in daily life, embedded in a clear rationale, provides patients with a useful tool to cope with their symptoms, and this may have a crucial role in the continuation of symptom improvement. The rationale for treatment that was provided to patients may also have contributed to patient compliance in our study: only 16 of 98 patients were lost to long-term follow-up. In a recently published trial, dropout was over 50%, which possibly explains why this study did not find greater efficacy for either relaxation training or cognitive behavioural therapy versus routine clinical care in IBS[18]. Although some of our patients were sceptical towards the concept of RT as treatment for IBS, all were enthusiastic once the rationale had been clarified.

We acknowledge that inclusion of patients in the CON group who were initially randomized to RT but were unable to attend the scheduled training sessions, may have introduced selection bias. Additional analyses, in which these patients were included in the RT group (RT, n=65; CON, n=33), showed similar results for reduction in IBS composite score, overall symptom rating and gain in number of symptom-free days compared to the primary analysis, but statistical significance was not reached (data not shown). In our opinion, this is not surprising as 13 of 65 'RT' patients (20%) in this analysis did not receive treatment. When these 13 patients were excluded from the analysis (RT, n=52; CON, n=33), which has been recommended by some authors[25], the IBS composite score was significantly reduced in the RT group

compared to CON (data not shown), suggesting that RT is indeed beneficial in IBS patients who are treated with RT. Since demographical, clinical and psychological characteristics did not differ between these 13 patients and other patients (data not shown), we believe that adding these patients to the control group (which remained stable during the one year follow-up) did not change outcome in this group.

Whereas some trials included only referred patients[11], we recruited Rome II-positive patients from both the hospital and from the general population, i.e. not only those who seek health care. This strategy was chosen to avoid selection bias, because patients who seek health care represent only a minority of the entire IBS population[27], and symptoms in this subgroup are usually more severe[24,28]. However, inclusion of patients with mild symptom severity may also complicate the interpretation of our results, as less improvement can be expected in this group. Although no additional analysis was performed, it is likely that patients with high symptom severity benefit most from RT simply because their symptom scores can decrease more than low baseline symptom scores. However, our primary finding that, on average, a mixed group of IBS patients having both severe and mild symptoms profits from RT further highlights the potential benefit of this therapy in an individual patient.

We aimed for a reliable distinction between responders and non-responders and therefore used the strict Jacobson and Truax criteria to measure clinical significant improvement[23] in IBS composite score. It is clinically relevant to use outcome measures that represent symptom improvement, since this is the primary outcome of interest in IBS[16]. Most trials have used such endpoints, for instance overall symptom rating[15] and symptom reduction scores[11,17], although some investigators used other outcome measures such as satisfaction with treatment[12]. According to the Jacobson and Truax criteria, significantly more treated patients (23%) than controls (3%) were improved 12 months after therapy. However, the reliable change index (RC) that was utilized to define responders is in part dependent on pre-treatment score as it is calculated by the difference between pre- and post-treatment scores divided by the standard error of the difference in the whole group. As a consequence, significant improvement could not be measured in 12 patients in the CON group and 15 in the RT group due to low pre-treatment scores (data not shown). The higher pre-treatment symptom severity we found in the responder group is therefore associated with the definition of responder according to the Jacobson and Truax criteria. This may underestimate true improvement.

A limitation of our study is the comparison of RT to a standard medical care control group. We cannot exclude that the efficacy of RT is the result of non-specific therapy factors, such as attention and support. A number of control interventions are available for comparison with psychological treatment, but not all of them are appropriate[25]. For instance, a waiting list control group, in which patients do not

receive any treatment until the trial ends, may generate negative expectations with respect to symptom improvement, and these patients may be less inclined to report improvement[25]. Furthermore, the use of a placebo pill might discourage patients who are interested in trying behavioural intervention to participate, while most IBS patients have already tried several drugs to improve their symptoms, without the expected results[25].

We are aware that therapist attention and support might contribute to a positive effect of RT. This may explain the difference in doctor visits between the two groups, since patients in the control group had no additional scheduled interactions whereas patients in the RT group did. Yet, we did not control for this because RT is a minimal intervention and contains elements of patient education as part of the treatment. It is likely that an intervention controlling for attention and support also contains these elements and thereby resembles RT. Controlling for the amount of contact time (5 times 90 minutes in this study) by employing an inert patient-therapist interaction may create an artificial situation. This may further increase the likelihood that patient education or some other form of IBS-related support takes place.

Although using standard medical care as a control intervention has methodological restrictions, such as creating a negative expectation with respect to improvement when assigned to 'more of the same treatment', we expected this effect to be less prominent than in the case of a waiting list control group. Nevertheless, informing these patients that they would not receive any other but their present treatment makes symptom improvement in this group less probable. This may have amplified the differences between treated patients and controls. We attempted to minimize the possible effects of non-specific therapy factors, such as attention and support, by providing highly structured training sessions to patients in the RT group. In addition, all patients in the CON group had free access to medical support from a senior gastroenterologist during the trial period, allowing patients in this group to receive the attention and support they demanded, while we were able to monitor medical consumption. In general, our main objective was to determine the efficacy of group RT as such, inspired by a previous smaller pilot study[17], rather than to assess in detail which aspect of RT is responsible for its beneficial effect (i.e., relaxation, attention, support, group dynamics, etc.).

Finally, it is important to recognize that standard medical care, which was provided to all patients, is essential in treating IBS and cannot be replaced by relaxation training alone. Dietary advice, which is considered the mainstay in IBS treatment, may improve symptoms considerably, especially in patients who report symptom deterioration after a meal. Evidence suggests that some dietary components, such as dairy products and cereals, are involved in abnormal colonic fermentation and increased colonic gas production, leading to postprandial symptom worsening[29].

Furthermore, patient education on the natural course and prognosis of IBS and reassurance with respect to the benign character of IBS symptoms are also essential. These are hallmarks in present-day treatment of IBS and should not be left out.

In conclusion, our study has demonstrated short and long term beneficial effects of RT compared to standard medical treatment, which highlights this treatment as a promising intervention for IBS. RT reduces symptom severity, increases the number of symptom-free days and improves general health satisfaction immediately after therapy. Symptom improvement increases over time until at least 12 months after RT. Patient selection may be important since those patients with high symptom severity are likely to benefit most from RT. The efficacy of RT compared to sham intervention remains to be clarified, but the cost-effectiveness of RT compared to other psychological therapies for IBS deserves further evaluation.

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REFERENCES

1. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut 1999;45 Suppl 2:II43-7.
2. Jones R, Lydeard S. Irritable bowel syndrome in the general population. BMJ 1992;304:87-90.
3. Inadomi JM, Fennerty MB, Bjorkman D. Systematic review: the economic impact of irritable bowel syndrome. Aliment Pharmacol Ther 2003;18:671-82.
4. Donker GA, Foets M, Spreeuwenberg P. Patients with irritable bowel syndrome: health status and use of health care services. Br J Gen Pract 1999;49:787-92.
5. Camilleri M, Heading RC, Thompson WG. Clinical perspectives, mechanisms, diagnosis and management of irritable bowel syndrome. Aliment Pharmacol Ther 2002;16:1407-1430.
6. Mertz HR. Irritable bowel syndrome. N Engl J Med 2003;349:2136-46.
7. Rajagopalan M, Kurian G, John J. Symptom relief with amitriptyline in the irritable bowel syndrome. J Gastroenterol Hepatol 1998;13:738-741.
8. Clouse RE, Lustman PJ, Geisman RA, Alpers DH. Antidepressant therapy in 138 patients with irritable bowel syndrome: a five-year clinical experience. Aliment Pharmacol Ther 1994;8:409-16.
9. Novick J, Miner P, Krause R, et al. A randomized, double-blind, placebo-controlled trial of tegaserod in female patients suffering from irritable bowel syndrome with constipation. Aliment Pharmacol Ther 2002;16:1877-88.
10. Camilleri M, Northcutt AR, Kong S, Dukes GE, McSorley D, Mangel AW. Efficacy and safety of alosetron in women with irritable bowel syndrome: a randomised, placebo-controlled trial. Lancet 2000;355:1035-40.
11. Creed F, Fernandes L, Guthrie E, et al.. The cost-effectiveness of psychotherapy and paroxetine for severe irritable bowel syndrome. Gastroenterology 2003;124:303-17.
12. Drossman DA, Toner BB, Whitehead WE, et al. Cognitive-behavioural therapy versus education and desipramine versus placebo for moderate to severe functional bowel disorders. Gastroenterology 2003;125:19-31.
13. Svedlund J, Sjodin I, Ottosson JO, Dotevall G. Controlled study of psychotherapy in irritable bowel syndrome. Lancet 1983;2:589-92.
14. Gonsalkorale WM, Houghton LA, Whorwell PJ. Hypnotherapy in irritable bowel syndrome: a large-scale audit of a clinical service with examination of factors influencing responsiveness. Am J Gastroenterol 2002;97:954-61.
15. Gonsalkorale WM, Miller V, Afzal A, Whorwell PJ. Long term benefits of hypnotherapy for irritable bowel syndrome. Gut 2003;52:1623-9.
16. Talley NJ, Owen BK, Boyce P, Paterson K. Psychological treatments for irritable bowel syndrome: a critique of controlled treatment trials. Am J Gastroenterol 1996;91:277-83.
17. Blanchard EB, Greene B, Scharff L, Schwarz-McMorris SP. Relaxation training as a treatment for irritable bowel syndrome. Biofeedback Self Regul 1993;18:125-32.
18. Boyce PM, Talley NJ, Balaam B, Koloski NA, Truman G. A randomized controlled trial of cognitive behavior therapy, relaxation training, and routine clinical care for the irritable bowel syndrome. Am J Gastroenterol 2003;98:2209-18.
19. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33.
20. Derogatis LR, Rickels K, Rock AF. The SCL-90 and the MMPI: a step in the validation of a new self-report scale. Br J Psychiatry 1976;128:280-9.
21. Toner BB, Stuckless N, Ali A, Downie F, Emmott S, Akman D. The development of a cognitive scale for functional bowel disorders. Psychosom Med 1998;60:492-7.

22. Brazier JE, Harper R, Jones NM, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 1992;305:160-4.
23. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol 1991;59:12-19.
24. Longstreth GF, Hawkey CJ, Mayer EA, et al. Characteristics of patients with irritable bowel syndrome recruited from three sources: implications for clinical trials. Aliment Pharmacol Ther 2001;15:959-64.
25. Whitehead WE. Control groups appropriate for behavioural interventions. Gastroenterology 2004;126:S159-63.
26. Heymann-Monnikes I, Arnold R, Florin I, Herda C, Melfsen S, Monnikes H. The combination of medical treatment plus multicomponent behavioural therapy is superior to medical treatment alone in the therapy of irritable bowel syndrome. Am J Gastroenterol 2000;95:981-94.
27. Talley NJ, Zinsmeister AR, Melton LJ. Irritable bowel syndrome in a community: symptom subgroups, risk factors, and health care utilization. Am J Epidemiol 1995;142:76-83.
28. Longstreth GF, Wilson A, Knight K, et al. Irritable bowel syndrome, health care use, and costs: a U.S. managed care perspective. Am J Gastroenterol 2003;98:600-7.
29. King TS, Elia M, Hunter JO. Abnormal colonic fermentation in irritable bowel syndrome. Lancet 1998;352:1187-9.