

Long-Term Follow-Up of Gut-Directed Hypnotherapy vs. Standard Care in Children With Functional Abdominal Pain or Irritable Bowel Syndrome

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OBJECTIVES: We previously showed that gut-directed hypnotherapy (HT) is highly effective in the treatment of children with functional abdominal pain (FAP) and irritable bowel syndrome (IBS). Aim of this follow-up study was to investigate the long-term effects of HT vs. standard medical treatment plus supportive therapy (SMT).

METHODS: All 52 participants of our previous randomized controlled trial (RCT) were invited to complete a standardized abdominal pain diary, on which pain frequency and pain intensity were scored. Furthermore, the Children's Somatization Inventory (CSI) and a general quality of life (QOL) questionnaire were filled out. Clinical remission was defined as >80% improvement in pain scores compared with baseline.

RESULTS: All 27 HT patients and 22 out of 25 SMT patients participated in this study. Two patients of the SMT group were lost to follow-up and one refused to participate. After a mean duration of 4.8 years follow-up (3.4–6.7), HT was still highly superior to conventional therapy with 68 vs. 20% of the patients in remission after treatment ($P=0.005$). Pain intensity and pain frequency scores at follow-up were 2.8 and 2.3, respectively, in the HT group compared with 7.3 and 7.1 in the SMT group ($P<0.01$). Also, somatization scores were lower in the HT group (15.2 vs. 22.8; $P=0.04$). No differences were found in QOL, doctors' visits, and missed days of school or work between the two groups.

CONCLUSIONS: The beneficial effects of gut-directed HT are long lasting in children with FAP or IBS with two thirds still in remission almost 5 years after treatment, making it a highly valuable therapeutic option.

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INTRODUCTION

Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) are the common disorders in the pediatric population. Both conditions typically present with chronic or recurrent abdominal pain and, in case of IBS, with a disturbed defecation pattern, ranging from lumpy or hard stools to loose, watery diarrhea or both (1). Estimates on the prevalence range from 0.3 to 19%, with the highest prevalence between 4 and 6 years of age and early adolescence (2). FAP and IBS in children and adolescents have been associated with significant impairment in self-reported quality of life (QOL) scores, increased rates of school absenteeism, and a higher risk for depressive symptoms and social isolation (3,4). Many children and adolescents with mild symptoms of FAP or IBS will improve with physician reassurance and time, but long-

term follow-up studies have shown that a significant number of patients continue to experience symptoms into adulthood (5).

The management of patients with persistent or severe illness often presents a challenge for pediatricians and pediatric gastroenterologists. To date, scientific data are lacking to support the routine use of pharmacological agents, dietary interventions, such as extra fibers or probiotics (6,7). Cognitive-behavioral therapy is an effective treatment option in children with recurrent or chronic abdominal pain and for many pediatricians; it is the therapy of choice if standard medical care has failed (8,9). However, parents of children with FAP or IBS can be reluctant in accepting the existence of psychosocial influences on their child's symptoms and often refuse to engage with psychological services (10). Between 2002 and 2005, we conducted a randomized controlled trial (RCT) to study the

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effect of gut-directed hypnotherapy (HT) in 52 pediatric patients with long-lasting FAP or IBS. HT was introduced to parents and children as a method influencing and reducing pain through the brain and was, therefore, by most parents not perceived as a psychological intervention. At 1 year follow-up, successful treatment was accomplished in 85% of the HT group compared with only 25% of the group, receiving standard medical treatment plus supportive therapy (SMT) (11).

Aim of the present study was to investigate and compare the long-term effects (>4 years) of HT and SMT in children with FAP or IBS in terms of symptom improvement, medication use, school or work absenteeism, and QOL. For this purpose, all participants of the original study were contacted and asked to fill out abdominal pain diaries.

Non-gastrointestinal (non-GI) somatic complaints like headache, chronic fatigue or joint pain are common in children and adults with functional GI disorders, and the common overlap with other functional disorders is well recognized (12,13). Our gut-directed HT protocol addresses mainly abdominal discomfort and a possible side effect of our treatment could be a shift from abdominal complaints toward other functional somatic symptoms. We therefore also inquired our patients about the presence of extraintestinal problems.

METHODS

Patients and procedure

All patients, participating in our previous RCT (11), were eligible for inclusion and were contacted by telephone or mail. If the phone number or address proved wrong, the investigators tried to obtain new contact details from the patient's last known general practitioner. After the patient had given informed consent, a set of questionnaires was mailed. Patients were asked to complete and return the questionnaires within 2 months and received several reminders if necessary.

Questionnaires

Participants were asked to keep a 7-day pain diary card, on which they recorded daily intensity and frequency of abdominal pain. Participants were familiar with this abdominal pain diary, since it had been used in the original study as well (11). 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). Afterwards, 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 = 1–30 min pain, 2 = 31–120 min pain, and 3 = >120 min pain per day. Again, the data for 7 days were totaled giving a pain frequency score (PFS).

The Dutch version of the Children's Somatization Inventory (CSI) was used to score somatic complaints (14,15). The CSI contains 35 items that have to be rated on a 5-point scale, ranging from not at all (0) to a whole lot (4), reflecting the extent to which symptoms were experienced in the last 2 weeks. A total score can be computed by summing the scores across all items, with higher

scores indicating a higher intensity of somatic complaints. The CSI has been shown to be a reliable and valid instrument for assessing somatization symptoms in children and adolescents. Because we were interested to evaluate if HT had also resulted in a change in non-GI symptoms and since a number of items on the CSI are items concerning abdominal pain, a separate CSI score without GI complaints was also calculated (CSI-non-GI). The following CSI items were left out in this CSI-non-GI: nausea, constipation, diarrhea, epigastric pain, vomiting, and bloating.

For studying the QOL, two different questionnaires were used. Children under 16 years of age received the TNO-AZL Questionnaire for Children's Quality of Life (TACQOL), whereas patients aged 16 years and older received the TNO-AZL Questionnaire for Adult's Quality of Life (TAAQOL) (16–20). The TACQOL and TAAQOL have been developed as generic instruments intended for health-related QOL assessment in medical research and clinical trials for children aged 8–15 years and >15-year old, respectively, and validated by a pool of >1,100 Dutch children. In these questionnaires, health-related QOL is defined as the combination of health status and the affective evaluation of problems in health status. The TACQOL contains seven health status scales of eight items each; physical complaints, motor functioning, autonomy, cognitive functioning, social functioning, negative, and positive emotions. The items are scored on a 0–4 scale. The TAAQOL consists of 45 questions divided into 12 scales (most of them four items each): gross motor functioning, fine motor functioning, cognition, sleep, pain, social contacts, daily activities, sex, vitality, happiness, depressive mood, and anger. The questionnaire measures the emotional impact of self-reported functional problems in the same way the TACQOL does. Finally, the participants were asked about visits to a physician for their abdominal pain, use of medication, and school or work absenteeism, all in the past 12 months.

Statistical analysis

All analyses were performed using the intention to treat principle. Differences in pain and other scores between the two therapy groups at 5-year follow-up were analyzed by means of χ^2 or *t*-test. Primary outcome of this study was the percentage of patients still in complete remission of their abdominal pain. Clinical remission was defined as a decrease of the PIS and PFS of >80% compared with baseline; 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 (11). χ^2 test was used to test groups of treatment effect. To evaluate effects of possible covariates, logistic regression analysis was performed. For all statistical analyses, statistical significance was set at the 0.05 level, and all tests were two-tailed. Statistical analysis was performed using SPSS version 18.0 (IBM, Amsterdam, The Netherlands). This trial has been registered as an International Standard Randomized Clinical Trial, number ISRCTN 26628553. There was no external funding source.

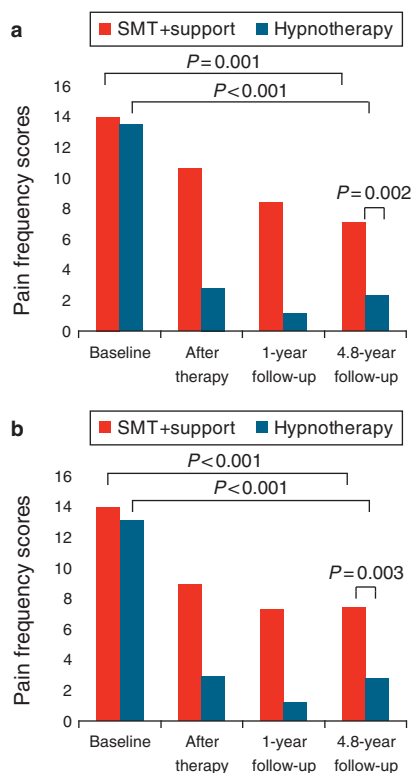
RESULTS

All patients of the original HT group agreed to participate in this study. Two out of twenty-five patients who had received SMT

Table 1. Baseline characteristics of participants by treatment group

	Hypnotherapy (n=27)	SMT+support ^a (n=22)
<i>Demography</i>		
Girls (%)	67	86
IBS/FAP (%)	41/59	41/59
Age at follow-up (years)	17.5 (2.5)	17.6 (3.2)
Duration of follow-up (years)	4.8 (0.7)	4.7 (0.8)
<i>Abdominal complaints at baseline</i>		
Pain frequency score	13.5 (5.9)	14.0 (4.7)
Pain intensity score	13.5 (3.9)	14.2 (4.1)
Duration of complaints (years)	3.7 (0.5)	3.2 (0.5)

FAP, functional abdominal pain; IBS, irritable bowel syndrome; SMT+support, standard medical treatment+supportive therapy.
^aData are mean (s.d.).

**Figure 1.** Change in pain scores. (a) Pain frequency scores (PFSs) before and after treatment. (b) Pain intensity scores (PISs) before and after treatment. SMT, standard medical treatment.

were lost to follow-up and one child refused to participate. One SMT patient had received HT shortly after SMT had failed, but was analyzed in the SMT group according to the intention to treat principle. Therefore, 27 HT patients and 22 SMT patients with a mean follow-up of 4.8 years \pm 0.8 after treatment and a mean age of 17.8 years (12.5–23.5) were included in this study. There were

no differences between the two treatment groups with respect to demographic characteristics and baseline measures of pain intensity and pain frequency (Table 1).

PIS and PFS

In both treatment groups, the PFSs were still significantly decreased at long-term follow-up compared with baseline (Figure 1a). PFSs in the HT group decreased from 13.5 \pm 5.9 at baseline to 2.3 \pm 4.0 at 5-year follow-up ($P<0.001$) and from 14.0 \pm 4.7 to 7.1 \pm 6.0 in the SMT group ($P=0.001$). Compared with the follow-up scores at 12 months post treatment, a trend toward a slight increase was seen in the HT group ($P=0.08$); in the SMT group, scores had remained the same ($P=0.5$). HT remained highly superior, with a significantly greater reduction in PFS compared with SMT ($P=0.002$).

Similar results were found for the PIS, with the difference between HT and SMT after 5 years still highly significant ($P=0.003$) (Figure 1b). PIS in the HT group decreased from 13.5 \pm 3.9 at baseline to 2.9 \pm 4.4 ($P<0.001$) and from 14.2 \pm 4.1 to 7.7 \pm 5.3 in the SMT group ($P<0.001$). Again, a slight increase in PIS was seen in the HT group compared with the score at 12 months post treatment ($P=0.1$), whereas the PIS had remained stable in the SMT group ($P=0.9$).

Treatment success

Four participating patients had not filled out a complete diary, so treatment success could only be determined in 20 SMT patients and 25 HT patients. In the SMT group, eight patients (40%) had shown no effect of treatment, eight patients (40%) were significantly improved, and four (20%) were in clinical remission. One of these four was the patient who had received HT after failing SMT. In the HT group, 3 patients (12%) had no effect of treatment, 5 (20%) had improved, and 17 (68%) were in clinical remission ($P=0.005$). The type of functional gastrointestinal disorder, age, and gender did not influence treatment success.

Somatization scores

The two groups differed significantly in their CSI scores at follow-up: 15.2 \pm 12.7 in the HT group vs. 22.8 \pm 11.8 in the SMT group ($P=0.04$). A separate CSI score without GI symptoms was also lower in the HT group: 10.6 \pm 10.4 vs. 15.5 \pm 8.3 ($P=0.08$).

QOL and other variables

The TAAQOL (children ≥ 16 years) was filled out by 15 SMT and 20 HT patients. No differences were seen in QOL scores between the two groups in all 12 scales. Furthermore, no significant differences were found between QOL scores of this sample of children with abdominal pain compared with healthy controls (data not shown). Also for the TACQOL (children < 16 years) no differences were found between the six HT and the six SMT patients. In all, 7 patients of the 22 SMT patients had missed 6 or more days of school/work vs. 3 of 27 HT patients ($P=0.09$). No differences were found in last year's visits to a physician (5/22 vs. 6/27) and use of other/complementary therapies (4/22 vs. 6/27) for abdominal complaints.

DISCUSSION

We conducted a long-term follow-up study of our previously reported RCT on gut-directed HT vs. SMT in the treatment of children with FAP or IBS (11). To our knowledge, this is the first study to report results from a follow-up period of > 12 months on the long-term effects of gut-directed HT in children with FAP or IBS. After a mean follow-up of 4.8 years, beneficial effects of HT were shown to be long lasting with HT still highly superior to conventional therapy with 68 vs. 20% of patients being in clinical remission. One child in the SMT group had received successful HT shortly after failing SMT, but was analyzed in the SMT group according to the intention to treat principle. Results on treatment success are therefore a slight underestimation of the real difference between both treatments. The low percentage of recovered patients in our SMT group is in sharp contrast to a recent study that showed that close to 70% of children with FAP/IBS will become symptom free over time (21). This might be caused by the fact that we only included children with long-lasting complaints of a least 1 year, who had been treated previously with standard medical care and/or psychological therapies (11).

Our finding of on-going beneficial effects of HT is in accordance with long-term results in adults with IBS (22). Gonsalkorale *et al.* conducted a study with duration of follow-up ranging from 1 year to >5 years. In the original cohort of 273 patients 71% had responded to HT. In 81% of these initial responders, beneficial effects of HT maintained. Favorable effects were similar in patients who received HT >5 years ago as in those completing HT only 1 year ago (22).

In our HT group, a trend toward a slight deterioration in both PFS and PIS was seen within time. Still, the scores remain significantly lower compared with pre-treatment scores. The same phenomenon is reported in adult IBS patients (22). This can represent the natural course of symptoms, which are known to fluctuate over a period of years (23) or might indicate that in some patients the effect of HT can fade out in due time. Because we did not document whether patients were still practicing (self-) hypnosis exercises, we do not know if this trend in deteriorating pain scores is related to cessation of practicing self-hypnosis in some patients. In the Gonsalkorale follow-up study in adults maintained improvement did not appear to be associated with continuation of self-hypnosis (22).

It is known that many children with functional gastrointestinal disorders also experience non-GI somatic complaints (12). Apparently, HT can have an effect on these extracolonic symptoms as well, as demonstrated by a trend toward lower somatization scores for non-GI symptoms in the HT group. This is a remarkable finding, because the HT protocol used in our study, mainly addresses abdominal symptoms. The common occurrence of non-GI symptoms in children with functional GI disorders is thought to be caused by a general amplification of sensory responsiveness throughout the whole body (12). The cause of this hypersensitivity for abdominal pain and other somatic signals in IBS and FAP is probably multifactorial and it is not unlikely that HT intervenes in several of these factors. First, brain imaging studies

have shown that cerebral pain processing is altered in IBS patients, with a greater activation of the amygdala and the anterior cingulate cortex (24). Interestingly, hypnotic suggestions modulate activity of these particular brain areas (25). So far, however, no studies have been performed to analyze changes in these central processes in IBS patients before and after HT. It is also known that many IBS patients have dysfunctional cognitions, with a tendency toward attentional bias toward bodily sensations and catastrophic thinking (26). Treatment effect in functional bowel disorders often depends on a reduction in these negative cognitions (27). Indeed, Gonsalkorale *et al.* (28) showed that improvement in adult IBS after HT is associated with cognitive change. Whether HT brings about cognitive changes through directly influencing cognitions, which then help to improve symptoms, or through influencing pain and gut functioning, leading to a change in cognitions, remains to be seen. Finally, a third mechanism, through which HT may exert its effect in functional bowel disorders, may be through a reduction in stress and its concomitant changes in the hypothalamo-pituitary-adrenal axis. IBS patients may have abnormalities in the hypothalamo-pituitary-adrenal axis (26) and it has been shown that hypnosis can modulate these (29).

QOL scores at follow-up did not differ between both groups, despite the fact that both PFS and PIS were significantly lower in the HT group. It is reasonable to assume that children with enduring FAP/IBS have become accustomed to their abdominal complaints and may have learned to cope with them, without interference of daily activities. It is known that pediatric patients with chronic abdominal pain can exhibit different pain coping strategies (30). To our knowledge, however, no longitudinal studies have been performed to investigate whether these coping profiles may indeed change over time as children become older and develop themselves. The fact that we used a general QOL questionnaire instead of an IBS-specific QOL questionnaire could also explain that QOL scores did not differ between both groups.

Strengths of this study include the long period of follow-up of 5 years and the fact that only three patients from our original cohort were lost to follow-up (11). The presence of a control group, which had received not only SMT but also supportive therapy to correct for patient-therapist time, strengthens the results found. The relatively small sample size of this follow-up study can be considered as a limitation, but so far, this is the largest follow-up study available. Another limitation relates to the generalizability of our findings: in this study, HT was performed by only one hypnotherapist with 15 years of experience. Future studies need to evaluate the results in other therapists.

In conclusion, this follow-up study clearly shows that beneficial effects of gut-directed HT sustain over a period of 5 years in children with FAP or IBS. With more than two third of patients still in clinical remission, gut-directed HT can be considered as a highly valuable therapeutic option for children with long-lasting complaints of IBS or FAP. RCTs of more sufficient sample size should be conducted in the future to confirm our long-term results.

CONFLICT OF INTEREST

Guarantor of the article: Arine M. Vlieger, MD, PhD.

Specific author contributions: A.M. Vlieger generated the general idea for this study, coordinated data analysis and was responsible for writing this report. J.M.T.M. Rutten participated in data analysis and writing the report. A.M.A.P. Govers collected and compiled the data. C. Frankenhuys carried out the HT and participated in data collection. M.A. Benninga coordinated the project and contributed to writing this report.

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Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Gut-directed hypnotherapy (HT) is an effective therapy for children with functional abdominal pain and irritable bowel syndrome with most children symptom free 1 year after treatment.
- ✓ Neither the long-term effect of HT nor the effect on other functional symptoms is unknown.

WHAT IS NEW HERE

- ✓ This follow-up study shows that the beneficial effects of HT are long lasting with 68% of the patients still in clinical remission after 4.8 years of follow-up.
- ✓ Patients also experienced a reduction in non-gastrointestinal symptoms.

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