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ORIGINAL ARTICLE

Pilot Study of a Self-Administered Hypnosis Intervention for Functional Dyspepsia

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Abstract

Background Functional dyspepsia (FD) is a chronic disorder of the upper gastrointestinal tract that currently lacks substantially effective therapy options.

Aims To evaluate the feasibility and potential impact on FD symptoms and well-being of a fully automated gut-directed hypnosis intervention delivered via audio recordings.

Methods FD patients were enrolled at a single medical center and given access to a password-protected website where they completed 7 bi-weekly audio-recorded hypnosis sessions over a 3-month period. Study questionnaires including the Patient assessment of upper gastrointestinal symptom severity index, Short-Form Nepean Dyspepsia Index, the Visceral Sensitivity Index, and the Brief Symptom Inventory (BSI-18) were completed online pre-treatment, mid-treatment, post-treatment and at 3-month follow-up.

Results Of 23 enrolled patients (18 females; mean age = 38 years), 96% completed the entire treatment program and 3-month follow-up. Intention-to-treat analyses showed significant improvement at both end of treatment and 3-month follow-up in dyspepsia severity and quality of life, as well as in gut-specific anxiety and psychological distress. 68% of treatment completers reported that their FD symptoms were improved. Improvement in FD severity was significantly positively correlated with baseline PAGI-SYM total scores and BSI Global Severity Index scores.

Conclusions The fully automated hypnosis audio treatment program, which requires no therapist or clinician involvement, demonstrated excellent feasibility and resulted in significant improvement in FD symptoms, quality of life and emotional well-being. The results indicate that the intervention has high potential as adjunctive therapy for FD and warrants further investigation in a randomized controlled trial.

Keywords Functional dyspepsia · Disorders of gut-brain interaction · Hypnotherapy · Brain-gut psychotherapy

Introduction

Functional Dyspepsia (FD) is one of the most commonly diagnosed disorders of gut-brain interaction (DGBI), affecting 4.8–7.2% of the global population according to Rome IV criteria [1]. It is characterized by upper gastrointestinal (GI) tract symptoms, including epigastric pain, post-prandial fullness, and early satiety [2]. These symptoms occur in the absence of structural abnormalities [3]. FD has significant economic impact due to the financial costs related to health care utilization as well as indirect costs associated with missed work and impaired work performance. Due to the chronic nature of this condition, patients continue to seek medical care for poorly managed symptoms, including multiple physician office visits and investigative procedures. Patients with FD also report significant reductions in quality

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of life and have increased rates of psychological distress [4]. There are few effective treatment options for FD, with no FDA-approved medications for the condition. Medical therapy typically includes trials of proton pump inhibitors, prokinetic agents, or tricyclic anti-depressants [5]. However, these treatments have limited efficacy, and current approaches to management of the disorder are considered unsatisfactory [5, 6].

Psychological treatments are increasingly recognized as an effective treatment option for DGBI, particularly irritable bowel syndrome (IBS). Gut-directed hypnotherapy has been studied extensively as a treatment for IBS, with more than twenty published trials including 10 randomized controlled trials [7]. These studies consistently demonstrate significant improvements in the central IBS symptoms (abdominal pain and abnormal bowel habits) following a course of hypnotherapy [7]. FD and IBS are thought to have overlapping pathophysiology, including altered gut motility, visceral hypersensitivity, and abnormal central processing of visceral signals. In fact, the two conditions have high rates of comorbidity, with 46% of patients with FD also meeting criteria for IBS [8]. Many of these underlying mechanisms in FD can potentially be targeted by hypnotherapy via brain-gut pathways. For example, hypnosis has been shown to experimentally decrease gastric emptying time in patients with FD [9]. However, there has been limited research examining the effectiveness of psychological treatments for FD. The few trials that have been conducted have involved diverse forms of psychotherapy and have had varying degrees of reported success. To date, the most successful and best-designed trial has been Calvert et al.'s randomized controlled study of gut-directed hypnotherapy for FD [10]. In this trial, 126 patients with FD were randomized to either gut-directed hypnosis treatment, supportive therapy plus medication, or medical treatment for 16 weeks. The trial found that 73% of patients in the hypnotherapy group had significant improvements in dyspeptic symptoms at long-term follow-up (56 weeks), compared to 34% of patients receiving supportive therapy and 43% of patients receiving medical treatment. Additionally, patients in the hypnotherapy group had dramatic reductions in medication use and physician consultation at follow-up. However, it is notable that the intervention tested by Calvert et al. consisted of a 12-session course of treatment with a specialized GI hypnotherapist, which means that generalizability of this approach is limited due to the significant cost barriers and limited availability of therapy expertise. In fact, these are common criticisms of brain-gut psychotherapies as a whole. Even though brain-gut psychotherapies have very good efficacy for conditions like IBS, these treatments are not accessible by most patients due to limited availability of highly specialized GI psychology providers.

The current study was designed to improve accessibility of gut-directed hypnotherapy for FD by developing a self-administered and convenient treatment that allows patients to complete the entire treatment course at home without any therapist involvement by using web-based audio recordings. This methodology has been used previously in hypnotherapy trials for IBS and pediatric abdominal pain with good results [11, 12]. For example, a published pilot study of hypnotherapy for IBS delivered entirely through audio recordings found that IBS patients who completed a 7-session self-administered audio home hypnosis treatment course were twice as likely (53% vs. 26%) to have a reduction in their gastrointestinal symptoms by half or more at 6 months compared to matched control patients who only received usual medical care [11].

The purpose of the present trial was to pilot test a seven-session self-administered hypnotherapy treatment program for FD. The primary aim was to evaluate the feasibility and acceptability of this treatment program. A second aim of the study was to evaluate preliminary evidence of the effectiveness of the treatment at improving FD symptoms and quality of life, and evaluate the short-term maintenance of treatment effects by assessing these outcome parameters again 3 months after treatment was completed. We hypothesized that participants would report significant reductions in pre-treatment to end-of-treatment FD symptom scores as well as improvements in psychological indices and disease-specific quality of life, and that the therapeutic effects would be maintained at 3-month follow-up. Our final aim was to assess potential predictors of treatment response.

Methods

Participants and Procedure

Participants were adults (> 18 years) with FD recruited between June 2019 and April 2020 and enrolled at a single academic medical center. All participants were referred by a gastroenterology provider and had undergone an evaluation, including an upper endoscopy, to evaluate their symptoms and confirm the FD diagnosis. Seventy-eight percentage of participants also met Rome IV criteria for FD at enrollment [3]. Although all participants met diagnostic criteria during the initial screening interview with the study coordinator, a subset of participants' symptoms did not meet the threshold for diagnosis on the Rome IV FD module that was administered as one of the pre-treatment assessment questionnaires. Exclusion criteria included concomitant organic gastrointestinal disease; diagnosis or presentation of serious mental illness (e.g., eating disorder, schizophrenia, psychosis, obsessive–compulsive disorder, post-traumatic stress disorder, or a dissociative disorder); cognitive or language barriers that would make completing the questionnaires difficult or limit understanding of the verbal intervention; and lack of access

to the Internet via laptop or desktop computer, smartphone or tablet.

All eligible potential participants met with a clinical health psychologist (Dr. Kinsinger, the study PI), for a screening evaluation prior to being enrolled in the study. The purpose of this evaluation was to conduct a clinical interview to confirm that patients met eligibility criteria and that there were no contraindications for hypnotherapy treatment (e.g., active post-traumatic stress disorder). Furthermore, the visit provided education on FD, informed potential participants about the study design and included completion of written consent for patients choosing to participate.

Participants received the study treatment at no cost and received $25 gift cards for each completed research assessment (pre-treatment, mid-treatment, and 3-month follow-up) and a $50 gift certificate for the end of treatment assessment. The Institutional Review Board at Loyola University Medical Center approved the study, which was registered at www.clinicaltrials.gov prior to data collection (NCT03884270). Informed consent was obtained from all individual participants included in the study.

Treatment

Participants enrolled in the study were given access to a password-protected website containing the hypnotherapy treatment materials. They were instructed by the study coordinator to log on to the website within one week to complete baseline assessment questionnaires and watch an instructional video. The video was recorded by Dr. Kinsinger (study PI), and included educational information about the patient's diagnosis, provided rationale for hypnotherapy treatment, set expectations for treatment, and dispelled myths about hypnotherapy. The video also provided instructions for implementing the treatment protocol, including guidance on selecting a time and place to complete the hypnotherapy audio sessions and recommendations for weekly practice with audio recordings (5×/week).

Study investigators (Palsson and Kinsinger), co-wrote the scripted 7-session hypnosis protocol for functional dyspepsia that was used in the study. It was similar in structure and general treatment approach to Dr. Palsson's University of North Carolina scripted hypnosis protocol for IBS that has been tested in clinical trials and has been adapted for other GI conditions (e.g., functional heartburn, inflammatory bowel disease) [13]. The FD protocol used in this study was not adapted from this earlier protocol and contained unique content. The hypnosis intervention for this study was designed to specifically focus on mechanisms that contribute to functional dyspepsia symptoms, such as impaired relaxation of the stomach and visceral hypersensitivity. Study participants were given access to audio recordings of the scripted intervention sessions (recorded by Dr. Kinsinger) via secure online streaming.

The participants accessed all treatment materials and study questionnaires on a secure web page where they logged in with a unique username and password. Once the participants were logged in, they were presented with an online audio player that enabled them to play one of the seven biweekly main hypnosis sessions, which were presented in a fixed sequence and became automatically available at the appropriate pre-programmed intervals. These main therapy sessions were half-hour long on average. The web system asks participants to press a button after listening to each of the main hypnosis sessions to indicate that they had completed it which then allowed the participant to move on to the next hypnosis session at the correct time (i.e., two weeks later). In between the main sessions, the participants completed a 15-min hypnosis practice exercise that was to be used five times per week. Participants were also asked to push a button after listening to each practice session which allowed the web system to track frequency with which participants were using the practice sessions. The participants could listen to the hypnosis audio recordings either on their computers or on their mobile phones, via a mobile-adapted version of the study website. When it was time for participants to complete study questionnaires, a button would become visible within the patient web portal with instructions to click it to complete the appropriate questionnaire. By using a separate study management web page, study staff periodically monitored the participants' compliance with their use of the hypnosis sessions and questionnaire completion, and a staff member contacted the patients with reminders via e-mail or phone if needed.

Measures

At baseline (week 0), mid-treatment (week 6), end of treatment (week 12), and 12 weeks following the end of treatment (i.e., at 3-month follow-up) participants completed study questionnaire evaluations as described below via Qualtrics Research Suite Software.

In the baseline assessment, immediately before the first main hypnosis session, participants completed demographic questions (e.g., age, gender, education) as well as disease-related information (symptom severity, medication use). They also completed the Rome IV Dyspepsia Module used to assess whether individuals meet Rome IV FD criteria [3].

The Patient Assessment of Upper Gastrointestinal Symptoms Severity Index (PAGI-SYM) was administered to assess FD symptom severity at all evaluation time points. The PAGI-SYM measures 20 dyspeptic symptoms on a 6-point Likert scale, 0 (no complaints) to 5 (severe complaints), subdivided into six subscales: heartburn/regurgitation, nausea/vomiting, post-prandial fullness/early satiety,

bloating, upper abdominal pain, and lower abdominal pain. The measure has demonstrated good reliability and validity for measuring symptom severity in patients with functional dyspepsia [14].

The Short-Form Nepean Dyspepsia Index (NDI-SF) was used to assess disease-specific quality of life at all evaluation time points. The NDI-SF is a 10-item quality of life questionnaire developed for clinical trials in functional dyspepsia. The NDI has been established to have excellent psychometric properties [15] and responsiveness to treatment change has been confirmed [16] and the 10-item short form is recommended for use in clinical trials [17].

The Visceral Sensitivity Index (VSI) was used to assess gastrointestinal-specific anxiety [18] at all evaluation time points. It is a 15-item questionnaire that assesses fears of GI symptoms and is a predictor of symptom severity in patients with disorders of gut-brain interaction. The VSI uses a 6-point Likert scale response format with total scores ranging from 0 to 75 (higher scores indicate more severe symptom-related anxiety).

The Brief Symptom Inventory (BSI) was used to assess psychological distress at all evaluation time points. The BSI is an 18-item questionnaire using a 5-point Likert scale with total scores ranging from 0 to 68 to assess global distress (higher scores indicate greater distress) as well as three subscales assessing depression, anxiety and somatization [19].

Thought Impact Scale-Short Form (TIS-SF) is a 17-item questionnaire that measures a personality trait, subconscious connectedness, which has been found to be associated with clinical response to hypnosis treatment. The TIS-SF was administered at baseline only to assess whether the scores correlated with the degree of FD symptom improvement in the study. Scores on this trait are conceptualized to represent the extent to which people's non-conscious mental functions communicate with their consciousness in everyday life. For example, high TIS-SF scorers experience more time-appropriate unprompted reminders from their memory, and more frequent spontaneous creative impulses, than do other people. They also more readily experience dissociation from the here-and-now and narrowed focus of attention (i.e., mental absorption), both of which are relevant to responsiveness to hypnosis [20].

Health Care Utilization was assessed by asking participants at baseline and end of treatment to report the number of outpatient visits and procedures they had within the last 3 months related to their functional dyspepsia symptoms. They were also asked to report any changes in medications they were using for their functional dyspepsia symptoms.

Satisfaction with Treatment and Global Outcome ratings were obtained from the participants at the end of treatment only by asking them two questions: (1) "On a scale from 1 to 7, with 1 being "extremely dissatisfied" and 7 being "extremely satisfied", please rate your overall satisfaction with the hypnosis treatment" and (2) "Compared to how they were at the beginning of the hypnosis treatment, how are your Functional Dyspepsia symptoms now?" (from "Very Much Worse" to "Very Much Improved").

Satisfaction with the Web Platform was assessed at the end of treatment by asking participants 2 questions. (1) "Please indicate how difficult or easy the web platform for receiving this treatment was to use", with 1 being "extremely easy" and 7 being "extremely difficult" and (2) "Please describe any difficulties you had using the web interface and audio recordings and/or suggestions on ways we could improve the website".

Adherence to Hypnosis Practice was recorded automatically by the audio player page on the treatment website, to track frequency of hypnotherapy home practice by study participants.

Statistical Analysis

We calculated descriptive summary statistics as frequency counts and percentages for all categorical variables, and as means and standard deviations for ordinal and continuous variables. Among all participants consented, the proportion of participants who completed the hypnosis treatment program was calculated as a measure of feasibility. Treatment satisfaction was calculated as the proportion of patients who started the treatment (dropouts included) who reported that they were satisfied with the treatment (i.e., endorsed either "Somewhat satisfied", "Very satisfied" or "Extremely satisfied" on the 7-point treatment satisfaction measure).

Mixed linear effects regression analysis was used to estimate treatment effects. Each total score and subscale was regressed against the fixed effect of time period in a separate linear mixed effects regression model that included random intercepts to account for within-participant correlation. Adjusted mean differences from baseline were calculated for end of treatment and 3-month follow-up. Effect size Cohen's d was reported as the mean difference over the standard deviation of the difference [21]. Finally, the association between baseline summary scores with change in PAGI-SYM was assessed for statistical significance using Pearson's correlation coefficients. All analyses were performed as intention-to-treat, with the last available data carried forward for the participant. Analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC).

Results

Patient Characteristics

A total of 23 patients were enrolled in the study (18 females; mean age = 38 years, range 18–65 years). Table 1 summarizes the patient demographics.

Feasibility and Acceptability of Treatment

Of the 23 patients enrolled, 22 (96%) completed the entire treatment program (i.e., all 7 main hypnosis treatment sessions) and 3-month follow-up. The only participant who dropped out did so after completing the first hypnosis intervention session. Satisfaction scores were generally positive, with 83% (19/23) of participants reporting being "somewhat, very, or extremely satisfied" with the treatment, and 91% (21/23) rating the web platform as "extremely, moderately, or slightly easy" to use.

Table 1 Participant characteristics

	Overall $N = 23$
Age, mean (SD) [range]	38 (17) [18–65]
Female, *n* (%)	18 (78.3)
Race/ethnicity, *n* (%)	
White/caucasian (non-hispanic)	17 (73.9)
Black/African American (non-hispanic)	3 (13.0)
Hispanic (of any race)	2 (8.7)
Other	1 (4.3)
Relationship status, *n* (%)	
Single	7 (30.4)
Committed relationship	6 (26.0)
Married	10 (43.5)
Divorced	0 (0.0)
Education, *n* (%)	
High school	3 (13.0)
Some college	3 (13.0)
Technical school or associates degree	2 (8.7)
Undergraduate degree	8 (34.8)
Some graduate school	1 (4.3)
Graduate degree	6 (26.0)
Employment, *n* (%)	
Full-time	15 (65.2)
Part-time	2 (8.7)
Not working	4 (17.3)
Retired	2 (8.7)
Prior mental health diagnosis, *n* (%)	11 (47.8)
FD Rome criteria met, *n* (%)	
Postprandial distress syndrome (PDS) only	6 (26.1)
Epigastric pain syndrome (EPS) only	2 (8.7)
Both PDS and EPS	10 (43.5)

Practice Session Compliance

The use of the shorter hypnosis practice session varied greatly among participants. The mean number of practice sessions completed by participants was 32.4 (range = 7–96). Due to the design of the automated online delivery program, all program completers were required to listen to all 7 of the main therapy sessions, but they were highly variable in their compliance with the recommended 5 times per week use of the shorter hypnosis exercise between those main sessions.

Treatment Outcomes

Table 2 presents a summary of all outcome measures and treatment effects at pre-treatment, mid-treatment, post-treatment, and 3-month follow-up. Mixed effects linear regression showed significant, large reductions in PAGI-SYM total scores (reflecting overall functional dyspepsia symptom severity) at post-treatment ($d = 1.01$) and these effects were maintained at the 3-month follow-up ($d = 1.02$). Figure 1 illustrates the improvement in PAGI-SYM symptoms from baseline to end of treatment and at 3-month follow-up. All PAGI-SYM subscale scores, except for lower abdominal pain, also demonstrated significant reductions from pre- to post-treatment with medium to large effect sizes. The mean difference scores for the PAGI-SYM total and the 6 subscales fall within or exceed the minimal difference (0.30–0.70) that is recommended to demonstrate clinically significant improvements with this measure (see Table 2) [22]. We also examined the proportion of individual participants who experienced clinically significant magnitude of change on this measure and found that 65% ($n = 15$) of participants met or exceeded this minimal difference criteria (0.30) on the PAGI-SYM total scale at post-treatment and 74% ($n = 17$) met these criteria at 3-month follow-up.

Additionally, a majority of patients reported significant symptom improvement on a single-item global rating scale with 68% (15/22) of treatment completers rating their symptoms as "somewhat, moderately, or very much better" at the end of treatment.

Mixed effects linear regression showed significant, large improvement in NDI-SF total scores at post-treatment ($d = 1.13$) and 3- month follow-up ($d = 0.78$). All NDI-SF subscale scores also demonstrated significant improvements from pre- to post-treatment with medium to large effect sizes. The pre- to post-treatment reduction in the NDI-SF total score in our sample (34.1 to 24.7) corresponds to a clinically meaningful change for this measure (i.e., a 10 point change on the NDI total scale is considered clinically meaningful) [23]. We also examined the proportion

Table 2 Dyspepsia symptom severity, health-related quality of life, GI-specific anxiety and emotional well-being

	Baseline	Mid-treatment	End of treatment	3-month follow-up	End of treatment minus baseline			3-month follow-up minus baseline		
	Mean (SD)				Adjusted mean difference (SE)	*p*-value	Effect size $\|d_z\|$	Adjusted mean difference (SE)	*p*-value	Effect size $\|d_z\|$
PAGI-SYM total score	2.3 (1.0)	1.6 (0.9)	1.6 (0.9)	1.5 (0.8)	− 0.73 (0.12)	< 0.001	1.01	− 0.82 (0.12)	< 0.001	1.02
Nausea/vomiting	1.4 (1.3)	0.9 (1.0)	0.9 (1.1)	0.9 (0.9)	− 0.45 (0.17)	0.01	0.41	− 0.51 (0.17)	0.004	0.57
Post-prandial fullness	2.9 (1.5)	1.8 (1.2)	1.9 (1.2)	1.7 (1.2)	− 1.00 (0.20)	< 0.001	0.91	− 1.24 (0.20)	< 0.001	0.96
Bloating	3.0 (1.5)	2.3 (1.5)	2.4 (1.5)	2.3 (1.4)	− 0.59 (0.19)	0.003	0.54	− 0.65 (0.19)	0.001	0.66
Upper abdominal pain	3.2 (1.1)	2.1 (1.1)	2.1 (1.2)	2.0 (1.3)	− 1.07 (0.18)	< 0.001	1.01	− 1.20 (0.18)	< 0.001	1.20
Lower abdominal pain	1.6 (1.5)	1.2 (1.1)	1.2 (1.2)	1.3 (1.2)	− 0.46 (0.25)	0.07	0.35	− 0.30 (0.25)	0.225	0.19
Heartburn/regurgitation	1.8 (1.4)	1.1 (1.0)	1.0 (0.9)	0.8 (0.8)	− 0.82 (0.15)	< 0.001	0.91	− 0.99 (0.15)	< 0.001	1.10
NDI-SF Total score*	34.1 (8.9)	23.6 (9.4)	24.7 (10.0)	24.4 (12.1)	− 9.43 (1.75)	< 0.001	1.13	− 9.65 (1.75)	< 0.001	0.78
Tension	7.1 (2.2)	4.7 (2.0)	5.1 (2.3)	5.0 (2.4)	− 2.00 (0.42)	< 0.001	0.92	-2.09 (0.42)	< 0.001	0.77
Interference w/activities	6.3 (2.7)	4.3 (2.4)	4.8 (2.6)	4.5 (2.8)	− 1.52 (0.45)	0.001	0.63	− 1.83 (0.45)	< 0.001	0.65
Eating/drinking	7.5 (2.0)	5.3 (2.3)	4.9 (2.2)	5.5 (2.6)	− 2.65 (0.43)	< 0.001	1.25	− 2.04 (0.43)	< 0.001	0.75
Knowledge/control	7.0 (1.7)	5.2 (2.0)	5.5 (2.2)	4.8 (2.2)	− 1.52 (0.45)	0.001	0.71	− 2.22 (0.45)	< 0.001	0.81
Work/study	6.1 (2.4)	4.2 (2.4)	4.3 (2.4)	4.6 (3.0)	− 1.74 (0.44)	< 0.001	0.78	− 1.48 (0.44)	0.001	0.52
BSI GSI	63.9 (11.5)	58.5 (9.7)	58.0 (11.0)	54.7 (8.4)	− 5.91 (1.34)	< 0.001	0.77	− 9.22 (1.34)	< 0.001	1.07
Somatization	63.7 (10.0)	58.7 (9.3)	57.9 (9.5)	57.1 (8.5)	− 5.83 (1.38)	< 0.001	0.81	− 6.61 (1.38)	< 0.001	0.84
Depression	59.9 (14.9)	54.0 (13.4)	54.6 (13.9)	51.3 (11.8)	− 5.26 (1.54)	0.001	0.69	− 8.61 (1.54)	< 0.001	0.89
Anxiety	63.0 (10.7)	57.2 (9.4)	57.8 (10.0)	52.1 (9.0)	− 5.22 (1.51)	0.001	0.58	− 10.96 (1.51)	< 0.001	1.13
VSI[a]	41.8 (16.0)	47.9 (15.5)	50.4 (17.6)	52.2 (18.3)	8.61 (2.73)	0.002	0.62	10.39 (2.73)	< 0.001	0.62

PAGI-SYM patient assessment of upper gastrointestinal symptom severity index, *NDI* Napean Dyspepsia Index, *BSI* Brief symptom inventory, *VSI* Visceral Sensitivity Index, *SE* standard error

*The NDI-SF measures disease-specific quality of life impairment with lower scores representing better quality of life

[a]These are non-reversed VSI raw scores: Higher scores mean less gut-specific anxiety

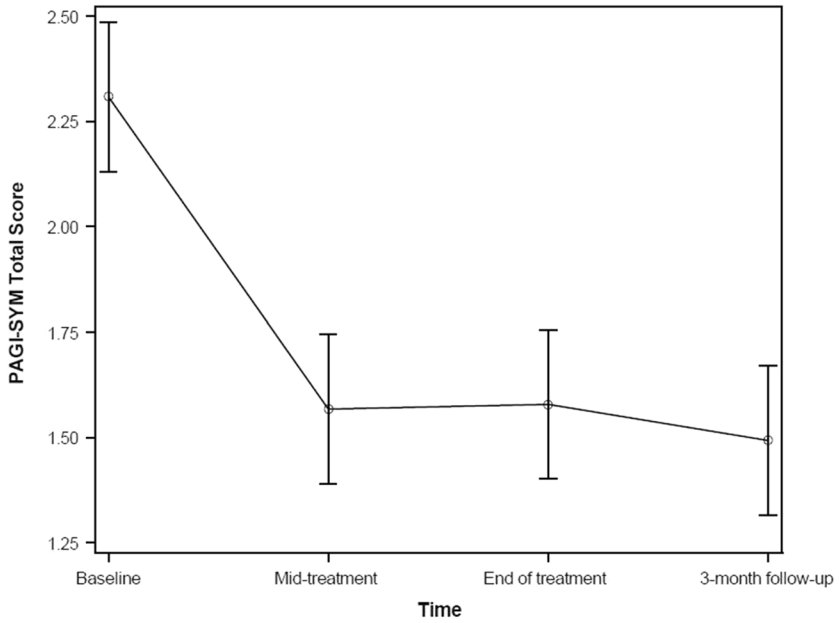

Fig. 1 Mean dyspepsia symptom severity scores at baseline, mid-treatment, at the end of the hypnosis treatment program, and at 3-month follow-up

of individual participants who experienced clinically significant change scores on the NDI-SF total score and found that 39% ($n=9$) of participants met these criteria (10 point reduction) at post-treatment and 52% ($n=12$) met this criteria at 3-month follow-up.

Psychological indices also demonstrated significant improvements, including the BSI Global Severity Index with scores significantly improving at post-treatment ($d=0.77$) and demonstrating further improvements at the 3-month follow-up ($d=1.07$). The three BSI subscales (somatization, depression, and anxiety) also showed significant improvements with medium to large effect sizes at post-treatment and 3-month follow-up. It is notable that baseline scores on the BSI-GSI and two of the subscales (somatization and anxiety) were in the clinically significant range based on published norms (T-score > 63)[19], indicating that participants were experiencing significant psychological distress at the start of treatment and these scores decreased to non-significant clinical levels by post-treatment and further improved at 3-month follow-up.

Finally, the visceral sensitivity index showed significant improvements in scores from baseline to post-treatment ($d=0.62$) and remained stable at the 3-month follow-up ($d=0.62$), indicating improvements in gastrointestinal-specific anxiety following treatment.

Assessment of Predictors of Treatment Response

Baseline scores on the PAGI-SYM, BSI-GSI, VSI, TIS-SF, and frequency of home practice were correlated with improvement in FD severity (baseline to end-of-treatment) to identify predictors of treatment response (see Table 3). Of the tested variables, higher baseline PAGI-SYM ($r=-0.51$, $p=0.01$) and BSI Global Severity Index ($r=-0.59$, $p=0.003$) scores were significantly correlated with greater reduction in FD symptoms after treatment.

Table 3 Correlations of baseline characteristics with change in PAGI-SYM scores at end of treatment (negative correlation values indicate associations with the amount of reduction in symptoms compared to baseline)

	Pearson's correlation coefficient (95% CI)	*p*-value
Baseline PAGI-SYM	−0.51 (−0.76, −0.11)	0.01
BSI GSI	−0.59 (−0.80, −0.22)	0.003
VSI	0.29 (−0.15, 0.62)	0.18
Frequency of home practice	−0.28 (−0.61, 0.16)	0.20
TIS total score	−0.27 (−0.61, 0.17)	0.22

PAGI-SYM patient assessment of upper gastrointestinal symptom severity index, *BSI* brief symptom inventory, *VSI* Visceral Sensitivity Index, *TIS*, Thought Impact Scale, *CI* confidence interval

Discussion

The fully automated hypnosis treatment program for functional dyspepsia that was tested in this trial demonstrated excellent feasibility and showed significant improvements in all primary and secondary outcome variables that were measured. Two-thirds (68%) of the patients reported significant symptom improvement on a global rating scale, and the study results showed clinically meaningful reductions in dyspeptic symptoms on a validated symptom severity

measure following treatment. The effect size for the primary treatment outcome variable was very large and was fully maintained at the 3-month follow-up period. Additionally, disease-specific quality of life improved significantly following treatment, with a very large effect size, and this was maintained at the 3-month follow-up assessment. Gastrointestinal-specific anxiety scores also improved significantly with a medium effect size and remained improved at the 3-month follow-up. Finally, psychological distress scores demonstrated significant improvements post-treatment with large effect sizes and improved further at the 3-month assessment. Collectively, these findings indicate that the hypnosis treatment program we tested has the potential to not only improve dyspepsia symptoms, but also to normalize psychological distress and help correct the impairment in quality of life that results from the disorder.

Our findings furthermore indicate that the automated delivery format we used is highly appealing to patients. We had very high adherence rate, with 96% of participants enrolled completing the treatment program, as well as very high satisfaction ratings for the treatment program and the web-based platform. These findings are encouraging and demonstrate that patients are not only receptive to a home-based treatment, but also remain engaged throughout the entire treatment program.

The significant associations we observed between symptom improvement and baseline FD severity and psychological distress suggest that this automated delivery method may be more effective for patients with severe dyspeptic symptoms or higher levels of psychological distress than for other FD patients. However, that is somewhat at odds with prior research showing that patients with higher rates of anxiety did not respond as well to a home-based hypnosis intervention for IBS [11]. It is also possible that this could represent regression to the mean. This potential moderating effect of severity of GI and psychological symptoms and treatment response should be explored further in a larger-scale trial.

Even though shorter audio-recorded practice sessions in between the main treatment sessions (which are generally in person with a therapist) are commonly used in GI hypnosis treatment, and we followed that convention in designing our program, our analyses suggest that the extent to which patients use these supplemental sessions may have little effect on clinical outcomes. This is consistent with findings in a pilot study of audio-recorded hypnosis treatment for IBS by Palsson et al. [11], where there was no difference in frequency of use of such hypnosis practice sessions among treatment responders versus non-responders. As reducing or eliminating practice sessions in between the main therapy sessions would save patients time and effort, the impact of including such supplemental practice sessions in treatment protocols needs to be further evaluated in future GI hypnosis research.

The goal of this pilot study was to establish feasibility and acceptability, and obtain preliminary information regarding therapeutic impact, of the automated hypnosis treatment program. As an initial pilot study intended to provide guidance as to whether more extensive investment in research on this novel treatment approach for FD is warranted, this investigation has some limitations. The primary limitation of the study is the uncontrolled trial design, which does not control for factors such as time and expectancy that may have influenced symptom improvement. However, given the very large effect sizes for all outcome variables in the trial, we find it unlikely that the results are entirely due to factors other than the active effects of the treatment itself. Given these very promising preliminary findings, we believe the treatment program we tested warrants further study with a randomized controlled trial. An additional limitation is that the sample was predominantly female, non-Hispanic White and well-educated, which may limit the generalizability of the results.

Gut-directed hypnotherapy is gaining popularity among providers and patients as an effective treatment option for DGBI; however, many patients do not have access to a specialized GI hypnotherapist, and this approach has not been adequately disseminated. The results from this study indicate that this home-based hypnotherapy program could, if further validated by additional research, become a widely available, effective, and affordable treatment option for FD and a viable alternative for patients that do not have access or the means to pursue in-person psychological brain-gut treatment.

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Declarations

Conflict of interest The authors report no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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