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ORIGINAL REPORT

FUNCTIONAL MAGNETIC STIMULATION IN CONSTIPATION ASSOCIATED WITH PARKINSON'S DISEASE

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Objective: **The aims of this study were: (*i*) to investigate the effect of functional magnetic stimulation on total colonic transit time in patients with Parkinson's disease; (*ii*) to compare the changes in dynamic recto-anal behaviour during filling and defaecation in response to this regimen; and (*iii*) to study the carry-over effects with a 3-month follow-up.**

Design: **A longitudinal, prospective before-after trial.**

Subjects: **Sixteen patients with Parkinson's disease enrolled in this study. No subject withdrew from the study as a result of serious adverse events.**

Methods: **A 3-week magnetic conditioning protocol, consisting of a 20-min stimulation session twice daily. Colonic transit time, Knowles-Eccersley-Scott Symptom Questionnaire and the dynamics of defecography were carried out before the intervention and on the final day of the protocol.**

Results and conclusion: **There was a statistically significant reduction in colonic transit time and in the questionnaire score following the intervention. The difference in the anorectal angles between resting and evacuating process and the changes in pelvic floor descent all reached significance after the intervention. The therapeutic effects that achieved significance remained constant in the 3-month follow-up result. Functional magnetic stimulation may facilitate colonic motility in Parkinson's disease and straighten the anorectal angle, allowing smooth access of rectal contents to the anal canal.**

Key words: constipation, Parkinson's disease, functional magnetic stimulation, colonic transit time, defecography.

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INTRODUCTION

Most patients with Parkinson's disease (PD) are affected by constipation, experiencing this common non-motor problem as their condition progresses (1). The pathophysiology of constipation appears largely to include defaecatory dysfunction and slow colonic transfer time (2, 3). The slowing of colonic transfer time may relate to the direct involvement of PD in the colonic myentric plexus, in which the disease appears to impair coordination of the pelvic floor and the anal sphincter (2). Constipation may be exacerbated by slow intestinal transit time and obstructions.

Most patients with PD with associated constipation are required to modify their diets and take laxatives, stool softeners and bulk-forming agents to produce a bowel movement (4). Where the condition is more extreme, patients may use enemas or manual rectal stimulation (5).

Nevertheless, paradoxical puborectalis contraction in PD is usually a persistent condition that remains unresponsive to treatment in spite of various therapies currently available to relieve constipation (3).

In previous research, functional magnetic stimulation (FMS) has been shown to stimulate the colon and to facilitate bowel emptying and colonic transit in both animals and humans (6–8). In our own previous studies, we demonstrated that, by carrying out FMS to the T9 and L3 spinal process, the mean colonic transit time for all spinal cord injured patients decreased from 62.6 to 50.4 h, and the effect of a certain number of stimuli could be carried over up to 3 months post-treatment (9). The rationale of FMS in improving bowel function following spinal cord injury (SCI) is based on the theory that FMS is capable of directing stimulation of the spinal nerves and contraction of the deep muscles, which is needed to facilitate bowel emptying, by modulating the different relaxation times between the movement of the peri-anal striated sphincter muscle and the rectum in aiding the evacuation of stool (8).

While the basic principles of the earlier study were similar, we now aimed to enhance bowel movements and harmonize the anorectal dyssynergia in patients with PD. The objectives of this study were: (*i*) to investigate the effect of FMS on total colonic transit time; (*ii*) to compare the changes in dynamic anorectal behaviour during filling and defaecation in response to FMS; and (*iii*) to study the carry-over effects of FMS with a 3-month follow-up.

METHODS

Study design

This was a prospective, intrinsically controlled study measuring baseline and post-FMS therapeutic responses. The methods and patients' informed consent were in accordance with the local institutional review board protocols for human subjects and in compliance with Occupational Health and Safety Administration regulations. We recruited 16 patients with PD, who met the clinical diagnostic criteria, including undertaking a magnetic resonance imaging scan and responding well to levodopa. The patients' average daily levodopa requirement during the period of this study was 200 mg (range 100–300 mg). Although dopaminergic drugs reportedly facilitate the functioning of the lower gastrointestinal (GI) tract, we nevertheless allowed our patients to continue taking levodopa during this study, since it is difficult for patients with PD to stop levodopa medication. None of the patients took anti-cholinergic agents.

The group comprised 14 men and 2 women, mean age 73.8 years (age range 54–89 years), mean duration of illness 10.1 years (range 3–22 years). The severity of illness ranged from 1 to 4 on the Hoehn and Yahr scale, with a median value of 2. We followed a modified version of the Rome criteria for the definition of constipation: "2 or fewer bowel movements a week, the use of laxatives or enema more than once a week or digital evacuation of faeces on all occasions" (10). Neither faecal incontinence nor diarrhoea was noted in any of the patients.

Functional magnetic stimulation protocol

We adopted the MagPro R30 Magnetic Stimulator (Medtronic, Skovlunde, Denmark) stimulation protocol to use as the conditioning protocol for this study. The instrumental setting and study paradigm has been described previously elsewhere (9). In brief, each subject was placed in a sitting position and each session began with the centre of the coil being placed at the T9 spinal process with 10 min of thoracic nerve stimulation, and the coil was then placed at the L3 spinal process by another 10 min of lumbosacral nerve stimulation. The stimulation intensities were set at 50% of maximal output (2.2 Tesla) on the first day, 60% on the second day and for the remainder of the study were stabilized at 70%. The stimulation frequency, burst length, and inter-burst intervals were fixed, respectively, at 20 Hz, 2 seconds, and 28 sec. Each subject underwent a 3-week stimulation period of 20-min stimulation sessions twice daily on an outpatient basis.

Colonic transit study

Colonic transit time (CTT) was assessed according to previously described methodology (9, 11). Each patient ingested one capsule per day, containing radiopaque markers on 3 consecutive days, a total of 3 capsules, then underwent one abdominal radiograph. Every capsule (Sitzmark radiopaque capsule, Konsyl Pharmaceuticals, Inc. Easton, USA) contains 24 differently shaped radiopaque markers, each of which is separately identifiable when viewed on abdominal films.

The patients began the CCT assessment before and after FMS. Abdominal radiographs were taken the day after the third capsule was ingested. The patients all had to suspend laxative medication, enema use or digital manoeuvring for 3 days during the CCT testing to prevent disturbing their colonic motility.

By identifying bony landmarks and gaseous outlines, we localized the markers on the abdominal films, a process described by Arhan et al. (12). Using this method, it was established that 3 days after ingestion of the first capsule, all 72 markers had been retained: an estimated transit of 72 h, which yielded a value of the upper limit for CCT, according to this method.

Defecography

A number of procedures are currently accessible to record images of the dynamics of defecology (13–16). We used the technique of positioning the patient on the fluoroscopic table (GE, Prestige II, Milwaukee, USA) in the left lateral position. A total of 500 g (250 ml) of thick barium paste was then injected into the patient's rectum. The paste has a similar consistency to normal stool, and 500 g (250 ml) produces a sensation of rectal fullness.

The table was then positioned upright at 90° and the patient was seated on a radiolucent commode. While the patient was thus at rest, lateral radiographs were taken of the voluntary contractions of the anal sphincter and of the pelvic floor muscles when they were straining downwards. We recorded the dynamics of evacuation using a computer video image analysis program. The residual barium paste in the rectum was rated on a scale of 1 to 3, with 1 indicating complete evacuation or the residual part of the paste occupying the lower third of the rectum; 2 indicating the residual part of the paste occupying two-thirds of the rectum; 3 indicating the residual part of the paste, which is occupying the whole rectum. The assessments were conducted by a radiologist who had no knowledge of the previous history and investigation results of our patients.

Knowles-Eccersley-Scott-Symptom questionnaire

The Knowles-Eccersley-Scott-Symptom (KESS) questionnaire (17) was completed for all patients prior to carrying out the FMS procedures, and again on the last day of the study. We continued the questionnaire by telephone at 2-week intervals between 2 weeks and 3 months following FMS. A detailed account of the KESS questionnaire used to assess the frequency or severity of bowel symptoms, in a similar paradigm, has been described elsewhere (9, 17). The interviews were conducted by a researcher who had no knowledge of the previous history and investigation results of the patients. For each question, the interviewer was required to elicit the single most appropriate answer at the time of the interview, and to avoid entering into discussions with the interviewees.

Statistical analysis

The Wilcoxon signed-rank test was used to analyse the information recorded from the CTT test, KESS scores and the changes in dynamic recto-anal behaviour, and to obtain an estimate of the patients' comparative baseline and post-FMS values. For repeated measurements' dependency, we used the generalized estimating equations (GEE) method (18) to examine the improvements in serial KESS scores compared with the baseline value, representing the clinical progression within 3 months of follow-up. An α-level of less than 0.05 was used to indicate significance.

Table I. *Clinical characteristics of 16 patients with Parkinson's disease*

Age, years	Sex	Severity of illness*	Duration of illness, years	Bowel care
81	M	2	11	Lax
69	M	4	7	Lax + Ene
70	F	2	8	Lax
77	M	3	7	Lax + Ene
73	M	2	10	Lax + Ene
54	M	1	3	Lax
89	M	2	12	Ene + Ene
57	F	2	5	Ene
69	M	4	12	Lax + Ene
58	M	4	5	Lax + Ene
73	M	2	11	Lax + Ene
80	M	2	15	Lax
83	M	2	16	Lax + Ene
76	M	3	13	Lax + Ene
86	M	2	22	Lax + Ene
87	M	1	12	Lax

*On the Hoehn and Yahr scale (1–4).

F: female; M: male; Lax: laxatives; Ene: enema.

Table II. *Data summary of defecography, colonic transit time and score of Knowles-Eccersley-Scott-Symptom (KESS) questionnaire at baseline and post-functional magnetic conditioning*

	Rest ARA, degree	Evacuation ARA, degree	Difference, degree†	Pelvic floor descent, cm	Residual barium amount, score	Colon transit time, hours	KESS score
Baseline, mean (SD)	94.0 (9.9)	97.9 (10.8)	6.0 (10.9)	1.38 (2.0)	2.63 (0.5)	64.9 (9.4)	17.5 (5.8)
Post-FMS, mean (SD)	100.8 (12.2)	117.3 (14.5)	19.3 (15.6)	2.75 (2.2)	1.88 (0.8)	53.6 (16.9)	11.4 (5.7)
p-value*	0.063	<0.001	<0.001	0.002	<0.001	<0.001	<0.001

**p*-values obtained from Wilcoxon signed-ranks test.
†Difference between rest and evacuation ARA.
ARA: anorectal angle; FMS: functional magnetic stimulation; SD: standard deviation.

RESULTS

Sixteen patients met the aforementioned inclusion criteria. The characteristics of their condition that we analysed included staging of severity, duration of illness and methods of bowel managements are demonstrated in Table I. Across all 16 patients, pre-and post-FMS bowel function showed significant decreases in their scores ($p < 0.05$), including the items: frequency of bowel movement, unsuccessful evacuation, enema/digitations, relative difficulty with evacuation, and time needed for bowel hygiene (Table II).

In comparison with the baseline values, significant improvement in KESS scores was found from the second to the eighth evaluation. The therapeutic effects of the FMS remained constant from the carrying out of the intervention to the last of the 3-month post-FMS measurements (Fig. 1). There was a statistically significant reduction in CTT and KESS scores following FMS intervention. The values are given in Table III. The differences in anorectal angles between resting and straining during evacuation, the changes in the pelvic floor muscles when straining downwards, and changes to the amounts of barium paste remaining in the rectum after evacuation, all reached significance following FMS intervention (Table III).

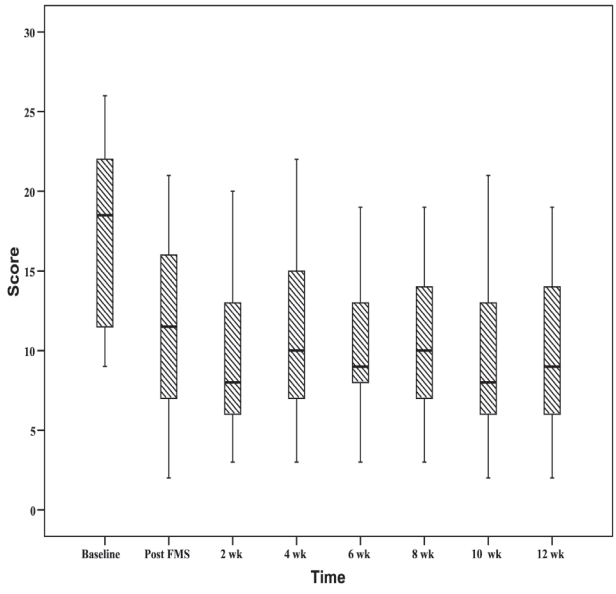

Fig. 1. Knowles-Eccersley-Scott-Symptom (KESS) scores were obtained every 2 weeks until 3 months after functional magnetic stimulation (FMS) intervention. In comparison with the baseline values, significant improvement in KESS scores was found from the second to the eighth evaluation.

DISCUSSION

In this study, we demonstrated: (*i*) that FMS enhanced CTT in patients with PD; (*ii*) that a significant increase in the anorectal angle and pelvic floor descent was noted during stool evacuation; and (*iii*) that FMS continues to be effective at 3 months post-intervention.

The cause of constipation in PD is multifactorial, but disturbance in autonomic regulation, leading to a delay of CTT in a majority of patients with PD, is the major underlying cause of constipation (19, 20). The activation of the colon in patients with SCI, resulting in an improvement of CTT, has been shown by our team and other authors to occur after FMS (8, 9). This study also showed that FMS of the colon facilitated colon transit in patients with PD. These results should be interpreted in the context of several factors: first, prolonged CTT in rectosigmoid segment and smaller amplitude of phasic rectal contractions were demonstrated in patients with PD (3). Electric stimulation to sacral nerves significantly increased pan-colonic antegrade propagating sequence frequency in patients with slow-transit constipation (21). The propagating action potentials originating in the proximal colon are an important precursor to initiate rectal contraction waves and stool expulsion (22). Secondly, the placement of the magnetic coil at T9 activates all the spinal nerves between T6 and T12 – with the corresponding innervated abdominal muscles – resulting in abdominal massage-like contractions. It elicited rectal wave along with bowel sensation and intermittent defaecation in constipation associated with myelopapthy (23). Abdominal massage, adjuvant to a traditional bowel program for patients with SCI, has also been proven to facilitate total CTT (24). The somato-autonomic reflex via pressure-sensitive nerves and autonomic ganglia may underlie this condition.

Previous studies on ineffective defaecation in patients with PD have found a correlation between paradoxical contractions of the pelvic floor and the external anal sphincter muscles during straining (25–28). This accentuates the flap-valve action of the anorectal angle to block the passage of stool (29). However, FMS of the lumbosacral nerves in patients with puborectalis paradoxical syndrome led to rectal pressure elevation and balloon expulsion on rectal distension without significant change

Table III. *Self-esteem distribution of the Knowles-Eccersley-Scott-Symptom (KESS) questionnaire at baseline and post-functional magnetic stimulation intervention for 16 patients*

Symptoms	KESS score	Baseline, %	Post-FMS, %	*p*
Laxative use				
None	0	6.25	31.25	0.086
Occ or short duration usage	1	18.75	6.25	
Regular or long duration usage	2	56.25	56.25	
Long duration, ineffective	3	18.7	6.25	
Frequency of bowel movement (using current therapy)				
1–2 times per 1–2 days	0	6.25	75	0.004*
2 or less times per week	1	75	18.75	
Less than once per week	2	12.5	6.25	
Less than once per 2 weeks	3	6.25	0	
Unsuccessful evacuation				
Never/rarely†	0	6.25	18.75	0.002*
Occasionally	1	6.25	37.5	
Usually	2	31.25	25	
Always (manual evacuation)	3	56.25	18.75	
Feeling of incomplete evacuation				
Never	0	25	18.75	0.677
Rarely	1	12.5	25	
Occasionally	2	18.75	6.25	
Usually	3	12.5	43.75	
Always	4	31.25	6.25	
Abdominal pain				
Never	0	68.75	62.5	1.0
Rarely	1	12.5	12.5	
Occasionally	2	6.25	18.75	
Usually	3	6.25	6.25	
Always	4	6.25	0	
Bloating				
Never	0	50	50	0.656
Perceived by patient only	1	31.25	37.5	
Visible to others	2	12.5	12.5	
Severe, causing nausea	3	0	0	
Severe, with vomiting	4	6.25	0	
Enema/digitations				
None	0	12.5	68.75	0.001*
Occ enema/suppository usage	1	31.25	18.75	
Regular enema/suppositories usage	2	56.25	12.5	
Occasional manual evacuation	3	0	0	
Manual evacuation always	4	0	0	
Time taken (min at each evacuation/ evacuation attempt)				
<5	0	0	25	0.005*
5–10	1	12.5	18.75	
10–30	2	37.5	50	
>30	3	50	6.25	
Difficult evacuation causing painful effort				
Never	0	0	12.5	0.001*
Rarely	1	6.25	12.5	
Occasionally	2	6.25	6.25	
Usually	3	18.75	56.25	
Always		68.75	12.5	
Stool consistency				
Soft/loose/normal		18.75	68.75	0.008*
Occasionally hard		37.5	12.5	
Always hard		6.25	0	
Always hard, usually pellet-like		37.5	18.75	

*Wilcoxon signed-rank test showed significant differences at $p<0.05$ (17).†Rarely: <25% of the time; occasionally: 25–50% of the time; usually ≥50% of the time. FMS: functional magnetic stimulation; Occ: occasional.

in the intragastric pressure (30). Magnetic conditioning can coordinate rectal and anal sphincter activities through the different length of relaxation periods between visceral and striated muscle contractions after being co-activated to facilitate stool evacuation in patients with PD. We demonstrated in this study that FMS intervention allows the pelvic floor to relax considerably, which allows the rectum to descend and enables the anorectal angle to increase during straining (25). This phenomenon during defaecation is the first to show in patients with PD treated with FMS.

We monitored and analysed the carry-over effects of the FMS intervention through the total KESS questionnaire. Since the questionnaire was designed for the assessment and diagnosis of functional constipation, it was feasible to use the same questionnaire to monitor treatment efficacy.

It is significant to note that our patients demonstrated an increase in the frequency of bowel movement, in ease of evacuation, and a decrease in the time taken for defaecation within 3 months after FMS. The 3-month prolongation of the effects of this treatment in the present study raises the possibility of using FMS to generate autonomic reorganization in patients with PD.

This was a preliminary study that followed the guidelines of the pioneering research on FMS in patients with SCI (8). We did not design a randomized, double-blind model. To verify the validity of FMS on patients with PD, a sham-controlled evaluation would be required in future studies.

In conclusion, the importance and potential of these findings for patients with PD with constipation, and the considerable improvement in their lifestyle and dignity, are noteworthy. We conclude, firstly, that FMS of the thoracic and lumbosacral nerves can facilitate bowel movement in patients with PD, and secondly, that the therapeutic effects of this intervention continue 3 months after intervention.

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