

## Hypnotherapy for Children With Functional Abdominal Pain or Irritable Bowel Syndrome: A Randomized Controlled Trial

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**Background & Aims:** Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) are highly prevalent in childhood. A substantial proportion of patients continues to experience long-lasting symptoms. Gut-directed hypnotherapy (HT) has been shown to be highly effective in the treatment of adult IBS patients. We undertook a randomized controlled trial and compared clinical effectiveness of HT with standard medical therapy (SMT) in children with FAP or IBS. **Methods:** Fifty-three pediatric patients, age 8–18 years, with FAP (n = 31) or IBS (n = 22), were randomized to either HT or SMT. Hypnotherapy consisted of 6 sessions over a 3-month period. Patients in the SMT group received standard medical care and 6 sessions of supportive therapy. Pain intensity, pain frequency, and associated symptoms were scored in weekly standardized abdominal pain diaries at baseline, during therapy, and 6 and 12 months after therapy. **Results:** Pain scores decreased significantly in both groups: from baseline to 1 year follow-up, pain intensity scores decreased in the HT group from 13.5 to 1.3 and in the SMT group from 14.1 to 8.0. Pain frequency scores decreased from 13.5 to 1.1 in the HT group and from 14.4 to 9.3 in the SMT group. Hypnotherapy was highly superior, with a significantly greater reduction in pain scores compared with SMT ( $P < .001$ ). At 1 year follow-up, successful treatment was accomplished in 85% of the HT group and 25% of the SMT group ( $P < .001$ ). **Conclusions:** Gut-directed HT is highly effective in the treatment of children with longstanding FAP or IBS.

Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) in childhood are pediatric functional gastrointestinal disorders that are characterized by chronic or recurrent abdominal pain and in the case of IBS with altered bowel movements and/or relief of pain after defecation. There is no objective evidence of an underlying organic disorder.<sup>1</sup> Both FAP and IBS have reported prevalences of 1% to 19% and are among the most common reasons for consultation in pediatrics.<sup>2,3</sup> Quality of life scores of children with FAP are comparable to children with inflammatory bowel disease, highlighting the clinical significance of these functional disorders.<sup>4</sup> Spontaneous remis-

sion is high, but long-term follow-up studies have shown that a significant number, 25% to 66%, continues to experience symptoms even in adulthood.<sup>5–8</sup> For this group of patients with persisting abdominal complaints therapeutic options are limited.<sup>9,10</sup>

Gut-directed hypnotherapy (HT) has been shown to be very effective in the treatment of adult patients with IBS, functional dyspepsia, and noncardiac chest pain, with the majority of patients showing long-term improvement in symptoms and quality of life.<sup>11–17</sup> Several uncontrolled studies have shown the feasibility of the use of (self-) hypnosis in children with chronic abdominal pain, but so far no randomized controlled trials have been performed.<sup>18–20</sup> We report the findings of a randomized controlled trial conducted in pediatric patients with long-lasting complaints of IBS or FAP, recruited from a tertiary medical center. We compared the effect of gut-directed HT with that of standard medical therapy (SMT), consisting of education, dietary intervention, and intervention on stress factors.

### Materials and Methods

#### Study Participants

Children were recruited from the Department of Pediatric Gastroenterology of the Academic Medical Centre Amsterdam, the Netherlands. All children between 8 and 18 years who were diagnosed with either FAP or IBS according to the Rome II criteria<sup>1</sup> and with a history of abdominal complaints of at least 12 months were invited to participate. Exclusion criteria were: the use of medication influencing gastrointestinal functions, a concomitant organic gastrointestinal disease, functional constipation, treatment by another health care professional for abdominal symptoms, mental retardation, neurologic or psychiatric problems, and insufficient knowledge of the Dutch language. All patients and/or parents gave written

*Abbreviations used in this paper:* FAP, functional abdominal pain; HT, hypnotherapy; IBS, irritable bowel syndrome; PFS, pain frequency score; PIS, pain intensity score; SMT, standard medical therapy.

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informed consent. The study protocol was approved by the medical ethics committee of the hospital.

### *Design*

Patients were randomly allocated using a computerized random-number generator for concealment to either HT or standard medical care. Hypnotherapy was carried out by C. M. and consisted of 6 sessions of 50 minutes over a 3-month period. C. M. is a registered nurse with 4 years of training and 15 years of experience in HT. The protocol used was the Manchester protocol of gut-directed HT adapted for children.<sup>21</sup> We used the same protocol in both children (<14 years) and adolescents; the only difference was the language used, adapted to the child's developmental age. It is still unclear whether FAP and IBS are heterogeneous disorders with different pathologic mechanisms or represent variable expressions of the same disorder. Therefore we decided to treat children with FAP and IBS using the same protocol.

Hypnotherapy consisted of general relaxation, control of abdominal pain and gut functions, and ego-strengthening suggestions. Hypnosis was not used to analyze the existence of causal or compounding psychologic factors. The first session was always used to have the participant become familiar with hypnosis and the therapist. In addition, the participant was given information on the "body-mind connection" and the mind's ability to regulate bodily functions. Specific techniques aiming at control of the abdominal pain, and if necessary normalization of gut functions, were then introduced. For example, after a hypnotic induction, the participant was invited to create visualizations of a normal working gut, using metaphors adapted to the child's interests, such as a car running at a normal speed. In another session, the participant was asked to place both hands on the belly and was given suggestions for positive effects on abdominal discomfort. No fixed hypnotic scripts were used, and subsequent sessions were often modified on the basis of feedback from the participant. Apart from gut-directed suggestions, treatment also included a variety of nonanalgesic suggestions for relaxation, sleep improvement, and ego-strengthening suggestions to increase self-confidence and well-being. Every participant received a compact disc with a standardized hypnosis session and was encouraged to listen to it on a daily basis or to practice self-hypnosis.

Patients in the control group received standard care consisting of education, dietary advice, extra fibers, and pain medication or proton-pump inhibitors if considered necessary. Moreover, they received 6 half-hour sessions of supportive therapy over a 3-month period with M. A. B. or A. M. V. In these sessions symptoms of the previous weeks were discussed and possible contributory triggers—such as dietary products, emotional problems, and stressful events—were explored.

Outcomes were measured at baseline, 1, 4, 8, and 12 weeks after randomization and 6 and 12 months after therapy. Participants were asked to keep a 7-day pain diary card, on which they recorded daily the intensity and frequency of abdominal pain as well as associated symptoms (nausea, vomiting, loss of appetite, flatus, nocturnal pain, pain upon awakening, and pain related to meals).<sup>11,22</sup> Pain intensity was scored using an affective facial pain scale with faces showing no pain at all (face A) to faces showing severe pain (face I).<sup>22</sup> Afterward, these scores were transposed to a daily score of 0 = no pain, 1 = faces A-C, 2 = faces D-F, and 3 = faces G-I. The data for 7 days were totaled, giving a maximum pain intensity score (PIS) of 21. Pain frequency was daily scored as follows: 0 = no pain, 1 = 1 to 30 minutes of pain, 2 = 31 to 120 minutes of pain, 3 = more than 120 minutes of pain per day. Again, the data for 7 days were totaled giving a pain frequency score (PFS). Every associated gut symptom, as mentioned previously, was given 1 point if it occurred at least twice a week and 0.5 point if it occurred only once. The total of the associated symptoms was the associated symptom score, with a maximum of 7. Furthermore, the existence of headache was scored separately. Pain diaries were analyzed by S. W. (medical student), who was blinded to the treatment arm. Primary outcomes were the percentages of patients with complete remission of abdominal pain after the treatment phase and at 1 year follow-up. Clinical remission was defined as a decrease of the PIS and PFS of >80%; significant improvement was defined as a decrease of PIS and PFS between 30% and 80% and treatment was considered unsuccessful if the scores improved <30% or got worse. Secondary outcomes were the 3 different scores after treatment and at 1 year follow-up.

### *Statistical Analysis*

All analyses were performed using the intention to treat principle. Differences between the 2 therapy groups at baseline were analyzed by means of a  $\chi^2$  or *t* test. Missing data of the diary values were handled using replacing missing values with estimates computed with the linear interpolation method. The last valid value before the missing value and the first valid value after the missing value were used for interpolation. Predetermined end points for the study included results after the intervention period and at 6 and 12 months follow-up. For the analysis of differences of therapy effect within patients in time, a general linear model (repeated measures) was used. As mentioned previously, 3 groups of treatment effects between baseline and end point values were determined: no effect, significantly improved, and complete remission. The  $\chi^2$  test was used to test groups of treatment effect between therapies. For each therapy group, analysis of repeated measures was used to examine the differences in treatment effects in time between patients with IBS and FAP and the differences of age and

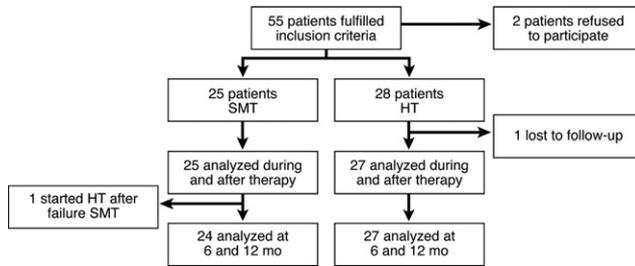


Figure 1. Trial profile.

gender effects within patients in time. For all statistical analyses, statistical significance was set at the .05 level, and all tests were 2-tailed. Statistical analysis was performed using SPSS version 14.0 (SPSS, Chicago, IL). This trial is registered as an International Standard Randomized Clinical Trial, number ISRCTN 26628553. There was no external funding source.

## Results

Between October 2002 and June 2005 a total of 55 children with abdominal pain fulfilling the Rome II criteria for FAP or IBS were referred by general pediatricians, pediatric gastroenterologists, and psychiatrists to the outpatient clinic of our tertiary centre (Figure 1). Of these patients 53 children agreed to participate in the study. Twenty-five patients were allocated to SMT and 28 to HT. Only 1 patient of the HT group did not provide baseline assessments and refused further therapy; therefore 27 patients in

Table 1. Baseline Characteristics of Participants, by Treatment Group

	HT (n = 27)	SMT (n = 25)
Demography		
Age (y) <sup>a</sup>	13.2 (2.5)	13.4 (2.9)
Girls (%)	67	84
Clinical features		
IBS <sup>a</sup> (%)	41	44
FAP <sup>a</sup> (%)	59	56
Duration of symptoms (y) <sup>a</sup>	3.7 (2.5)	3.1 (2.4)
Associated symptoms (%?)		
Nausea	44	68
Nocturnal pain	70	76
Headache	48	60
School absenteeism (%)	78	68
Hospitalization (%) for IBS/FAP <sup>a</sup>	14	23
Stress at school/home (%)	32	36
Previous psychological treatment (%)	33	24
Family member with abdominal pain (%)	67	48
Abdominal pain scores		
Pain intensity score	13.5 (3.9)	13.9 (4.1)
Pain frequency score	13.7 (5.9)	14.1 (4.7)
Associated symptom score	3.1 (1.4)	3.8 (1.5)

IBS, irritable bowel syndrome; FAP, functional abdominal pain.

<sup>a</sup>Data are mean (SD).

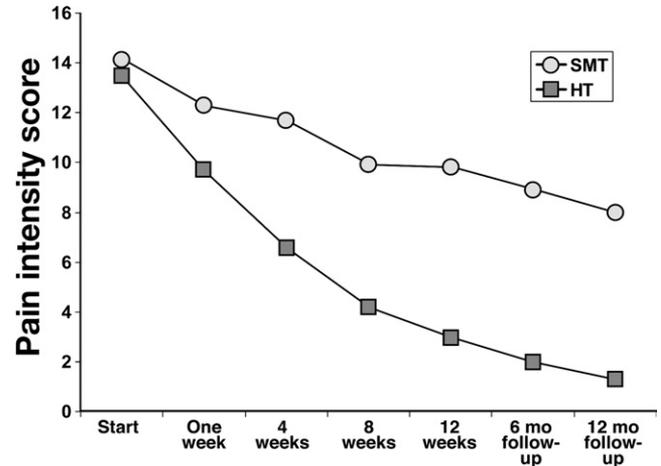


Figure 2. Changes in pain intensity scores during and after treatment.

this group contributed to the data analysis. One patient, not responding to the SMT, was subsequently treated with HT at the request of his parents. His pain scores at 6 and 12 months follow-up are lacking (Figure 1).

There were no differences between the 2 treatment groups with respect to demographic characteristics, clinical features, and baseline measures of pain intensity, pain frequency, and associated symptoms that could explain treatment effects (Table 1).

### Pain Intensity and Frequency Scores

In both treatment groups the PISs decreased significantly during and after treatment. The PISs decreased from 13.5 to 1.3 at the final end point 1 year after therapy in the HT group ( $P < .001$ ) and from 14.1 to 8.0 in the SMT group ( $P = .002$ ). Hypnotherapy was, however, highly superior, with a significantly greater reduction in PIS compared with SMT ( $P < .002$ ; Figure 2). Also the PFSs decreased during and after therapy in both groups (Figure 3); the figures for the PFSs were 13.5 to 1.1 in the HT group ( $P < .001$ ) and 14.4 to 9.3 in the SMT group

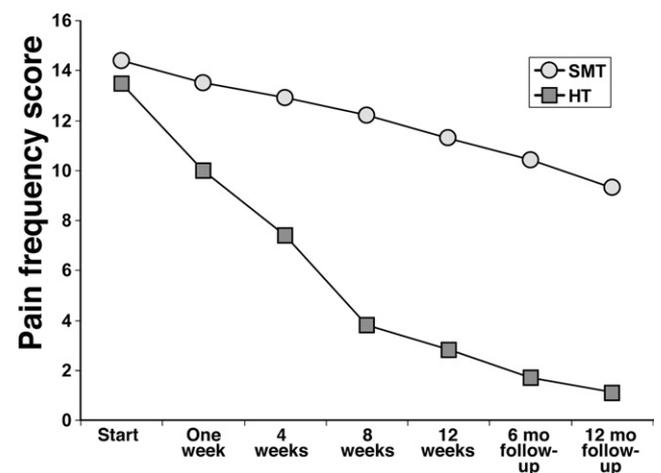
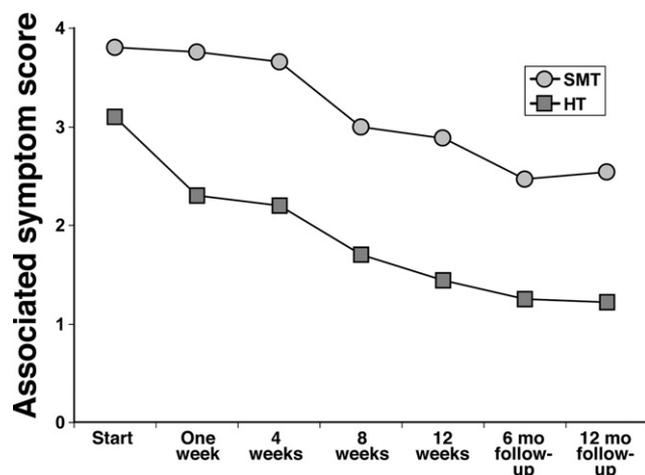


Figure 3. Changes in pain frequency scores during and after treatment.



**Figure 4.** Changes in associated symptoms score during and after treatment.

( $P = .007$ ). Again, HT was significantly more effective in reducing the scores compared with SMT ( $P < .001$ ).

### Associated Symptoms

The associated symptom scores decreased from 3.1 at the start to 1.2 at 1 year follow-up ( $P < .001$ , Figure 4) and from 3.8 to 2.5 ( $P = .002$ ) in the HT and SMT group, respectively. There was no difference in treatment effect in time between the HT and SMT group ( $P = .661$ ). In both groups the percentage of patients with headaches increased slightly but not significantly, from 48% to 52% and from 60% to 67% at 1 year follow-up in the HT and SMT group, respectively.

### Treatment Success

At the end of the 3-month treatment period, 16 of 27 patients (59%) in the HT group showed a clinical remission versus 3 of 25 (12%) in the SMT (Table 2;  $P < .001$ ). At 6 months follow-up, 19 of 27 (71%) patients in the HT group were in clinical remission, compared with only 4 of 24 (17%) in the SMT group. One year after the end of therapy, a further improvement had occurred in both groups, with a remission in 22 of 26 patients (85%) in the HT group and 6 of 24 (25%) in the SMT group (Table 2;  $P < .001$ ). After therapy, only 1 child in clinical remission in the HT group had worsening of symptoms at 6 months. She was in clinical remission again 6

months later. All other children in the HT group remained in clinical remission during follow-up.

The type of functional gastrointestinal disorder (IBS or FAP) did not influence the response to therapy. Moreover, no relation could be found between the pain severity and pain frequency pretreatment and the effect of therapy or between gender and treatment effect. Age, however, did affect treatment response: children  $< 14$  years showed a significantly better treatment response than older patients during treatment up until 6 months after therapy. No difference in therapeutic effect between the 2 age groups was found at 1 year follow-up. The effect of age on treatment efficacy was similar in both treatment groups.

## Discussion

This randomized controlled study is the first to demonstrate that gut-directed HT is highly effective in the treatment of children with long-lasting complaints of either IBS or FAP. Treatment was successful in 85% of the participants at 1 year follow-up, whereas only 25% of the children were in clinical remission after standard medical care, given by an experienced pediatric gastroenterologist and an experienced general pediatrician. This high success rate is remarkable, given that most children were referred by other hospitals after receiving no benefit from extensive other therapies, such as treatment with proton-pump inhibitors, laxatives, and psychotherapy.

Our results corroborate earlier data in 3 uncontrolled trials in children. Self-hypnosis or a combination of guided imagery and relaxation, a technique almost identical to hypnosis, was successfully used in 90% of the children in these trials.<sup>18-20</sup> The high success rate of our study is also in accordance with reports in adult IBS patients, where response rates to HT of 61% to 100% have been reported.<sup>11-15</sup> A difference, though, is the number of HT sessions. In our study, children underwent only 6 sessions of HT, whereas in studies in adult IBS patients, 7 to 12 sessions were performed. Children are generally more hypnotizable than adults and our results seem to confirm our hypothesis that 6 sessions would be sufficient.

Most children with IBS and FAP have other gut-related symptoms, such as nausea, nocturnal pain, vomiting, and loss of appetite. Also, these associated symptoms de-

**Table 2.** Percentage of Patients in Clinical Remission

	After therapy		At 6 mo follow-up		At 1 y follow-up	
	SMT group (n = 25)	HT group (n = 27)	SMT group (n = 24)	HT group (n = 27)	SMT group (n = 24)	HT group (n = 27)
No effect	56%	15%	66%	7%	46%	4%
Improved	32%	26%	17%	22%	29%	11%
Clinical remission	12%	59%	17%	71%	25%	85%

$P < .001$  between the treatment groups at all end points.

creased significantly during therapy. Interestingly, the proportion of children with headaches did not decrease after HT. An explanation might be that during HT no specific suggestions were given for headache; during therapy the focus was on abdominal pain and gut function. We have now adapted our HT protocol to also address headaches and other associated complaints, if considered necessary.

In accordance with the adult studies, therapeutic gains of HT were maintained for at least 1 year after treatment and some patients continued to experience further improvement in symptoms after ending therapy.<sup>23</sup> This posttreatment effect could be caused by hypnotic suggestions that benefits of the treatment would persist and become even more effective over time or by the ongoing use of self-hypnosis by the participants. However, it might also be possible that further improvement was caused by either the natural course of the disease or an aspecific learning effect, given that in the SMT group symptoms also further ameliorated after ending therapy, although to a smaller degree.

Predictors of treatment response—such as the severity of the abdominal pain or the type of functional gastrointestinal disorder—could not be identified. Gonsalkorale et al reported in their analysis of 250 patients that males with a diarrhea-predominant bowel pattern had a statistically significantly lower response rate than other IBS patients.<sup>23</sup> We could not observe such a difference, because our study group was small and contained only a few patients with diarrhea-predominant IBS. We did find, however, that children below the age of 14 had a significantly greater response to both therapies compared with older children. These differences disappeared at 1 year follow-up. Further studies are needed to examine whether this difference is caused by a higher suggestibility in younger children or by differences in motivation, expectancy, or symptom severity.

There are some limitations to this study. The study was only a single-blind trial, with all outcomes assessed by an investigator who was blinded for treatment allocation. It was inevitable that the recipients were not blinded to their form of treatment. It is known that response expectancy is an important mechanism of hypnotic pain reduction,<sup>24</sup> and it is therefore likely that expectancy, which was not recorded in this study, contributed to the treatment effect. However, we noticed that many patients allocated to the HT group were at first skeptical about HT, suggesting that expectancy initially was low. Another limitation is the fact that the HT was performed by only one therapist. Therefore, this study needs to be replicated with other therapists. Third, in this study we focused mainly on abdominal pain and did not investigate the influence of HT on other important outcome factors, such as school absenteeism, sleeping problems, and, more generally, quality of life.

One of the strengths of this study is the fact that we included only children with complaints lasting at least 1 year who had been treated previously with standard medical care or psychologic therapies. This might explain the relatively low percentage of patients who were cured in the SMT group (25%), which is considerably lower than the average placebo response rate in IBS trials (40%). Our strict use of Rome criteria for study entry might also account for the low response rate in the SMT group, given that it has been shown that this is also associated with lower placebo responses.<sup>25</sup>

Cognitive-behavioral therapy has been shown to be an effective treatment option in children with recurrent abdominal pain with long-lasting effects<sup>26–28</sup> and for many pediatricians, cognitive-behavioral therapy is the therapy of choice if standard medical care has failed. However, parents of children with FAP or IBS may be reluctant to accept the existence of psychosocial influences on their child's symptoms and often refuse to engage with psychologic services.<sup>29</sup> In our study, gut-directed HT was introduced to parents and children as a method of influencing and reducing the pain through the brain and was therefore probably not perceived as a psychologic treatment. This may be reflected by the fact that almost all of the invited patients agreed to participate in this study.

The mode of action of HT is not completely understood yet. There is some evidence that gut-directed HT impacts IBS through a combination of effects on gastrointestinal motility, visceral sensitivity, psychologic factors, and/or effects within the central nervous system. Whorwell et al demonstrated that hypnosis can have a relaxing effect on fasting colonic motility.<sup>30</sup> The effect of hypnosis on visceral sensitivity is somewhat less clear, with two studies demonstrating a reduction in fasting rectal sensitivity after hypnosis,<sup>31,32</sup> whereas two others failed to find such an effect.<sup>14,33</sup> Evidence suggests that an improvement in IBS symptoms after HT parallels improvement in psychological symptoms,<sup>14,23</sup> but whether this is a cause or a consequence of the treatment effect remains to be elucidated. Finally, brain imaging techniques have shown that the anterior cingulate cortex plays a key role in hypnotic pain modulation.<sup>34,35</sup> This is an interesting finding, given that the anterior cingulate cortex is one of the brain regions where IBS patients have been found to differ from healthy controls.<sup>36,37</sup> However, so far no published studies have evaluated the changes in anterior cingulate cortex function after HT in IBS patients. Not much is known yet on the pathophysiology of IBS and FAP in children, but there is no reason to believe it is much different from what is known on the pathophysiology of IBS in adults. It seems therefore plausible to assume that the mechanisms of the effects of gut-directed HT on IBS and FAP in children as seen in our study are also a combination of the above-described mechanisms, but further studies are needed to examine this.

In conclusion, this study clearly shows the efficacy of gut-directed HT in the treatment of children with longstanding IBS and FAP. We advocate that HT become the treatment of choice in children with persisting complaints of either FAP or IBS in whom first-line therapies such as education and dietary advice have failed. Furthermore, studies are needed to confirm our findings and to investigate whether HT might also be a treatment option for children with other functional gastrointestinal disorders.

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A. M. Vlieger participated in patient selection and treatment of the patients, coordinated data analysis and interpretation, and was responsible for writing this report. C. Menko-Frankenhuis carried out the HT and participated in data collection. S. Wolfkamp compiled the data. E. Tromp contributed to the data analysis and interpretation. M. A. Benninga generated the initial idea for the study, coordinated the project, participated in patient selection and patient treatment, and contributed to the writing of this report. All authors have seen and approved the final version.