

Prokinetic effect of gut-oriented hypnosis on gastric emptying

G. CHIARIONI, I. VANTINI*, F. DE IORIO* & L. BENINI*

Department of Gastroenterology, Rehabilitation Hospital of Valeggio s/M, University of Verona, Verona and *Department of Biomedical and Surgical Sciences, Section of Gastroenterology University of Verona, Verona, Italy

Correspondence to:

Dr G. Chiarioni, Divisione di Riabilitazione Gastroenterologica, C.O.C. Valeggio s/M, 37067 Valeggio sul Mincio (VR), Italy.
E-mail: chiarioni@tin.it

Publication data

Submitted 2 August 2005

First decision 19 August 2005

Resubmitted 31 January 2006

Resubmitted 8 February 2006

Accepted 10 February 2006

SUMMARY

Background

No data are available on the effect of hypnosis on gastric emptying.

Aim

To determine the effect of a hypnosis session on gastric emptying and dyspeptic symptoms.

Methods

We studied emptying by ultrasonography and epigastric sensations in 11 healthy subjects and in 15 patients affected by functional dyspepsia under three conditions according to a fixed schedule: (a) basal, (b) after cisapride and (c) during a 90 min hypnotic trance. Eight healthy subjects repeated an emptying study listening to relaxing music. Statistical analysis was performed using the Friedman test or RM-ANOVA.

Results

In dyspeptics, the postprandial increase in the antral area was significantly smaller during the hypnosis trance than under the basal and the cisapride conditions. For the patients gastric emptying was significantly shortened by cisapride, and even more by hypnosis (basal 274 ± 16.8 min; cisapride 227 ± 13.2 ; hypnosis 150 ± 9.7) whereas for healthy subjects it was shortened only by hypnosis. The repeated study in healthy subjects listening to relaxing music showed no significant difference compared with the basal. Epigastric sensations were improved in dyspeptics by hypnosis, but not by cisapride.

Conclusions

Gut-oriented hypnosis is effective in shortening gastric emptying both in dyspeptic and in healthy subjects.

Aliment Pharmacol Ther 23, 1241–1249

INTRODUCTION

Stress and psychological factors have been implicated in the pathogenesis of dysfunctions and symptoms in functional gastrointestinal disorders.¹ Experimental stress can delay gastric emptying and cause antral hypomotility.^{2, 3} In functional dyspepsia, patients report a collection of upper digestive distress symptoms in the absence of organic explanations. The pathophysiology of functional dyspepsia is unknown.⁴ Gastric dysmotility, described in up to 60% of patients, may play a role in determining at least some of the symptoms.⁵ The fact that cisapride accelerates gastric emptying in various functional disorders and is more effective than placebo in functional dyspepsia^{6–9} is consistent with this hypothesis. However, alternative explanations may be suggested, such as impaired gastric accommodation or visceral hypersensitivity, possibly related to psychological factors.^{10–12} Patients with functional dyspepsia report higher rates of anxiety and depression and higher levels of exposure to chronic social stressors than other functional gut syndromes.^{13, 14} Encouraging results have been obtained by psychodynamic psychotherapy,¹⁵ but this is a complex treatment requiring referral to a dedicated psychotherapist and may not be accepted by the patient.

Hypnosis is a well known relaxation and stress management technique that has been used by gastroenterologists to treat irritable bowel syndrome and to decrease peptic ulcer relapse.^{16, 17} Hyperemesis gravidarum¹⁸ and functional dyspepsia¹⁹ can also be improved by hypnotherapy.¹⁸ However, hyperemesis gravidarum is commonly believed to be psychogenic in origin with no impairment of gastric function.^{18, 20} It has been shown that hypnosis can be used to modulate gastric secretion,²¹ but no data are available on its potential effect on gastric motor function.^{22, 23} We postulate a gastroprokinetic influence of hypnosis that may be beneficial in functional dyspepsia.

Accordingly, the aim of the present study was to assess the effect of a single hypnosis session on gastric emptying in healthy subjects (HS) and in dyspeptic patients and to compare it with that of oral cisapride in a standard therapeutic regimen. In addition, the potential influence of hypnosis on dyspeptic symptoms reported during the gastric emptying study was evaluated both in dyspeptic patients and in HS.

MATERIALS AND METHODS

Subjects

Fifteen patients (seven males; age range: 23–58 years) referred to our department for severe chronic dyspepsia and fulfilling the Rome II criteria for functional dyspepsia (pain or discomfort in the upper abdomen for at least 3 months in the previous year in the absence of either organic disease or irritable bowel syndrome)²⁴ were recruited from our out-patient clinic between December 1999 and October 2000. All complained of various combinations of chronic, unremitting dyspeptic symptoms: pain and/or discomfort in the upper abdomen, nausea, fullness, early satiety, etc. (symptom duration: 2–10 years). They had already undergone abdominal ultrasonography and gastroscopy in the previous year without any pathological findings other than microscopic antral gastritis. All the patients had already been treated in the past with prokinetic and antisecretory drugs without achieving any lasting improvement. Most patients were referred by other gastroenterologists and were taking prokinetics only 'on demand', by the time of consultation.

A complete history was taken and physical examination performed in all patients. Further tests were carried out to exclude secondary causes of dyspepsia with certainty, only if deemed necessary. At the time of recruitment, four patients were *Helicobacter pylori*-positive at antral histology; *H. pylori* status was unknown in five and negative in six after successful eradication (¹³C-urea breath test). Formal psychological testing was not carried out, but none of the patients showed evidence of overt psychopathology.

All subjects were informed of the relevance of gastric dysfunction as a cause of dyspeptic symptoms. The potential benefits of relaxation techniques on gastric function were also discussed. All received a thorough explanation both of cisapride effects and of hypnosis, despite the fact that all of them had already used cisapride in the past. In Italy, cisapride used to be widely prescribed in functional dyspepsia up to early December 2000, when its use was first limited to documented gastroparesis, while since October 2001 the drug has been suspended owing to its cardiological side-effects.²⁵ Eleven members of the medical staff of our hospital (five males; age range: 27–60 years), unaffected by gastrointestinal complaints, were studied as HS.

All the subjects were totally naive to hypnosis and none of them reported previous experience of

psychotherapy or relaxation techniques (autogenic training, yoga, etc.).

After receiving a thorough explanation of the aims of the study, all the subjects signed an informed consent form. The study was approved by the Internal Review Board of our Department.

All the subjects were studied according to a fixed schedule (a-b-c) on three different days by means of gastric emptying tests and visual analogue scales of epigastric fullness and abdominal discomfort under three different conditions: (a) basal test: no premedication; (b) cisapride test: cisapride, 10 mg, one tablet 30 min before the meal; (c) hypnosis study: trance was induced for 90 min, after 30 min had elapsed since the end of the meal. A 1-week time interval was left between tests. In the week preceding the procedures, no medication other than antacids was allowed.

Gastric emptying study

The ultrasonographic method used for measuring gastric emptying has recently been described in detail and validated against concomitant scintigraphic measurement.²⁶ After an overnight fast, subjects were given a standard two-course meal (60 g of 'macaroni alla bolognese' with 70 g of meat sauce and then 50 g of ham, 50 g of soft fatty cheese, one roll and 250 mL of water; 800 Kcal, 15% from protein, 45% from fat and 40% from carbohydrates). The meals had to be eaten in 20 min, chewing *ad libitum*. Subjects were allowed to walk in quiet surroundings between measurements but were required to refrain from smoking and working. Smoking, alcohol, caffeine and physical exercise were not allowed on the day preceding the procedure.

Real-time ultrasonography was used to measure the diameters of the gastric antrum in the sagittal plane passing through the aorta. Measurements were taken before the meal (basal), immediately after ingestion (time 0) and at 30-min intervals thereafter. The mean of three readings was calculated at each time during interperistaltic relaxation. The antral section was calculated using the formula $S = d_1 \times d_2 \times \pi / 4$, where S represents the antral cross-sectional area, and d_1 and d_2 the measured diameters. Antral cross-sectional area was then plotted against time. Total emptying time was identified from the point where the trend line crossed the basal value. In our laboratory, the upper limit for gastric emptying of the test meal in control subjects is 320 min.²⁷ We used the total emptying time of ingested food to define gastric emptying time with

our ultrasonography technique. We have recently shown that this is a reliable index of gastric motor function both in health and in disease when compared with total emptying time measured by scintigraphy.²⁶ The maximal postprandial cross-sectional area was also measured, as it has been reported to be greater in dyspeptic patients than in asymptomatic controls.²⁸⁻³⁰

Gastrointestinal symptoms

Subjects filled in a visual analogue scale questionnaire on epigastric fullness and abdominal discomfort before the meal and at 30-min intervals till the end of emptying. Feelings were rated on a triangle, the base of which corresponded to the maximum possible value (10 cm²) and the apex to the minimum.³¹

This measurement had to be stopped between 30 and 120 min during trance. For this reason the comparison among groups was performed at fixed times (120 and 150 min), when data were available for all patients and at the end of gastric emptying rather than considering the area under the curve.

Trance

Trance was induced in all the subjects in the semirecumbent position, after 30 min had elapsed since the end of the meal. The method of progressive relaxation by verbal suggestions was used for induction. To deepen the trance, different methods were used in sequence beginning with the counting and breathing technique followed by the induction of limb heaviness and warmth.³² Then the subject was instructed to place the hypnotically warmed hand over the epigastrium and was given suggestions of well-being and improved gastric function mediated by the warmth of the hand. After 7-10 min, the subjects were directed to regain their original body position, with the arms resting at the side of the body, at which point the imagery part began. Images of water flowing in a river and in a waterfall were suggested and related both to general well-being, relaxation and to improved gastric function. Gut-oriented suggestions were developed according to the version used in irritable bowel syndrome.¹⁶ The hypnosis session was completed with the Hartland's classic ego-strengthening technique.³³ All sessions were conducted by one of the authors (G.C.). Trance duration was about 90 min.

Eight of the HS underwent an additional study to address the potential influence of both repeated testing

and posture, assuming a semirecumbent position 30 min after the end of the meal for 120 min and listening to relaxing music (so-called New-Age music). They were asked to relax without sleeping. An assistant watched to make sure subjects did not fall asleep. All subjects reported feeling comfortable and relaxed.

Statistical analysis

Results are expressed as mean \pm 1 S.E.M. The Kolmogorov–Smirnov one-sample test was used to confirm the normal distribution of results. The overall statistical significance of the differences between the three emptying studies was evaluated either by the Friedman test for paired data (for parameters not following a normal distribution), or by ANOVA for repeated measurements (for normally distributed parameters). Wilcoxon's or Student's *t*-test were used to evaluate the difference between individual studies, once the overall difference had been found to be significant. The significance cut-off in all cases was 0.05.

RESULTS

All subjects completed the tests without any major problems. During the cisapride test four subjects reported increased bowel sounds, another four defecated. None of the subjects reported difficulties in initiating or terminating the trance, or was trance resistance evident to the therapist. No trance-related side-effects were reported except for mild dizziness in one HS.

Figure 1 illustrates the results of antral cross-sectional areas in the fasting condition (left panel) and at peak postprandial dilatation (right panel) in HS and in dyspeptic patients. No differences were found in fasting antral sections in the three tests either when pooling all the study subjects or when considering HS and dyspeptic patients independently. There were no significant differences between dyspeptic patients and HS either in fasting or in peak postprandial increase in antral cross-sectional areas.

A significant overall difference in peak postprandial cross-sectional area in the three tests was found when only dyspeptic patients were considered ($P = 0.002$, ANOVA for repeated measurements). In patients, the antral area increased less in hypnosis compared both with the basal (mean difference: 292, 95% CI: 169–415 mm², $P < 0.001$) and with the cisapride tests (mean difference: 232, 95% CI: 65.0–399 mm², $P < 0.01$, paired Student's *t*-test).

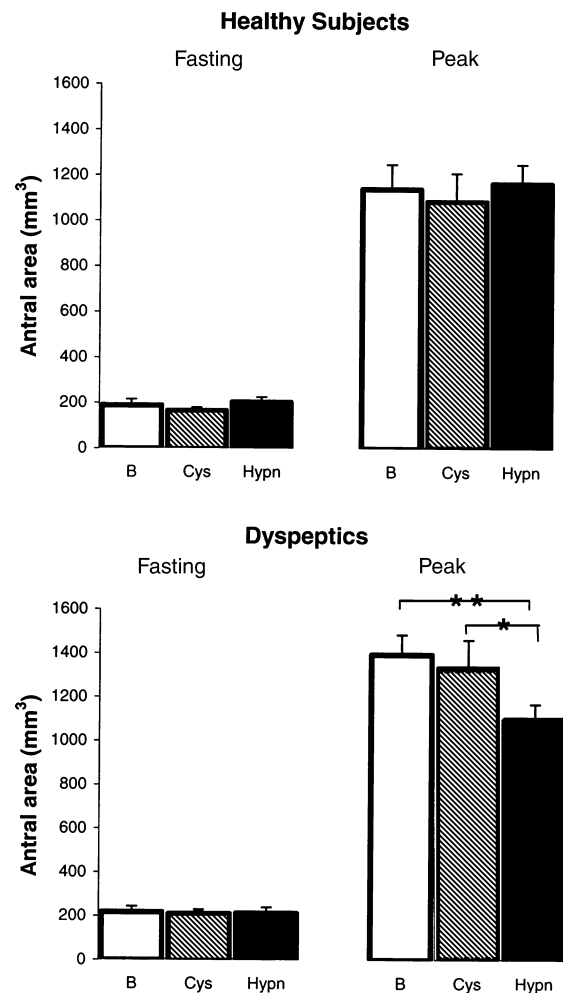


Figure 1. Values of antral cross-sectional areas measured before the meal ('fasting') and at the time of maximal postprandial dilatation ('peak') in healthy subjects (left panel) and in dyspeptic patients (right panel) during the three tests (basal: open bars; cisapride: shadowed bars; hypnosis: black bars). Values are expressed as mean (\pm 1 S.E.M.; * $P < 0.01$, ** $P < 0.001$).

Figure 2 illustrates the times required for total gastric emptying in controls and in dyspeptic patients. In the basal test, HS emptied their stomachs significantly more rapidly than dyspeptic patients (229 ± 12.3 min vs. 274 ± 16.8 min; mean difference: 44.9 min, 95% CI: 87.9–1.9 min, $P = 0.05$). This difference disappeared during the cisapride and hypnosis tests.

A significant overall difference in emptying times in the three tests was found both when pooling all subjects together and in controls and dyspeptic patients independently (P -value invariably < 0.001 , ANOVA for repeated measurements). The paired differences

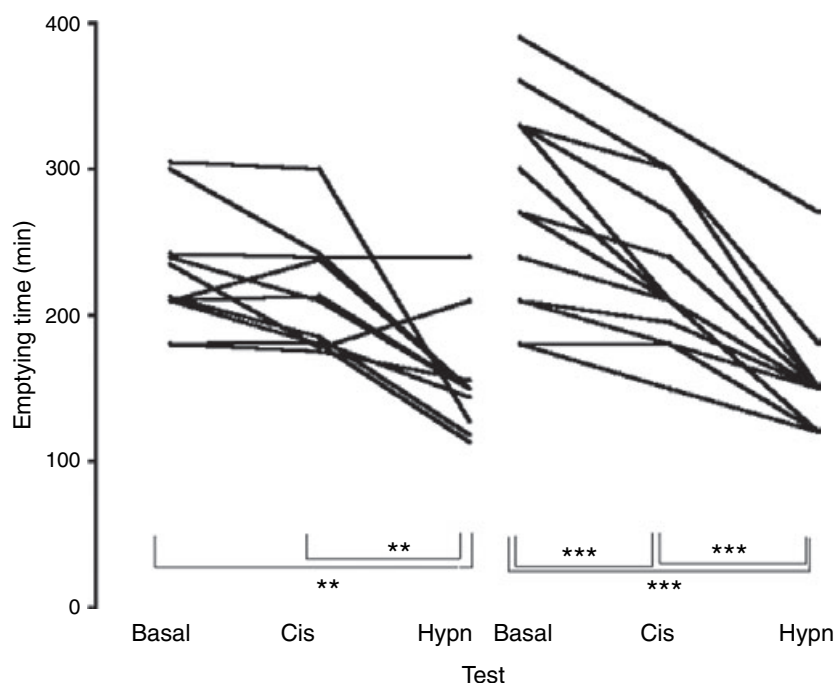


Figure 2. Values of total emptying times of the three test meals in healthy subjects (left panel) and in dyspeptic patients (right panel). * $P = 0.05$. ** $P < 0.005$. *** $P < 0.001$.

between the three experimental conditions and their statistical significances are shown in Table 1. In HS, only hypnosis significantly shortened gastric emptying compared with both the basal and the cisapride study (mean emptying times, basal: 229 ± 12.3 min; cisapride: 212 ± 11.8 ; hypnosis: 155 ± 11.3). In dyspepsia patients, cisapride significantly improved gastric emptying compared with the basal study. Hypnosis, however, was associated with a greater reduction in gastric emptying, which proved significant compared not only with the basal test but also with the cisapride test (basal: 274 ± 16.8 min; cisapride: 227 ± 13.2 ; hypnosis: 150 ± 9.7). In the eight HS in whom an additional study was conducted with the subjects listening to relaxing music, there was no noticeable difference in emptying time between the basal study and this one (232 ± 15.8 vs. 243 ± 25.6 min, respectively, N.S.; Figure 3).

Symptoms

The distribution of symptom scores was not normal and therefore non-parametric tests were used.

Tables 2 and 3 show the fullness and discomfort scores (on a scale from 0 to 10) during the three tests. A significant difference between test scores was found for epigastric fullness and discomfort at times 120 and 150. This held true both when pooling all subjects together and when considering only dyspeptic patients, but not HS (in whom the discomfort was always rated as absent). The Wilcoxon test confirmed the statistical significance of the difference in symptom reduction between the hypnosis and both the basal and the cisapride tests but not between the basal and cisapride tests. There was no difference in the values of symptoms at the time of completion of gastric emptying. No correlation was found between

Table 1. Mean paired differences (95% confidence intervals of values) in total emptying times (min) between tests in healthy volunteers and in dyspeptic patients and their statistical significance (paired t -test)

	Control – cisapride	P -value	Control – hypnosis	P -value	Cisapride – hypnosis	P -value
Volunteers	16.3 (–2.5 to 35.2)	N.S.	73.6 (37.2–110)	<0.001	57.3 (20.7–93.8)	0.006
Dyspepsia patients	47 (30.1–63.9)	<0.001	124 (94.0–154)	<0.001	77 (57.9–96.1)	<0.001

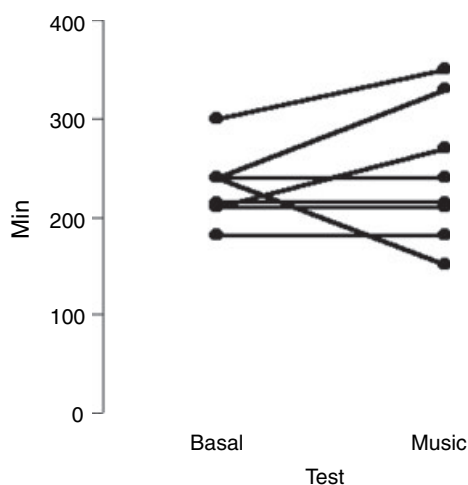


Figure 3. Values of total emptying times in the healthy subjects who repeated the basal test listening to relaxing music.

symptoms and either gastric emptying rates or maximal antral dilatation in HS and in dyspeptic patients.

DISCUSSION

The pathophysiology of functional dyspepsia is largely unknown.⁴ Delayed gastric emptying, impaired antral accommodation of ingested food and visceral hyperalgesia have been described with various frequencies.^{5, 10, 11} In addition, dyspeptic patients score higher than controls in terms of anxiety, depression and neuroticism, suggesting that psychological factors may

aggravate symptoms and that there may be a therapeutic role for psychological intervention.^{13–15} Better established is the efficacy of treatment with gastrokinetic drugs.⁹ Cisapride has been shown to accelerate gastric emptying and improve symptoms in functional dyspepsia.^{7, 8, 34}

In our study the aim was to compare the effect of cisapride with that of an established relaxation technique (hypnosis) reinforced by gut-oriented suggestions.^{16, 35} Acute administration of cisapride 10 mg p.o. was associated with a shortening of gastric emptying time in dyspeptic patients but not in HSs. Gut-oriented hypnosis accelerated gastric emptying more than cisapride both in dyspeptics and in HSs.

We are well aware of a number of possible objections to the design of the study. This is not a placebo-controlled study, and the anticipation of positive results by hypnosis may have played a role in improving gastric emptying in patients. In addition, all patients had already taken cisapride in the past without obtaining lasting improvement. This may have created a negative expectation with regard to the efficacy of the drug. A number of considerations, however, appear to argue against the placebo effect of the relaxation technique. Patients were affected by chronic, unremitting symptoms, and were mostly referred to our department by other gastroenterologists, after various medical treatments had yielded disappointing results. A low placebo rate was therefore anticipated. Even more relevant was the attitude of most of the HSs, who were rather sceptical as to the possible prokinetic action of hypnosis.

Table 2. Rates of fullness in healthy subjects and in patients with dyspepsia during the three different studies

	0'	30'	60'	90'	120'	150'
Healthy subjects						
Basal	0.06 ± 0.05	6.0 ± 1.0	5.6 ± 1.0	5.0 ± 1.1	4.6 ± 1.2	3.6 ± 1.1
Cisapride	0 ± 0.0	7.2 ± 1.0	6.0 ± 1.0	5.0 ± 1.0	4.2 ± 0.9	2.8 ± 0.7
Hypnosis	0.03 ± 0.02	7.5 ± 0.8	–	–	4.2 ± 0.9	2.4 ± 0.9
Significance*	N.S.	N.S.			N.S.	N.S.
Dyspepsia patients						
Basal	0.8 ± 0.4	8.8 ± 0.4	8.5 ± 0.5	8.0 ± 0.6	7.4 ± 0.7	7.3 ± 0.7
Cisapride	1.0 ± 0.5	8.6 ± 0.5	7.8 ± 0.7	7.4 ± 0.8	7.4 ± 0.7	6.7 ± 0.8
Hypnosis	1.0 ± 0.4	8.0 ± 0.6	–	–	4.5 ± 0.8	3.4 ± 0.7
Significance*	N.S.	N.S.			0.04	<0.001

* Levels significance of the differences among the values in the three studies within the two different groups of subjects, evaluated by the Friedman's non-parametric ANOVA for paired data.

Table 3. Rates of discomfort in healthy subjects and in patients with dyspepsia during the three different studies

	0'	30'	60'	90'	120'	150'
Healthy controls						
Basal	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0
Cisapride	0 ± 0.0	0.09 ± .08	0 ± 0.0	0 ± 0.0	0 ± 0.0	0 ± 0.0
Hypnosis	0 ± 0.0	0 ± 0.0	-	-	0 ± 0.0	0 ± 0.0
Significance*	N.S.	N.S.			N.S.	N.S.
Dyspepsia patients						
Basal	1.0 ± 0.6	2.0 ± 0.7	2.2 ± 0.8	2.4 ± 0.8	2.3 ± 0.8	1.7 ± 0.6
Cisapride	0.7 ± 0.3	2.1 ± 0.5	1.7 ± 0.4	1.8 ± 0.5	1.3 ± 0.4	1.4 ± 0.4
Hypnosis	0.9 ± 0.3	1.7 ± 0.4	-	-	0.1 ± 0.1	0.1 ± 0.1
Significance*	N.S.	N.S.			0.03	<0.001

* Levels significance of the differences among the values in the three studies within the two different groups of subjects, evaluated by the Friedman's non-parametric ANOVA for paired data.

An additional objection may concern the fixed schedule of the gastric emptying evaluations, with the hypnosis test always following the basal and cisapride tests. The reason for this choice was to avoid a carry-over effect, in view of the reported long-lasting effect of hypnotherapy on rectal sensitivity in functional bowel disorders.²³ We acknowledge the potential bias, as training in a medical procedure may decrease the procedure-related stress. However, we were unable to detect any influence of desensitization and/or different posture by repeatedly testing the HSs in a semirecumbent position while listening to relaxing music, compared with the basal test results. Moreover, when we developed and validated our method for measuring gastric emptying in our laboratory, no difference was found between repeated tests in the same subjects,³⁶ to suggests that no appreciable training effect is present.

Previous studies have described an enlarged antrum in functional dyspepsia, suggesting a relationship between antral distension and symptoms.²⁷⁻²⁹ Impaired gastric accommodation has been reported in functional dyspepsia, but our technique is not suitable for its measurement.¹⁰ Tack *et al.* reported that some dyspeptic symptoms seem to be related to altered gastric accommodation, because impaired accommodation of the fundus may lead to early diversion of the meal to an enlarged antrum.³⁷ As regards, peak antral dilatation was modified by hypnosis in dyspeptic patients only. No correlation was found, however, between symptomatic improvement and maximal antral dilatation in our patients.

The mechanism or mechanisms of action of gut-oriented hypnosis on gastric function are left unexplored by our study. The prokinetic action may be related to the generalized decrease in sympathetic system activity induced by trance (the so-called relaxation response).³⁸ Experimental stress delays gastric emptying and increases plasma levels of noradrenaline,³ and derangements of autonomic function have been reported in functional bowel disorders.³⁹ Acute stress may accelerate small bowel transit and increase rectosigmoid motor activity.^{40, 41} Hypnosis-induced relaxation has been reported to slow small bowel transit and inhibit colonic motility.^{22, 42} In addition, hypnosis may modulate acid gastric secretion,²¹ and omeprazole has been reported to delay gastric emptying of a solid meal.³⁶ We cannot rule out the possibility of an influence on gastric secretion, but no hypnotic suggestions (appearance, aroma, taste of food) specifically designed to increase acid secretion were given. Finally, there was no appreciable correlation between discomfort and fullness scores and either gastric emptying rate or maximal antral dilatation. The symptomatic improvement observed may be related to perceptive modulation at a cortical level (central analgesia) induced directly by hypnotic suggestions. This 'negative hallucination' due to hypnotic suggestions may underlie the analgesia and other kinds of reduced somatic perception observed under hypnosis.⁴³ In a recent study, hypnosis-modulated rectal perception without affecting rectal compliance or wall tension in irritable bowel syndrome patients.⁴⁴

In conclusion, a single session of gut-oriented hypnosis appears to be effective in shortening gastric emptying time of a solid meal both in functional dyspepsia patients and in HSs. Dyspeptic patients report a significant hypnosis-induced improvement in epigastric fullness and abdominal discomfort. Our study confirms an effect of hypnosis on gastric function and suggests that it may have a positive role in the clinical management of functional dyspepsia.

ACKNOWLEDGEMENTS

The authors are indebted to Luciano De Benedetti (PhD, deceased) and Andrea Gambacciani (MD) for training the principal author in hypnosis. We also wish to thank our technical assistants Monica Menegotti and Lara Salandini for carrying out part of the gastric emptying studies.

REFERENCES

- Mayer EA. The neurobiology of stress and gastrointestinal disease. *Gut* 2000; 47: 861–9.
- Thompson DG, Richelson E, Malagelada J-R. Perturbation of gastric emptying and duodenal motility via the central nervous system. *Gastroenterology* 1982; 83: 1200–6.
- Stanghellini V, Malagelada J-R, Zinsmeister AR, Go VLW, Kao PC. Stress-induced gastroduodenal motor disturbances in humans: possible humoral mechanisms. *Gastroenterology* 1983; 85: 83–91.
- Locke GR III. Nonulcer dyspepsia: what it is and what it is not. *Mayo Clin Proc* 1999; 74: 1011–5.
- Lin Z, Eaker EY, Sarosiek I, McCallum RW. Gastric myoelectrical activity and gastric emptying in patients with functional dyspepsia. *Am J Gastroenterol* 1999; 94: 2384–9.
- Corinaldesi R, Stanghellini V, Raiti C, Rea E, Salgemini R, Barbara L. Effect of chronic administration of cisapride on gastric emptying of a solid meal on dyspeptic symptoms in patients with idiopathic gastroparesis. *Gut* 1987; 28: 300–5.
- Jian R, Ducrot F, Piedeloup C, Mary JY, Najean Y, Bernier JJ. Measurement of gastric emptying in dyspeptic patients. Effect of a new gastrokinetic agent (cisapride). *Gut* 1985; 26: 352–8.
- Jian R, Ducrot F, Ruskone A, Rambaud JC, Modigliani R, Rain JD. Symptomatic, radionuclide and therapeutic assessment of chronic dyspepsia. A double-blind, placebo-controlled evaluation of cisapride. *Dig Dis Sci* 1989; 34: 657–64.
- Agreus L, Talley NJ. Dyspepsia: current understanding and management. *Annu Rev Med* 1998; 49: 475–93.
- Troncon LE, Bennett RJ, Ahluwalia NK, Thompson DG. Abnormal intragastric distribution of food during gastric emptying in functional dyspepsia patients. *Gut* 1994; 35: 327–32.
- Coffin B, Azpiroz F, Guarner F, Malagelada J-R. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 1994; 107: 1345–51.
- Berstad A. Functional dyspepsia – a conceptual framework. *Gut* 2000; 47 (Suppl. IV): 3–4.
- Jonsson B, Theorell T, Gotthard R. Symptoms and personality in patients with chronic functional dyspepsia. *J Psychosom Res* 1995; 39: 93–102.
- Bennett EJ, Piesse C, Palmer K, Badcock C-A, Tennant CC, Kellow JE. Functional gastrointestinal disorders: psychological, social, and somatic features. *Gut* 1998; 42: 414–20.
- Hamilton J, Guthrie E, Creed F, *et al.* A randomized controlled trial of psychotherapy in patients with chronic functional dyspepsia. *Gastroenterology* 2000; 119: 661–9.
- Whorwell PJ, Prior A, Faragher EB. Controlled trial of hypnotherapy in the treatment of severe refractory irritable bowel syndrome. *Lancet* 1984; ii: 1232–4.
- Colgan SM, Faragher EB, Whorwell PJ. Controlled trial of hypnotherapy in relapse prevention of duodenal ulceration. *Lancet* 1988; ii: 1299–300.
- Fuchs K, Paldi E, Abramovici U. Treatment of hyperemesis gravidarum by hypnosis. *Int J Clin Exp Hypn* 1980; 28: 313–23.
- Calvert EL, Houghton LA, Cooper P, Morris J, Whorwell PJ. Long-term improvement in functional dyspepsia using hypnotherapy. *Gastroenterology* 2002; 123: 1778–85.
- Maes BD, Spintz B, Ghoo YF, Hiele MI, Evenepoel P, Rutgeerts PJ. Gastric emptying in hyperemesis gravidarum and non-dyspeptic pregnancy. *Aliment Pharmacol Ther* 1999; 13: 237–43.
- Klein KB, Spiegel D. Modulation of gastric acid secretion by hypnosis. *Gastroenterology* 1989; 96: 1383–7.
- Beaugerie L, Burger AJ, Cadranet JF, Lamy P, Gendre JP, Le Quintrec Y. Modulation of oro-caecal transit time by hypnosis. *Gut* 1991; 32: 393–4.
- Prior A, Colgan SM, Whorwell PJ. Changes in rectal sensitivity after hypnotherapy in patients with irritable bowel syndrome. *Gut* 1990; 31: 896–8.
- Talley NJ, Stanghellini V, Heading RC, Koch KL, Malagelada J-R, Tytgat GNJ. Functional gastroduodenal disorders. *Gut* 1999; 45 (Suppl. II): 37–42.
- Nightingale SL. New warnings added to cisapride labeling. *JAMA* 1998; 280: 410–2.
- Benini L, Sembenini C, Heading RC, *et al.* Simultaneous measurement of gastric emptying of a solid meal by ultrasound and scintigraphy. *Am J Gastroenterol* 1999; 94: 2861–5.
- Benini L, Sembenini C, Vantini I. What is the status of gastric emptying of the successful dilatation? In: Giuli, R, Galliche, JP, Jamieson, GG, Scarpignato, C, eds. *The Esophago-Gastric Junction*, Vol. 2. Mount Rouge: John Libbey Eurotext, 1998: 632–5.
- Ricci R, Bontempo I, Labella A, De Tschudy A, Corazziari E. Dyspeptic symptoms and gastric antrum distension. An ultrasonographic study. *Ital J Gastroenterol* 1987; 19: 215–7.
- Hausken T, Berstad A. Wide gastric antrum in patients with non-ulcer dyspepsia: effect of cisapride. *Scand J Gastroenterol* 1992; 27: 427–32.

- 30 Hveem K, Jones KL, Chatterton BE, Horowitz M. Scintigraphic measurement of gastric emptying and ultrasonographic assessment of antral area: relation to appetite. *Gut* 1996; **38**: 816–21.
- 31 Turconi G, Bazzano R, Caramella R, Crovetto R, Porrini M. High-calorie fibre-rich breakfast: its effect on satiety. *J Hum Nutr Diet* 1993; **6**: 245–52.
- 32 Waxman D. *Hartland's Medical and Dental Hypnosis*, 3rd edn. London, UK: Harcourt Brace and Company Limited, 1998: 70–104.
- 33 Hartland J. Further observations on the use of ego-strengthening techniques. *Am J Clin Hypn* 1971; **14**: 1–8.
- 34 Eberl T, Barnert J, Dumitrascu DL, Fischer J, Wienbeck M. The effect of cisapride on dysmotility-like functional dyspepsia: reduction of the fasting and postprandial area, but not of the postprandial antral expansion. *Eur J Gastroenterol Hepatol* 1998; **10**: 991–5.
- 35 Heap M. The nature of hypnosis. *Eur J Gastroenterol Hepatol* 1996; **8**: 515–9.
- 36 Benini L, Castellani G, Bardelli E, *et al.* Omeprazole causes a delay in gastric emptying of digestible meals. *Dig Dis Sci* 1996; **41**: 469–74.
- 37 Tack J, Piessevaux C, Coulie B, Caenepeel P, Janssens J. Role of impaired gastric accommodation to a meal in functional dyspepsia. *Gastroenterology* 1998; **115**: 1346–52.
- 38 Benson H. Hypnosis and the relaxation response. *Gastroenterology* 1989; **96**: 1609–11.
- 39 Tougas G. The autonomic nervous system in functional bowel disorders. *Gut* 2000; **47** (Suppl. IV): 78–80.
- 40 Cann PA, Read NW, Cammack J, *et al.* Psychological stress and the passage of a standard meal through the stomach and the small intestine in man. *Gut* 1983; **24**: 236–40.
- 41 Narducci F, Snape WJ, Battle WM. Increased colonic motility during exposure to a stressful situation. *Dig Dis Sci* 1985; **30**: 40–4.
- 42 Whorwell PJ, Houghton LA, Taylor EE, Maxton DG. Physiological effects of emotion: assessment via hypnosis. *Lancet* 1992; **340**: 69–72.
- 43 Spiegel D. Negative and positive visual hypnotic hallucinations: attending inside and out. *Int J Clin Exp Hypn* 2003; **51**: 130–46.
- 44 Houghton LA, Calvert EL, Jackson NA, Cooper P, Whorwell PJ. Visceral sensation and emotion: a study using hypnosis. *Gut* 2002; **51**: 701–4.