



# Gut-directed hypnotherapy for functional abdominal pain or irritable bowel syndrome in children: a systematic review

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## ABSTRACT

**Objectives** Gut directed hypnotherapy (HT) is shown to be effective in adult functional abdominal pain (FAP) and irritable bowel syndrome (IBS) patients. We performed a systematic review to assess efficacy of HT in paediatric FAP/IBS patients.

**Methods** We searched Medline, Embase, PsychINFO, Cumulative Index to Nursing and Allied Health Literature databases and Cochrane Central Register of Controlled Trials for randomised controlled trials (RCT) in children with FAP or IBS, investigating efficacy of HT on the following outcomes: abdominal pain scores, quality of life, costs and school absenteeism.

**Results** Three RCT comparing HT to a control treatment were included with sample sizes ranging from 22 to 52 children. We refrained from statistical pooling because of low number of studies and many differences in design and outcomes. Two studies examined HT performed by a therapist, one examined HT through self-exercises on audio CD. All trials showed statistically significantly greater improvement in abdominal pain scores among children receiving HT. One trial reported beneficial effects sustained after 1 year of follow-up. One trial reported statistically significant improvement in quality of life in the HT group. Two trials reported significant reductions in school absenteeism after HT.

**Conclusions** Therapeutic effects of HT seem superior to standard medical care in children with FAP or IBS. It remains difficult to quantify exact benefits. The need for more high quality research is evident.

## INTRODUCTION

Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) are characterised by chronic or recurrent abdominal pain without evidence of any underlying organic disorder. By definition, according to the Rome III criteria, the defecation pattern is normal in patients with FAP, while altered bowel movements and/or relief of pain after defecation are typically seen in IBS.<sup>1</sup> These functional gastrointestinal disorders are among the most common complaints in paediatric patients, affecting approximately 20% of all children.<sup>2</sup> The pathophysiological mechanisms underlying functional gastrointestinal disorders are not completely understood.<sup>3</sup> Functioning of the gastrointestinal tract can become disrupted, for instance through dietary influences, lifestyle changes, psychological factors or after bacterial or viral gastroenteritis.<sup>4</sup> Studies using functional brain imaging techniques suggest that alterations in the brain-gut axis in response to visceral stimuli may result in visceral

## What is already known on this topic?

- ▶ Gut-directed hypnotherapy has been demonstrated to be effective in adult IBS patients who failed standard medical care and beneficial effects appear to be long lasting.
- ▶ Data on the efficacy of gut-directed hypnotherapy in children and adolescents with IBS or FAP are lacking.

## What this study adds?

This systematic review indicates that hypnotherapy is more effective than standard medical treatment in reducing symptoms in children with FAP or IBS.

hypersensitivity and an abnormal pattern of motility in the gastrointestinal tract. Interpretation of psychosocial factors can influence the brain-gut axis, thereby affecting symptom experience.<sup>4-5</sup>

Treatment of both conditions is often symptomatic, with standard medical care consisting of dietary advice, education and medication such as pain medication, laxatives, antidiarrhoeal or antispasmodic agents.<sup>6-7</sup> Furthermore, evidence exists that cognitive behavioural therapy can improve pain and disability.<sup>6-8</sup> Despite all available interventions, treatment is not effective in up to 50% of patients, and symptoms persist into adulthood.<sup>9</sup> Gut-directed hypnotherapy has been demonstrated to be effective in adult IBS patients who failed standard medical care, and the beneficial effects appeared to be long lasting.<sup>10-17</sup> In 2007, a Cochrane Review by Webb *et al*<sup>15</sup> concluded that data on the efficacy of gut-directed hypnotherapy in children and adolescents with IBS or FAP were lacking. Since then several studies in children and adolescents have been published and, therefore, our aim is to review the efficacy of gut-directed hypnotherapy systematically in these studies.

## METHODS

### Search strategy

An electronic literature search of Medline, Embase, PsychINFO, Cumulative Index to Nursing and Allied Health Literature databases and the Cochrane Central Register of Controlled Trials was



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conducted. Our search strategy was based on the strategy used by Webb *et al*<sup>15</sup> in their Cochrane Review. Search terms used combined items related to FAP and IBS in children and to hypnotherapy. To identify additional studies, reference lists of relevant studies identified in the literature search were searched by hand. This review covers literature on this subject published to February 2012. No language restriction was applied. The full search strategy and keywords are available from the authors.

### Study inclusion

Two authors independently assessed titles and abstracts of all potentially relevant studies identified in the literature search. In the case of disagreement between authors about the inclusion of a study, consensus was reached by discussion. Only studies in children and adolescents were included.

In hypnotherapy, a patient is induced into a hypnotic state and guided by a therapist to respond to suggestions for changes in subjective experience, alterations in perception, emotion, thought or behaviour.<sup>18</sup> This hypnotic state has several elements such as a feeling of ease or relaxation, an absence of judging and an absorbed attention on imageries. Guided imagery (GI) is a form of relaxed and focused concentration, in which children are encouraged by a therapist to imagine being in their favourite place or doing their favourite activity and image the sights, sounds and smell of that place/activity.<sup>19</sup> Although the hypnotic state is officially not induced during GI, the absorption in imageries often results in a hypnotic trance. GI, therefore, is a technique that is highly comparable to hypnotherapy, because both are using relaxation and imageries and both aim to change mental and physical experiences with the use of suggestions.<sup>18 19</sup> Because of these similarities, we included studies using either hypnotherapy or GI.

Hypnotherapy/GI could be performed by a qualified hypnotherapist or through self-exercises recorded on audio CD. Control treatment could include any standardised form of care such as medical care based on symptomatic treatment, psychological therapy, waiting list controls or no treatment. We only included studies in which diagnostic criteria of FAP or IBS were explicitly defined. Only randomised controlled trials (RCT) were included. Case reports, comments and letters were not included in this review.

### Data collection and analysis

The methodological quality of the included RCT was assessed using the Delphi list (table 1).<sup>20</sup>

Data on the following type of outcomes were extracted: (1) abdominal pain; (2) overall bowel symptom score; (3) general wellbeing or quality of life; (4) costs; (5) sick leave from school. We also extracted key characteristics of study populations, interventions, design and conduct of each included study. This information was used to assess the risk of bias of each study and to understand variability in results between included studies. If present, results on each type of outcome, including details on the measurements itself, were recorded.

Random effects models were used to meta-analyse and calculate summary estimated with corresponding 95% CI. Pooling was performed if there were at least four studies reporting on the same outcome and if those studies are comparable in design and conduct.

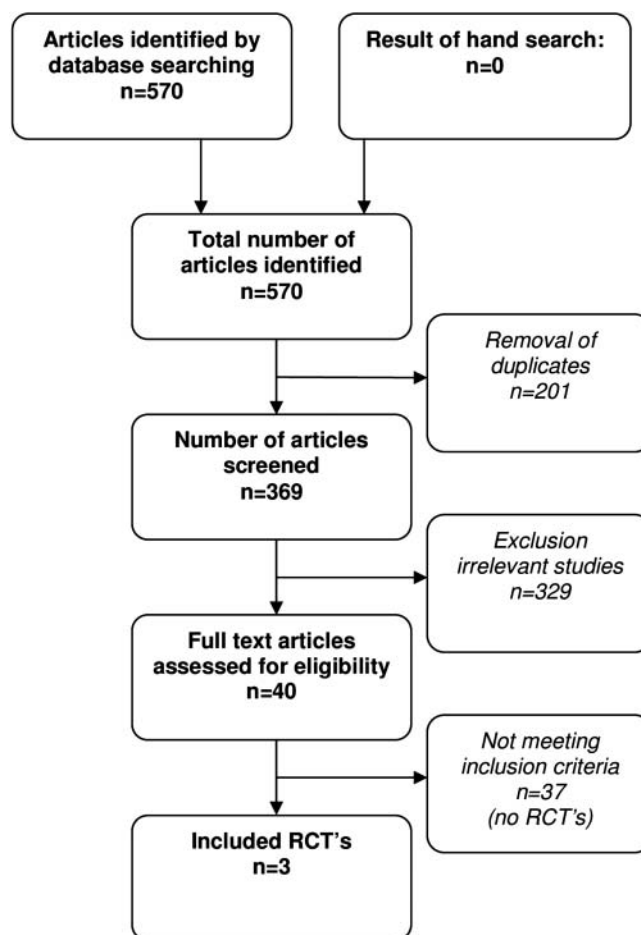
## RESULTS

A total of 570 potentially relevant studies was identified in our electronic literature searches. Cross-referencing did not identify any additional studies. After the exclusion of duplicates

**Table 1** The Delphi list

	Yes/no/don't know
<b>Study population</b>	
1. Was a method of randomisation performed?	
2. Was the allocation of treatment concealed?	
3. Were the groups similar at baseline regarding the most important prognostic indicators (age, gender, disease duration, disease severity)?	
4. Were both inclusion and exclusion criteria specified?	
<b>Blinding</b>	
1. Was the outcome assessor blinded?	
2. Was the care provider blinded?	
3. Was the patient blinded?	
<b>Analysis</b>	
1. Were point estimates and measures of variability presented for the primary outcomes?	
2. Did the analysis include an intention-to-treat analysis?	
3. Was the withdrawal/drop-out rate at <20% and equally distributed?	

(n=201), irrelevant studies (N=329) and studies not meeting the inclusion criteria (N=40), three RCT remained.<sup>21-23</sup> No RCT were excluded after full text evaluation. A flowchart of the retrieval and inclusion process is shown in figure 1.



RCT= randomized controlled trial

**Figure 1** Flowchart showing results of literature search and study inclusion. RCT, randomised controlled trial.

Sample sizes in the three included trials were 22, 34 and 52 patients, respectively, for a total of 108 patients.<sup>21–23</sup> A range of different outcomes was reported. When a similar outcome was reported, for example, abdominal pain, different instruments and measurement protocols were applied. One study reported long-term outcomes, with a follow-up period of at least 1 year, to assess whether the effects of hypnotherapy were sustained over time.<sup>23</sup> One study assessed general health-related quality of life.<sup>22</sup> Costs were not reported in any of the trials. School absenteeism was reported in two studies.<sup>21 22</sup> One study reported on school absenteeism at baseline, but did not report on these results after therapy.<sup>23</sup>

### Risk of bias

All included studies were randomised, but details on concealment of allocation were not reported in one trial.<sup>22</sup> In all studies the groups compared were similar at baseline with respect to the most relevant prognostic factors.

Because of the impossibility of blinding the intervention to patients and treating physicians results could be influenced by other factors besides the intervention. However, in the trial by Weydert *et al*<sup>21</sup> the research associate assessing the outcomes was blinded and in the trial by Vlieger *et al*<sup>23</sup> pain diaries were extracted by a blinded research associate.<sup>21 23</sup> Because symptoms were recorded by patients and/or parents in all trials, outcome measurements were not influenced by the judgement of an investigator.

Completeness of follow-up was adequate in all trials, so the risk of attrition bias was low. Table 2 shows scores on methodological quality. Two of the included trials examined hypnotherapy performed by a therapist,<sup>21 23</sup> while one trial examined hypnotherapy through self-exercises on audio CD.<sup>22</sup> The characteristics and results of these studies are shown in table 2 and below.

### Individual hypnotherapy by a therapist

The two trials examining hypnotherapy performed by a therapist included a total of 74 children aged 5–18 years.<sup>21 23</sup> In one study hypnotherapy was given by a single experienced and qualified hypnotherapist.<sup>23</sup> In the other study the number of experienced and qualified hypnotherapists participating in the treatment was not specified.<sup>21</sup> In both trials the hypnotherapy protocol used consisted of techniques that emphasise control of abdominal symptoms together with general relaxation, ego-strengthening and changing of cognitive perspective and coping skills.<sup>24</sup> The period of treatment was 1 month<sup>21</sup> and 3 months.<sup>23</sup> Patients in both studies had long-lasting symptoms, but different diagnostic criteria were used. Weydert *et al*<sup>21</sup> used Apley's criteria for recurrent abdominal pain, in which no differentiation is applied between FAP and IBS. Children with a history of at least three episodes of abdominal pain severe enough to affect normal activities, during the previous 3 months, were included. Participants were required to be stable on the current medication they were taking and were instructed not to add, delete, or change the dosing of medication. Patients in the control group received sessions of supportive therapy in which they received breathing exercises.

In the trial by Vlieger *et al*,<sup>23</sup> Rome II criteria for FAP and IBS were used to include children. Controls received standard medical care consisting of education, dietary advice, extra fibre and medication if necessary. They also received six sessions of supportive therapy with their paediatrician or paediatric gastroenterologist.

### Efficacy of hypnotherapy by a therapist

Both trials reported statistically significant lower levels of abdominal pain and symptom scores in patients receiving hypnotherapy at the end of therapy compared to controls (table 2). Due to difference in the outcome measures used, we refrained from pooling them.

Long-term results were only reported by Vlieger *et al*,<sup>23</sup> showing a significant effect in favour of hypnotherapy. After 1 year of follow up, 85% of children in the hypnotherapy group were in clinical remission compared to 25% of controls. A long-term follow-up study in the same group was recently published. Five years after treatment significantly more children who received hypnotherapy were still in remission compared to children receiving standard care plus supportive therapy: 68% vs 20%,  $p=0.005$ .<sup>25</sup> Results on quality of life and costs were not reported in either trial. Weydert *et al*<sup>21</sup> reported a significant decrease in the number of days on which children missed activities, such as school, sports and social activities, in favour of hypnotherapy. Vlieger *et al*<sup>23</sup> only reported school absenteeism at baseline. No harmful side effects were reported in either trial.

### Hypnotherapy through self-exercises on audio CD

A single randomised trial was included, which examined the efficacy of hypnotherapy induced by self-exercises on audio CD.<sup>22</sup> Van Tilburg *et al*<sup>22</sup> included 34 children aged 6–15 years, with a physician diagnosis of FAP, who had abdominal pain severe enough to disrupt activities at least once per week in the past 3 months. Patients were treated with standard medical care with or without home-based, GI. GI treatment was based on a protocol for developed by Palsson *et al*<sup>26</sup> and contained the same elements used in individual hypnotherapy given by a therapist.<sup>19</sup> Children were instructed to listen to the audio CD at least 5 days per week for 2 months.

### Efficacy of hypnotherapy through self-exercises on audio CD

At the end of treatment, levels of abdominal pain and symptom scores were significantly lower in patients undergoing hypnotherapy through self-exercises on audio CD compared to controls receiving only standard care. Treatment response was defined as a 50% or greater reduction in abdominal pain score. After treatment there were significantly more treatment responders in the group receiving hypnotherapy (63%) than in the group receiving standard care only (27%). After 6 months of follow-up, consolidation of this treatment effect was demonstrated, with 62.5% of treatment responders in the hypnotherapy group. The trial showed significantly improved quality of life scores in the hypnotherapy group. Results on costs were not reported. No difference in school absenteeism was demonstrated between both groups after treatment. The trial also did not report any harmful side effects.

### DISCUSSION

Our systematic review identified three RCT with a limited number of paediatric patients. All three trials indicated that both hypnotherapy given by a qualified therapist and hypnotherapy through self-exercises on audio CD are effective treatments in paediatric patients with FAP or IBS. Pain levels after treatment were significantly more reduced in patients receiving hypnotherapy compared to patients receiving various control treatments. Vlieger and colleagues<sup>23 25</sup> reported long-term treatment outcomes indicating that beneficial effects are long lasting, up to approximately 5 years after treatment.<sup>21 22</sup> Quality of life was only reported in one trial and showed a significant improvement

**Table 2** Study characteristics and results from included trials

Study features	Weydert <i>et al</i> , 2006 <sup>21</sup>	Vlieger <i>et al</i> , 2007, <sup>23</sup> Vlieger <i>et al</i> , 2012 <sup>25*</sup>	Van Tilburg <i>et al</i> , 2009 <sup>22</sup>
<b>No of patients:</b> Hypnotherapy/ self-exercises vs controls	14 vs 8	27 vs 25	19 vs 15
<b>IBS severity:</b> Duration of symptoms	>3 months	>1 year	>3 months
<b>Interventions:</b> Hypnotherapy/ self-exercises	Standard medical care +4 hypnotherapy sessions during 1 month	6 Hypnotherapy sessions during 3 months	Standard care + guided imagery; 3 biweekly sessions, including 1 booster session + 3 daily sessions. Listen to tape with self-exercises ≥5 days/week. Treatment period 2 months
Control	Standard medical care + supportive therapy including breathing exercises	Standard medical care + supportive therapy	Standard medical care
<b>Pain/symptom score:</b> Instrument	Pain days per month	Abdominal pain diary. Likert scale (0–4). Daily score summed total week score	Abdominal pain index. Likert scale (0–40)
Baseline	Hypnotherapy vs controls 23.0 vs 14.4	hypnotherapy vs controls PIS: 13.5 vs 13.9 PFS: 13.7 vs 14.1	Self-exercises vs control 18.7 vs 20.1
End of therapy	7.5 vs 11.3 % improvement: 67% vs 21%	PIS: 3 vs 10 PFS: 2.7 vs 11.6	9.0 vs 17 Absolute improvement: 9.7 vs 3.1
Direction/p value	Favours hypnotherapy (p = 0.05)	Favours hypnotherapy (p = 0.001)	Favours self-exercises (p=0.02)
Long-term results	% improvement at 1 month follow up: 82% vs 45% (p < 0.01)	% treatment success at 1 year: 85% vs 25% (p < 0.001) % treatment success at 5 years:* 68% vs 20% (p = 0.005)	No comparison reported (only pain scores at 6 months for self-exercise group)
<b>Quality of life/ wellbeing:</b> Baseline	Not reported	Not reported	Paediatric quality of life inventory: self-exercises vs. control 24.7 vs 32.4
End of therapy			28.2 vs 9.3
Direction/p value			Favours self-exercises (p=0.049)
<b>Costs</b>	Not reported	Not reported	Not reported
<b>School/work absenteeism</b>	Days with missed activities hypnotherapy vs controls: 4.0 vs 1.3	% of school absenteeism hypnotherapy vs controls: 78% vs 68%	Missed school days Self-exercises vs controls: 0.9 vs. 1.8
Baseline	% improvement: 85% vs 15% (p = 0.02)	Not reported	0.7 vs. 1.7
End of therapy	% improvement 1 month follow up: 95% vs 77% (p = 0.05)	% patients >6 days of school/work missed at 5 year follow-up:* 11% vs 32% (p = 0.09)	(favours self-exercises, p=0.2)
Long-term results			Not reported
<b>Methodological quality Score on Delphi list<sup>19</sup></b>	6	7	5

HT, hypnotherapy; IBS, irritable bowel syndrome; PFS, pain frequency score; PIS, pain intensity score.

in patients receiving GI.<sup>22</sup> Costs were not reported in the included trials.

Drawing firm conclusions on the results of those trials is difficult. Foremost, the body of evidence is still limited given that only three trials have been performed, all having very small sample sizes. The methodological quality of the studies was adequate, taking into account that blinding of patients and care providers was not possible.

The interpretation of results was also hampered by different types of control treatments and outcomes that were selected in

the trials. We decided to refrain from statistical pooling because of the low number of studies and many differences in design and reported outcomes.

The positive effects of hypnotherapy in children with FAP and IBS found in the three trials are in accordance with reports in adults. Since 1984, seven RCT on the efficacy of gut-directed hypnotherapy including a total of 337 adult IBS patients have been performed.<sup>10 11 13 14 16 17</sup> In six RCT hypnotherapy was given by a qualified therapist,<sup>10 11 13 16 17</sup> in one study hypnotherapy consisted of self-exercises on audio CD.<sup>14</sup> All trials

reported significantly lower pain levels and symptom scores in patients receiving hypnotherapy compared to various control treatments. Although sample sizes were relatively small (range 6–90 patients) and some methodological limitations were present, hypnotherapy can be considered a valuable therapeutic intervention for adult IBS patients.<sup>15</sup> Adult studies on long-term follow-up ranging from 1 to 7 years after treatment, show persisting effects of gut-directed hypnotherapy.<sup>12–27</sup> One trial in adult IBS patients suggested that the effectiveness of hypnotherapy is influenced by the setting in which it is given, with hypnotherapy given outside a highly specialised centre being less effective.<sup>16</sup> Future research has to show whether this may also be the case in children.

### Working mechanism of hypnotherapy

The mechanism by which hypnotherapy/GI acts in improving abdominal symptoms in FAP and IBS is still not well understood. It is hypothesised to have effects on both physiological and psychological processes.<sup>11</sup> Hypnosis has been demonstrated to lead to a change in colonic motility, but whether this effect persists when a patient is no longer in a hypnotic state is unknown.<sup>28</sup> The effect of hypnotherapy on visceral hypersensitivity is not well defined. Two studies in adult IBS patients identified a reduction in visceral sensitivity after hypnotherapy,<sup>29–30</sup> but one trial in children failed to find this effect.<sup>31</sup>

Hypnotherapy significantly reduces psychological factors such as somatisation and psychological stress, and this effect seems to persist over time.<sup>11</sup> Hypnotherapy may exert these effects by modulating the abnormal hypothalamo–pituitary–adrenal axis response to stress seen in IBS patients.<sup>32–33</sup> It is also known that many IBS patients have dysfunctional cognitions, and it has been demonstrated that symptom improvement in adult IBS patients receiving hypnotherapy is associated with a change in these negative cognitions.<sup>34</sup> The improvement in IBS symptoms is also associated with an improvement in general quality of life and reduction of psychopathology, such as depression and anxiety. It does, however, remain unclear whether an improvement in psychological factors causes the positive effects of hypnotherapy or is a consequence of it.<sup>35</sup> Hypnotherapy may also act on central nervous system processes, because FAP and IBS may be caused by altered central modulation of visceral stimuli. Pain processing regions in the brain, such as the anterior cingulate cortex and amygdala, appear to react more extensively in adult IBS patients,<sup>36</sup> and hypnotherapy seems to reduce this activity in these brain regions.<sup>37–38</sup> To date, no trials evaluating these brain regions in paediatric IBS patients after hypnotherapy are available.

### CONCLUSION

It remains difficult to quantify the exact benefits of hypnotherapy, because of the limited number of RCT on this subject, small sample sizes of the included studies, differences in control treatments used and inconsistency in reported outcome measurements. However, all three available randomised trials do provide an indication that hypnotherapy performed by a qualified therapist or through self-exercises on audio CD is more effective than standard medical treatment in reducing symptoms in children with FAP or IBS.

The need for more high quality RCT in this paediatric population is, however, evident. Future research must take into account the following factors: (1) sufficient samples sizes; (2) follow-up period of at least 1 year to determine whether treatment effects sustain; (3) using strict criteria for diagnosing FAP and IBS; (4) evaluation of both newly diagnosed and

treatment-resistant FAP and IBS patients; (5) quality of life; (6) costs; and (7) to assess whether the efficacy of hypnotherapy in children is influenced by the setting in which it is given and the level of experience of the hypnotherapist.

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### REFERENCES

- Rasquin A, Di Lorenzo C, Forbes D, *et al.* Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2006;130:1527–37.
- Chitkara DK, Rawat DJ, Talley NJ. The epidemiology of childhood recurrent abdominal pain in western countries: a systematic review. *Am J Gastroenterol* 2005;100:1868–75.
- Drossman DA. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology* 2006;130:1377–90.
- Ohman L, Simrén M. Pathogenesis of IBS: role of inflammation, immunity and neuroimmune interactions. *Nat Rev Gastroenterol Hepatol* 2010;7:163–73.
- Drossman DA, Camilleri M, Mayer EA, *et al.* AGA technical review on irritable bowel syndrome. *Gastroenterology* 2002;123:2108–31.
- Di Lorenzo C, Colletti RB, Lehmann HP, *et al.* Chronic abdominal pain in children: a technical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr* 2005;40:249–61.
- Weydert JA, Ball TM, Davis MF. Systematic review of treatments for recurrent abdominal pain. *Pediatrics* 2003;111:e1–11.
- Huertas-Ceballos A, Logan S, Bennett C, *et al.* Psychosocial interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. *Cochrane Database Syst Rev* 2008;(23):CD003014.
- Walker LS, Guite JW, Duke M, *et al.* Recurrent abdominal pain: a potential precursor of irritable bowel syndrome in adolescents and young adults. *J Pediatr* 1998;132:1010–15.
- Whorwell PJ, Prior A, Faragher EB. Controlled trial of hypnotherapy in the treatment of severe refractory irritable-bowel syndrome. *Lancet* 1984;2:1232–4.
- Palsson OS, Turner MJ, Johnson DA, *et al.* Hypnosis treatment for severe irritable bowel syndrome: investigation of mechanism and effects on symptoms. *Dig Dis Sci* 2002;47:2605–14.
- Gonsalkorale WM, Miller V, Afzal A, *et al.* Long term benefits of hypnotherapy for irritable bowel syndrome. *Gut* 2003;52:1623–9.
- Galovski TE, Blanchard EB. The treatment of irritable bowel syndrome with hypnotherapy. *Appl Psychophysiol Biofeedback* 1998;23:219–32.
- Forbes A, MacAuley S, Chiotakou-Faliakou E. Hypnotherapy and therapeutic audiotape: effective in previously unsuccessfully treated irritable bowel syndrome?. *Int J Colorectal Dis* 2000;15:328–34.
- Webb AN, Kukuruzovic RH, Catto-Smith AG, *et al.* Hypnotherapy for treatment of irritable bowel syndrome. *Cochrane Database Syst Rev* 2007;4:CD005110.
- Lindfors P, Unge P, Arvidsson P, *et al.* Effects of gut-directed hypnotherapy on IBS in different clinical settings—results from two randomized, controlled trials. *Am J Gastroenterol* 2012;107:276–85.
- Roberts L, Wilson S, Singh S, *et al.* Gut-directed hypnotherapy for irritable bowel syndrome: piloting a primary care-based randomized controlled trial. *Br J Gen Pract* 2006;56:115–21.
- Green JP, Barabasz AF, Barrett D, *et al.* Forging ahead: the 2003 APA division 30 definition of hypnosis. *Int J Clin Exp Hypn*. 2005;53:259–64.
- Rusy LM, Weisman SJ. Complementary therapies for acute pediatric pain management. *Pediatr Clin North Am* 2000;47:589–99.
- Verhagen AP, de Vet HC, de Bie RA, *et al.* The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 1998;51:1235–41.
- Weydert JA, Shapiro DE, Acra SA, *et al.* Evaluation of guided imagery as treatment for recurrent abdominal pain in children: a randomized controlled trial. *BMC pediatr* 2006;6:29–32.
- van Tilburg MA, Chitkara DK, Palsson OS, *et al.* Audio-recorded guided imagery treatment reduces functional abdominal pain in children: a pilot study. *Pediatrics* 2009;124:e890–7.

- 23 Vlieger AM, Menko-Frankenhuys C, Wolfkamp SC, *et al.* Hypnotherapy for children with functional abdominal pain or irritable bowel syndrome: a randomized controlled trial. *Gastroenterology* 2007;133:1430–6.
- 24 Gonsalkorale WM. Gut-directed hypnotherapy: the Manchester approach for treatment of irritable bowel syndrome. *Int J Clin Exp Hypn* 2006;54:27–50.
- 25 Vlieger AM, Rutten JM, Govers AM, *et al.* Long-term follow-up of gut-directed hypnotherapy vs. standard care in children with functional abdominal pain or irritable bowel syndrome. *Am J Gastroenterol* 2012;107:627–31.
- 26 Palsson OS, Turner MJ, Whitehead WE. Hypnosis home treatment for irritable bowel syndrome: a pilot study. *Int J Clin Exp Hypn* 2006;54:85–99.
- 27 Lindfors P, Unge P, Nyhlin H, *et al.* Long-term effects of hypnotherapy in patients with refractory irritable bowel syndrome. *Scand J Gastroenterol* 2012;47:414–20.
- 28 Whorwell PJ, Houghton LA, Taylor EE, *et al.* Physiological effects of emotion: assessment via hypnosis. *Lancet* 1992;340:69–72.
- 29 Lea R, Houghton LA, Calvert EL, *et al.* Gut-focused hypnotherapy normalizes disordered rectal sensitivity in patients with irritable bowel syndrome. *Aliment Pharmacol Ther* 2003;17:635–42.
- 30 Prior A, Colgan SM, Whorwell PJ. Changes in rectal sensitivity after hypnotherapy in patients with irritable bowel syndrome. *Gut* 1990;31:896–8.
- 31 Vlieger AM, van den Berg MM, Menko-Frankenhuys C, *et al.* No change in rectal sensitivity after gut-directed hypnotherapy in children with functional abdominal pain or irritable bowel syndrome. *Am J Gastroenterol* 2010;105:213–18.
- 32 Kennedy PJ, Clarke G, Quigley EM, *et al.* Gut memories: towards a cognitive neurobiology of irritable bowel syndrome. *Neurosci Biobehav Rev* 2012;36:310–40.
- 33 Wood GJ, Bughi S, Morrison J, *et al.* Hypnosis, differential expression of cytokines by T-cell subsets, and the hypothalamo–pituitary–adrenal axis. *Am J Clin Hypn* 2003;45:179–96.
- 34 Gonsalkorale WM, Toner BB, Whorwell PJ. Cognitive change in patients undergoing hypnotherapy for irritable bowel syndrome. *J Psychosom Res* 2004;56:271–8.
- 35 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.
- 36 Tillisch K, Labus JS. Advances in imaging the brain–gut axis: functional gastrointestinal disorders. *Gastroenterology* 2011;140:407–11.
- 37 Rainville P, Duncan GH, Price DD, *et al.* Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science* 1997;277:968–71.
- 38 Faymonville ME, Roediger L, Del Fiore G, *et al.* Increased cerebral functional connectivity underlying the antinociceptive effects of hypnosis. *Brain Res Cogn Brain Res* 2003;17:255–62.