Parkinsonism and Related Disorders xxx (2010) 1–6

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

LaserLight cues for gait freezing in Parkinson's disease: An open-label study

S. Donovan [a,1], C. Lim [a,1], N. Diaz [b], N. Browner [b], P. Rose [a], L.R. Sudarsky [c], D. Tarsy [a], S. Fahn [b], D.K. Simon [a,*]

[a] Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA
[b] Columbia University Medical Center, NY, USA
[c] Brigham and Women's Hospital, Harvard Medical School, Boston, USA

ARTICLE INFO

Article history:
Received 4 April 2010
Received in revised form
7 June 2010
Accepted 6 August 2010

Keywords:
Parkinson's disease
Falls
Freezing
Visual cue
Gait
Laser
Laserlight
Lasercane
Clinical trial

ABSTRACT

Freezing of gait (FOG) and falls are major sources of disability for Parkinson's disease (PD) patients, and show limited responsiveness to medications. We assessed the efficacy of visual cues for overcoming FOG in an open-label study of 26 patients with PD. The change in the frequency of falls was a secondary outcome measure. Subjects underwent a 1–2 month baseline period of use of a cane or walker without visual cues, followed by 1 month using the same device with the laserlight visual cue. The laserlight visual cue was associated with a modest but significant mean reduction in FOG Questionnaire (FOGQ) scores of 1.25 ± 0.48 ($p = 0.0152$, two-tailed paired *t*-test), representing a 6.6% improvement compared to the mean baseline FOGQ scores of 18.8. The mean reduction in fall frequency was 39.5 ± 9.3% with the laserlight visual cue among subjects experiencing at least one fall during the baseline and subsequent study periods ($p = 0.002$; two-tailed one-sample *t*-test with hypothesized mean of 0). Though some individual subjects may have benefited, the overall mean performance on the timed gait test (TGT) across all subjects did not significantly change. However, among the 4 subjects who underwent repeated testing of the TGT, one showed a 50% mean improvement in TGT performance with the laserlight visual cue ($p = 0.005$; two-tailed paired *t*-test). This open-label study provides evidence for modest efficacy of a laserlight visual cue in overcoming FOG and reducing falls in PD patients.

1. Introduction

Freezing of gait (FOG) is a significant clinical problem in Parkinson's disease (PD) that often shows little or no responsiveness to medications. FOG is characterized by a sudden inability to initiate or maintain adequate stepping movements [1]. When prominent, FOG interferes with daily functioning and quality of life and increases the risk of falls and injury [2–7]. FOG has been estimated to affect 32% of all PD patients [8], though a study using a specific questionnaire identified FOG in 60% of PD patients, appearing an average of 4.8 years after the onset of PD symptoms [9]. FOG is often resistant to dopaminergic therapy, with 90% of patients in this study reporting no improvement with levodopa [9]. Walking aids are frequently prescribed for PD patients with FOG, although standard wheeled walkers have failed to show any reduction in FOG [10,11].

Several small studies have tested various rehabilitation strategies using sensory cues for their impact on gait and falls in PD, but definitive data demonstrating on efficacy is lacking [11–14]. A study in 2000 by Kompoliti et al. showed no consistent benefits from the use of visual cues in overcoming FOG as measured by assessments of a timed gait task and freezing frequency, but falls or FOG in a community setting were not studied [15]. A study by Frazzitta et al. [16] assessed the impact of a visual cue on FOG in the office setting, but because the visual cue was used in combination with treadmill training or other rehabilitation methods, conclusions specifically regarding the impact of the visual cues are not possible from this study. Jiang et al. [17] provided evidence in a clinical laboratory for improvement in gait using transverse lines on the floor but did not address the impact of visual cues on FOG in a community setting. A limited pilot study in 3 PD patients and 3 controls suggested that optical stimulating glasses might provide a portable method for improving FOG in PD [18]. In a more recent study in 15 PD patients with various types of gait difficulties, glasses that generate a virtual image of a horizontal line led to a 12% improvement in performance on a timed gait task [19], though this study did not specifically require subjects to have freezing of gait.

* Corresponding author. Beth Israel Deaconess Medical Center; 330 Brookline Avenue, Room CLS-638, Boston, MA 02215, USA. Tel.: +1 617 735 3251; fax: +1 617 735 2826.
E-mail addresses: donovask@gmail.com (S. Donovan), chen.lim@gmail.com (C. Lim), NDiaz2@neuro.columbia.edu (N. Diaz), brownern@neurology.unc.edu (N. Browner), peggy@peggyrose.com (P. Rose), LSudarsky@partners.org (L.R. Sudarsky), dtarsy@bidmc.harvard.edu (D. Tarsy), fahn@neuro.columbia.edu (S. Fahn), dsimon1@bidmc.harvard.edu (D.K. Simon).
[1] Co-first authors; These 2 authors contributed equally to this study.

1353-8020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.parkreldis.2010.08.010

The "RESCUE" trial was a large trial of 153 PD patients randomized to early or later intervention with training by a therapist in the use of a device that provided auditory, visual, and somatosensory cues [20]. This study did not demonstrate any change in fall frequency, but did show a modest improvement of 5.5% on freezing as measured by the change in the FOGQ. However, because multiple types of sensory cues were used in the RESCUE study, the impact specifically of visual cues could not be determined. Thus, definitive studies of the impact of visual cues on FOG and fall frequency are lacking, particularly when considering the impact of visual cues outside of an office or laboratory setting. The aim of the current study was to address these issues.

2. Methods

All study procedures were carried out with the adequate understanding and written consent of the subjects involved and with the ethical approval of the authors' institutional review boards.

2.1. Subjects

Subjects were recruited from the Movement Disorders Centers at Beth Israel Deaconess Medical Center (BIDMC; Boston), Brigham and Women's Hospital (Boston), or Columbia University Medical Center (CUMC; New York). All study procedures were conducted at BIDMC or CUMC. 32 subjects were enrolled and 26 completed the study. Subjects dropped out due to medical illnesses unrelated to the study ($n = 3$) or were lost to follow-up ($n = 3$). Each of these 6 subjects who dropped out of the study did so prior to exposure to the laserlight visual cue. Therefore, data are presented only for the 26 subjects who completed the study. Subjects were diagnosed with levodopa-responsive Parkinson's disease by a neurologist with expertise in movement disorders (LRS, DT, SF, or DKS). Subjects were required to be ambulatory, to use a cane and/or walker, and to have a positive assessment for the "Questionnaire Used to Identify Freezing of Gait in PD Patients" [9] which for this study was defined as answering 'yes' to Question A: "Have you ever experienced a sudden and short-lasting (maximum 5 s) block of walking, as if your feet were glued to the floor?" and experiencing one of more of either a, b, c or d, which relate to FOG upon initiation of gait, while walking, in narrow spaces, or on turns. FOG episodes were required to occur an average of at least once per day during the week prior to the initial study visit, though in practice all enrolled subjects reported multiple freezing episodes on all or nearly all days and considered FOG to be a substantial problem. Subjects were excluded if they had experienced any syncopal episodes in the 6 months prior to the initial study visit or if they had prior exposure to a laserlight visual cueing device. Subjects with a mini-mental status exam score of less than 22 also were excluded. Subjects could not have visual impairment that might interfere with the ability to view the laserlight visual cue. Subjects with prominent signs of pyramidal dysfunction were excluded. All study assessments took place in the "on" state (on medications). Subjects were provided with a U-Step cane or Walking Stabilizer (hereafter referred to as walker), depending on which walking aid they had used prior to study entry. For patients who used a cane at times and a walker at other times, both devices were provided. Of the 26 subjects, 16 used a cane, 5 used a walker, and 5 used both at varying times. Of the 5 who used both, 3 used the walker the majority of the time and 2 primarily used the cane.

2.2. Study procedures

The study involved 3 visits. After enrollment at the initial study visit (visit 1), subjects used the new cane or walker without the laserlight visual cue for 1 or 2 months at which point visit 2 occurred. All 26 subjects were treated as a single group with respect to the primary outcome measure regardless of whether or not they had a 1 month or 2 month baseline period, but randomization to these 2 baseline period durations was performed to allow a secondary analyses to address the possibility that subjects improve over time with use of the walking aid regardless of the addition of the laserlight visual cue (see "secondary outcome measures" below). At Visit 2, the subjects continued to use the same cane or walker, except that the laserlight feature was turned on and the patient was instructed on its use. This feature allowed a laserlight line to be projected across the floor just in front of the subjects' feet. Subjects were instructed not to look constantly at the visual cue, but to do so whenever they experienced freezing of gait, at which point they were instructed to attempt to "step over" the laserlight line. Visit 3 for all subjects occurred one month after Visit 2. Subjects took the cane or walker home with them and were instructed to use the visual cue whenever they ambulated throughout this 1 month period. Data on the frequency of falls were available for 23 of the subjects, who were asked to keep daily logs of falls and freezing throughout the study. For the purposes of this study, subjects were instructed to record an event as a "fall" if a stumble occurred in which the individual unintentionally comes to a lower level, defined as a hand or knee or buttocks unintentionally touching the ground or floor. In order to facilitate accuracy and completeness of information, each subject received a weekly phone call to recount study information.

2.3. Outcome measures and statistical analyses

2.3.1. Primary outcome measure

The primary outcome measure was the mean change in the total FOG Questionnaire (FOGQ) [21,22] score with versus without the laserlight visual cue. The FOGQ consists of 6 questions, each rated 0–4 based on severity or frequency, with 0 representing no symptoms or never occurring. Question 1 relates to speed and independence of gait. Question 2 relates to the impact of gait difficulties on daily activities. Question 3 assesses the frequency of FOG, and question 4 assesses the duration of FOG episodes. Question 5 relates to the duration of start hesitations and Question 6 to the duration of turning hesitations. Details and validation data have been published previously [21,22]. Baseline FOGQ scores were measured as the average of the weekly FOGQ scores obtained during the 1 or 2 month baseline period of use of the walker or cane without the laserlight visual cue. This average was compared to the average weekly FOGQ scores during the subsequent 1 month during which the subject used the laserlight visual cue.

2.3.2. Secondary outcome measures

All subjects received the same order of treatment, first using the cane and/or walker without the laserlight visual cue and then later having the laserlight visual cue added. This strategy was chosen to limit subject dropouts that might otherwise have occurred if subjects perceived benefits from the laserlight visual cue and subsequently were reluctant to forego use of that cue during the second phase of the study. To test whether or not subjects improve over time with use of the walking aid independent of use of the laserlight visual cue, a secondary analysis was planned which required subjects to be pseudo-randomized to either a one or two month baseline duration between visit 1 and visit 2, hereafter referred to as Group 1 and Group 2, respectively. At each site, consecutive enrolled subjects were alternately assigned to Group 1 or Group 2, and informed of their group assignment only after having signed the informed consent form. After the 1 or 2 month baseline period, all subjects in Groups 1 and 2 subsequently used the laserlight visual cue for 1 month between visits 2 and 3. Among the subjects who completed the study 14 were in Group 1 and 12 were in Group 2. We then analyzed the mean changes in the FOGQ score from the first month to the second month separately for these 2 groups. If improvement occurs over time with use of the walking aid independent of use of the laserlight visual cue, then Group 1 (which continued to use the walking aid without the visual cue during the 2nd month) should show the same degree of improvement in the 2nd month (compared to the 1st month) as seen for Group 2 subjects, who used the laserlight visual cue during the 2nd month.

An additional secondary outcome measure was the mean change from baseline for each of the 6 individual questions composing the FOGQ scores. The mean change from baseline in total FOGQ scores also was assessed separately at each of the 4 weeks following visit 2 to allow an assessment of the sustainability of the effect of adding the laserlight visual cue at visit 2. The impact of the laserlight visual cue on performance of a timed gait test (TGT) was assessed as at visits 2 and 3 as another secondary outcome measure. For the TGT, subjects were instructed to walk a set distance of 20 feet including walking through a doorway and turning, followed by returning 20 feet back to the starting position. For subjects who used a cane at times and walker at other times, the TGT was performed using whichever walking aid was used for the majority of the time, and this remained constant for all TGTs. At visits 2 and 3, subjects completed the TGT once with the laserlight visual cue and once without the visual cue (in random order). To better assess the impact of the laserlight visual cue on individual patients, the protocol was modified for the final 4 patients who completed the study at Beth Israel Deaconess Medical Center, such that they performed the TGT a minimum of 6 times, alternating testing with and without the laserlight visual cue. The decision to perform the repeated TGT on these final four subjects was made prior to any exposure of those subjects to the laserlight visual cue.

A final secondary outcome measure was the change from baseline in the frequency of falls. Subjects were recruited without regard to the frequency of falls.

2.4. Statistical analyses

Baseline scores are defined as the average of all of the weekly FOGQ assessments completed during the 1 or 2 month period when the subjects used the walking aid without the visual cue. Mean changes in FOGQ scores from baseline were analyzed by a 2-tailed paired t-test, or by an equivalent 2-tailed 1-sample t-test with a hypothesized mean of 0. These data passed a D'Agostino & Pearson omnibus normality test ($p = 0.69$). Effect size was calculated as the difference in the means (mean baseline FOG scores versus mean FOG scores during the month of use of the laserlight visual cue) divided by the average of the SDs. Changes from baseline in absolute fall frequencies were compared using a two-tailed Wilcoxon signed-rank test, which avoids assuming a Gaussian distribution. A planned subgroup analysis was to analyze only subjects with at least one fall during the study. Because our statistical plan included analysis of the percentage change in fall frequency, it was necessary also to exclude subjects if they suffered no falls during the baseline period or if they experienced no falls during the subsequent period, as a percentage change

Please cite this article in press as: Donovan S, et al., LaserLight cues for gait freezing in Parkinson's disease: An open-label study, Parkinsonism and Related Disorders (2010), doi:10.1016/j.parkreldis.2010.08.010

cannot be calculated in such cases. A two-tailed one-sample *t*-test was used when comparing percentage changes in fall frequencies, which tend to be normally distributed. The mean time to complete the TGT with versus without the laserlight visual cue was analyzed by a 2-tailed paired *t*-test. The times to complete the repeated TGT with or without the laserlight visual cue were compared separately for each subject with a 2-tailed paired *t*-test with a bonferroni correction for 4 comparisons, leading to a threshold for significance of $p = 0.0125$. The threshold for significance for the primary analysis and for each of the other secondary analyses was $p = 0.05$. Graphpad Prism software (version 4.0) was used for these analyses.

3. Results

3.1. Subject characteristics

Of the 26 subjects who completed the study, 21 were male and 5 were female. Mean age at study entry was 71.0 years (range: 58–92). Mean years since diagnosis of PD was 10.5 ± 1.0 (standard error) years (range: 4–25). Mean motor UPDRS subscore while on medications at study entry was 26.1 ± 2.4. Median Hoehn–Yahr score at study entry was 3 (range: 2–4).

3.2. Change in FOGQ scores

The primary outcome measure was the change from baseline associated with use of the laserlight visual cue (Fig. 1A). The laserlight visual cue was associated with an improvement (reduction) in FOGQ scores of 1.25 ± 0.48 (95% CI: 0.26–2.23; $p = 0.0152$, two-tailed paired *t*-test). This represents a mean improvement of 6.6% relative to the mean baseline FOGQ score of 18.8 ± 0.5. The effect size (Cohen's d) is 0.42. As a secondary analysis, we also analyzed the change from baseline separately for each of the 6 individual questions that comprise the FOGQ. There was significant improvement ($p < 0.05$, 1-sample *t*-test with hypothesized mean of 0), meaning a lower score, for questions 3 (which relates to the frequency of FOG) and 5 (which relates to the duration of start hesitations), with a borderline significant result ($p = 0.056$) for question 4 (relating to the duration of FOG). Analyzed individually, there were no significant changes from baseline for results to questions 1, 2, 4, and 6.

In order to evaluate the sustainability of the effect of the laserlight visual cue on FOG over time, we analyzed separately the change from baseline in total FOGQ scores at each of the 4 weeks following visit 2 (Fig. 1B). The mean change from baseline at week 1 was −1.51 ± 0.68 ($p = 0.036$; 1-sample *t*-test with hypothesized mean of 0). At week 2, the mean change was −1.15 ± 0.67 ($p = 0.099$). At week 3, the mean change was −1.73 ± 0.65 ($p = 0.013$). At week 4, the mean change was −0.53 ± 0.43 ($p = 0.263$). The mean change at week 4 was not significantly different from the mean change at week 1, 2, or 3 ($p > 0.10$ for each comparison; unpaired *t*-test).

As an additional secondary measure to address the possibility that FOGQ scores might improve over time as subjects gain experience with the new cane or walker, the changes in FOGQ scores from the first to second month were determined separately for subjects in Group 1 randomized to a 1 month baseline versus subjects in Group 2 with a 2 month baseline (Fig. 2). FOGQ scores significantly improved in the second month for Group 1 subjects, who used the laserlight visual cue during the second month, with a mean improvement of 2.00 ± 2.32; (95% CI: 3.34–0.66; $p = 0.007$ two-tailed paired *t*-test). In contrast, Group 2 subjects, who continued to use the cane or walker without the laserlight visual cue during the second month, showed no significant change in FOGQ scores during that second month. Clinical features were not significantly different for Groups 1 and 2 (see Table 1), including age (Group 1 mean of 70.4, and range 58–92; Group 2 mean of 71.7, and range of 60–85), years since diagnosis (Group 1 mean of 11.3, and range of 4–25; Group 2 mean of 9.5 and range of 4–19), and mean baseline FOGQ scores (Group 1 mean of 18.9, range 15.3–21.6; Group 2 mean of 18.6, range of 11.2–23.9).

3.3. Fall frequency

The impact of the laserlight visual cue on the frequency of falls was assessed as a secondary outcome measure (Fig. 3). Of the 23 subjects for whom falls data were available, 13 experienced no falls during either the baseline period, the subsequent study period, or both. The remaining 10 subjects each experienced 1 or more falls during both the baseline and subsequent study periods. A predetermined subgroup analysis of subjects experiencing 1 or more falls during both the baseline and subsequent study periods reveal a mean reduction in fall frequency from 3.23 ± 1.31 to 2.12 ± 0.92 falls per week ($p = 0.02$, two-tailed Wilcoxan signed-rank test). The percentage reduction in fall frequencies associated with using the laserlight for this subset of subjects was 39.5 ± 9.3% (95% CI: 18.4–60.6%; $p = 0.002$ two-tailed

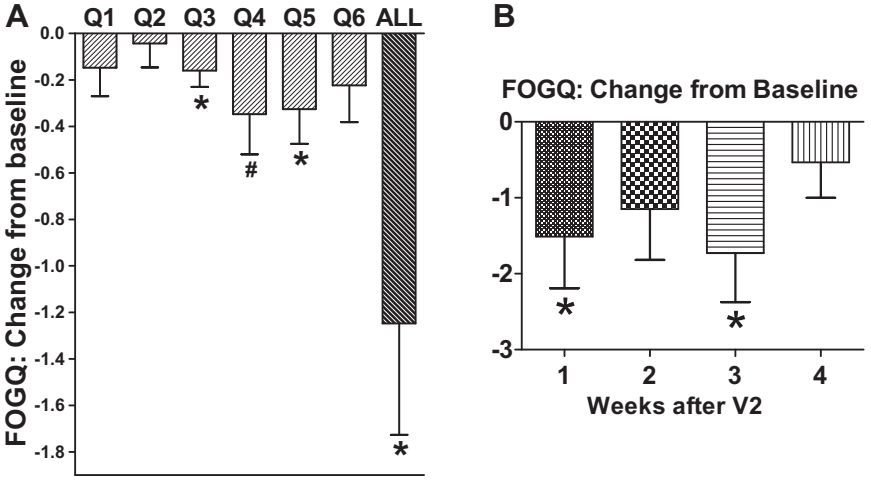

Fig. 1. A). Mean changes from baseline ± SE for each of the 6 questions that comprise the FOGQ, as well as the mean total change in the FOG score (ALL). Baseline scores are defined as the average of all of the weekly FOGQ assessments completed during the 1 or 2 month period when the subjects used the walking aid without the visual cue. The mean change is calculated by subtracting these baseline scores from the mean of the weekly FOGQ scores completed during the 1-month period when subjects used the laserlight visual cue. Negative results reflect lower (improved) scores associated with use of the visual cue. B). Mean changes from baseline ± SE in total FOGQ scores at each of the 4 weeks following visit 2. *$p < 0.05$, and $p = 0.056$ (two-tailed one-sample *t*-test with hypothesized mean of 0).

Please cite this article in press as: Donovan S, et al., LaserLight cues for gait freezing in Parkinson's disease: An open-label study, Parkinsonism and Related Disorders (2010), doi:10.1016/j.parkreldis.2010.08.010

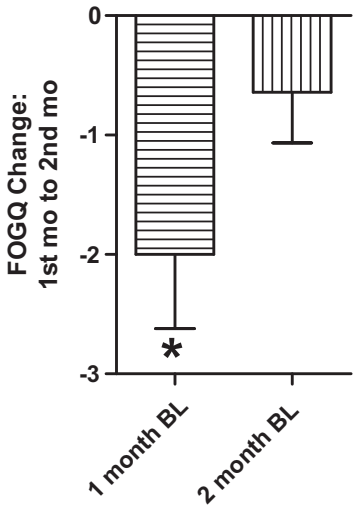

Fig. 2. Mean changes from baseline ± SE from month 1 to month 2 for subjects randomized to a 1-month baseline period (and thus used the laserlight visual cue during the 2nd month), and for subjects randomized to a 2 month baseline period (who continued to use the cane or walker without the laserlight visual cue during the 2nd month). "1-month BL" and "2 month BL" represent subjects randomized to 1 month (Group 1) or 2 months (Group 2) respectively between visit 1 and visit 2. BL = baseline. $^{*}p < 0.05$ (two-tailed one-sample *t*-test with hypothesized mean of 0).

one-sample *t*-test with a hypothesized mean of 0). The mean magnitude of improvement from baseline in the FOGQ scores for this subset of 10 subjects with frequent falls was (−1.36 ± 0.88), which was not significantly different from the mean for the overall group.

3.4. Timed gait test (TGT)

The time required to complete the timed gait test (TGT) did not significantly change in association with the laserlight visual cue when averaged across the entire group, with an average TGT time of 68.5 ± 26.2 s without the laserlight compared to an average of 57.6 ± 23.3 s with the laserlight visual cue ($p = 0.16$, two-tailed paired *t*-test). However, among the 4 subjects who underwent repeated testing of the TGT, one showed a mean improvement of 50% ± 11.7% (95% CI: 23.9–76.1%) in TGT performance with use of the laserlight visual cue (Fig. 4; $p = 0.005$; two-tailed paired *t*-test). There was no significant improvement for the other 3 subjects who underwent repeated testing for the TGT.

4. Discussion

These results demonstrate efficacy of a laserlight visual cue in overcoming FOG in PD patients, as measured by a modest but statistically significant reduction in FOGQ scores, and by a substantial reduction in the frequency of falls in PD patients with FOG who suffer frequent falls. A strength of this study is the use of a reliable and validated measure of FOG in PD in the outpatient setting (the FOGQ) [21,22]. As in the study of Kompoliti et al. [15], we saw no benefit in overall in performance with an in-office TGT. Although FOG often is not responsive to levodopa medications, it remains possible that we may have observed greater FOG, and hence had greater power to detect improvement with the visual cue, if we had conducted the TGT with patients in the "off" state. Still, we were able to document a significant improvement in one of 4 patients who underwent repeated TGT analyses, which remained statistically significant after adjustment for multiple comparisons. However, the lack of similar improvement in the other 3 subjects who underwent the repeated TGT indicates that this degree of improvement may be uncommon. The FOGQ score reflects the severity of FOG in every day life and may be a more responsive and clinically relevant outcome measure rather than an assessment of FOG in the doctor's office.

The significant reduction in frequency of falls seen in this study was surprising as patients with FOG were included in the study without regard to fall frequency, and only 10 subjects

Table 1
Baseline characteristics and change from baseline in FOGQ scores.

					Change from baseline.						
	AGE	GENDER	YEARS since Dx	BASELINE FOGQ	Q1	Q2	Q3	Q4	Q5	Q6	TOTAL
Group 1.	92	M	10	19	−0.33	0.48	−0.83	−1.31	−1.05	0.48	−2.57
	62	M	10	21.17	−0.37	0.00	−0.07	−0.23	−0.47	−0.03	−1.17
	77	M	6	19.17	0.17	0.00	0.20	0.00	−0.70	−0.43	−0.77
	75	M	4	20.4	0.00	0.00	0.20	−0.80	−0.80	−0.40	−1.80
	58	F	10	19.6	0.09	−0.51	−0.02	0.51	0.18	−1.07	−0.82
	62	M	20	18.33	0.00	−0.33	0.00	0.50	−0.33	0.00	−0.17
	66	M	8	18.8	−1.00	0.20	−0.80	−1.00	−1.40	−1.40	−5.40
	68	M	13	19	0.40	0.05	−0.75	−0.05	0.15	−0.30	−0.50
	71	M	25	17.33	−0.53	0.43	0.00	−0.40	−0.90	−0.27	−1.67
	66	M	12	15.33	0.33	−0.63	0.17	1.00	1.00	0.00	1.87
	78	M	6	20.2	0.00	−0.53	−0.33	−1.47	−2.73	−0.47	−5.53
	78	M	12	21.6	−1.65	−1.70	−0.75	−2.80	−0.65	−0.80	−8.35
	65	M	15	16	0.00	0.00	0.00	−0.83	−0.33	−0.33	−1.50
	67	M	9	18.2	0.00	−0.25	−0.15	−0.95	−0.90	−1.95	−4.20
Group 2.	66	M	12	17.67	0.00	−0.16	−0.47	0.69	0.29	−0.56	−0.21
	63	M	9	16.55	0.00	−0.38	−0.18	−0.44	−0.49	0.32	−1.17
	71	M	15	21.71	0.00	−0.36	0.00	−0.75	−0.18	2.73	1.45
	85	F	5	18.73	0.00	0.87	0.27	−0.27	−0.33	−0.63	−0.09
	79	M	9	19.38	0.00	0.21	−0.38	0.33	0.13	0.10	0.39
	64	M	6	21	0.10	0.50	0.30	0.90	0.60	0.10	2.50
	73	M	6	11.2	0.50	0.10	0.40	0.30	0.60	−0.10	1.80
	81	M	4	17	−2.20	0.88	0.00	0.38	−0.35	0.00	−1.30
	75	M	8	23.89	0.78	0.13	0.00	−1.60	−0.60	−0.73	−2.01
	76	F	19	15.25	−0.20	0.30	−0.20	0.20	0.40	−0.07	0.43
	67	F	9	20	0.07	−0.43	−0.57	−0.93	0.50	0.00	−1.36
	60	M	12	20.9	0.00	0.00	−0.20	0.00	−0.10	0.00	−0.30

Please cite this article in press as: Donovan S, et al., LaserLight cues for gait freezing in Parkinson's disease: An open-label study, Parkinsonism and Related Disorders (2010), doi:10.1016/j.parkreldis.2010.08.010

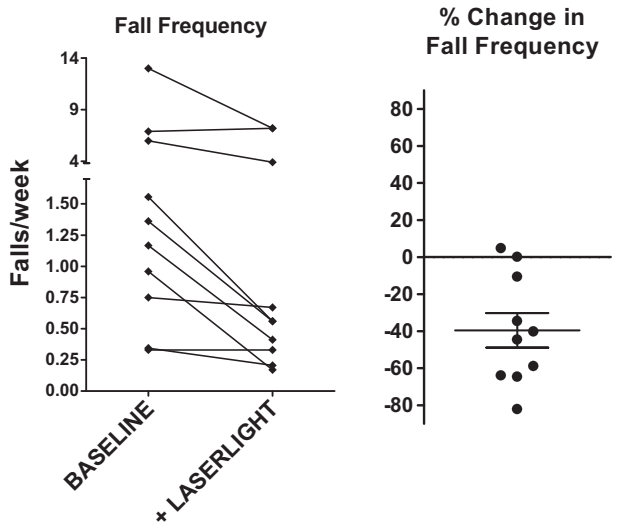

Fig. 3. Change in frequency of falls per week at baseline (without a visual cue) compared to the 1 month with the laserlight visual cue (+laserlight) for the 10 subjects who experienced 1 or more during the baseline period and also during the period of use of the laserlight visual cue. The right hand histogram shows the percentage decrease in fall frequency for each subject ($p = 0.002$; two-tailed one-sample t-test with a hypothesized mean of 0).

suffered 1 or more falls during both the baseline and the intervention phases of the study. Yet use of the laserlight visual cue was associated with a nearly 40% reduction in the fall frequency (mean number of falls per week) for these 10 subjects ($p = 0.002$). This analysis must be interpreted with caution, as it included only 10 subjects, and it does not address the question of whether or not a visual cue can help to reduce falls in patients with less frequent falls. Still, this finding is intriguing as falls are an important cause of morbidity in PD patients [2], and FOG is a common source of falls in PD patients [3–7].

It is important to consider the limitations of this study. One limitation is the inability to conduct the study in a blinded manner. Expectation of benefit (placebo effect) may have influenced performance, or may have biased recall on questions regarding FOG and falls. Another limitation is the relatively short duration of one month of use of the laserlight visual cue. It is possible that patients will habituate to the visual cue after longer periods of use, potentially limiting its long-term efficacy. An additional limitation is that subjects were analyzed during the "on" state. For some subjects, FOG might have been more severe in the "off" state, and an impact of the laserlight visual cue on "off" state freezing or falls would have been missed. FOG may be associated with cognitive impairment [6,23], but because subjects with dementia were excluded from this study, the results may not apply to PD patients with substantial cognitive impairment. All subjects used the cane and/or walker without the laserlight visual cue first and subsequently added the laserlight visual cue. However, Group 1 subjects showed a significant improvement during the second month when the laserlight was added ($p = 0.007$) whereas Group 2 subjects showed no significant improvement in the second month during which they continued to use the walking aid without the laserlight visual cue. These data support the interpretation that the benefit associated with the laserlight visual cue is not simply a reflection of improvement over time but instead reflects an impact of use of the laserlight visual cue. An additional concern is that the benefits of the visual cue may fade over time. Arguing against this, we identified a trend towards improvement at each of the 4 weeks following visit 2, with a statistically significant improvement at weeks 1 and 3. Although the magnitude of improvement appears less at week 4, the change in FOGQ from baseline at week 4 is not significantly different from the change at weeks 1, 2, or 3. However, although these data do not provide clear evidence for a loss of benefit over time, longer-term and larger studies may be necessary to more definitively address this possibility.

The individual questions that comprise the FOGQ include questions relating to the frequency and duration of FOG episodes. For example, question 3 of the FOGQ addresses the *frequency* of FOG episodes, whereas questions 4, 5, and 6 each address the *duration* of FOG episodes. As expected, the improvement in scores for question 5 and borderline improvement for question 4 is consistent with the *a priori* notion that the laserlight visual cue would help patients to more quickly overcome a FOG episode when it occurs. However, the improvement in question 3 suggests that the laserlight visual cue also may reduce the frequency of FOG episodes. The significance of these changes in individual questions must be interpreted with caution as this was a secondary analysis without correction for multiple comparisons.

FOG is common in PD and is associated with a reduced quality of life and an increased risk of falls. FOG typically is resistant to dopaminergic therapy and does not improve with a standard wheeled walker. Thus there is a strong clinical need for more effective strategies for overcoming FOG in PD. The current study demonstrates that adding a laserlight visual cue to a cane or walker can lead to a modest reduction in FOG and may substantially reduce the frequency of falls in PD patients with FOG and falls.

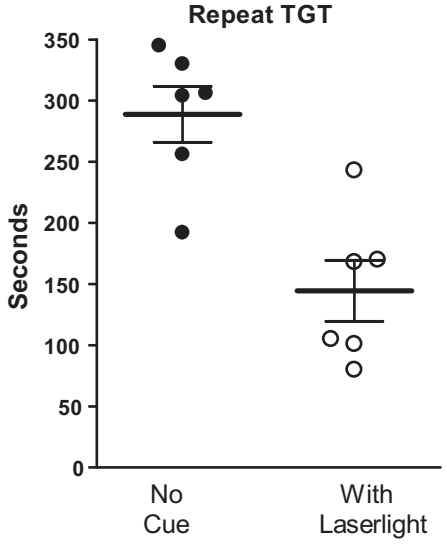

Fig. 4. Results of the repeated timed gait test (TGT) for a subject who underwent the test 12 times alternating with and without the laserlight visual cue (6 times each); $p = 0.005$ two-tailed paired t-test.

5. Financial disclosures

None of the authors have any financial relationships to disclose related to research covered in the article. Full financial disclosures for the previous 12 months are listed below:

C. Lim reports no disclosures
S. Donovan reports no disclosures
Dr. Diaz reports no disclosures
Dr. Browner reports no disclosures
P. Rose reports no disclosures
Dr. Sudarsky reports no disclosures

Please cite this article in press as: Donovan S, et al., LaserLight cues for gait freezing in Parkinson's disease: An open-label study, Parkinsonism and Related Disorders (2010), doi:10.1016/j.parkreldis.2010.08.010

Dr. Tarsy has received unrestricted education grants from Allergan Pharmaceuticals, Medtronic, Boehringer Ingelheim, Valeant, Teva Neurosciences, and Glaxo Smith Kline. Dr. Tarsy has received a lecture honorarium from UCB Pharma, and research grants from Solvay, the Parkinson Study Group, and the Michael J. Fox Foundation.

Dr. Fahn has served on science advisory boards for IMPAX Pharma, Boehringer Ingelheim, Vernalis, Intec Pharma, Merz Pharma, RJG Foundation, and Oxford Biomedica. Dr. Fahn has received research grants from the Smart Family Foundation (no salary support). Dr. Fahn directs the Columbia Parkinson's Disease Research Center and Fellowship Training Program that receives support from the Parkinson's Disease Foundation (no salary support). Dr. Fahn received a grant from the US Department of Defense's Telemedicine and Advanced Technology Research Center (TATRC) for the World Parkinson Congress 2010 (no salary support).

Dr. Simon has received consulting income from the Gerson Lehrman Group, MediaCorp, Decision Resources, and Easton Associates. Dr. Simon has received one-time consulting fees from Link Medicine and a lecture honorarium from UCB Pharma. Dr. Simon has received honoraria for service on National Institutes of Health (NIH) and Michael J. Fox Foundation (MJFF) grant review committees, from lectures given to St. Lukes and Carney Caritas Hospitals, and for a Harvard sponsored CME course. Dr. Simon has received a small honorarium for a one-time consultation for WeMOVE. Dr. Simon has received research grant support from the National Institutes of Neurological Disorders and Stroke (NINDS), American Federation for Aging Research (AFAR), National Parkinson Foundation (NPF), and the MJFF.

Acknowledgements

This work was funded by a grant to Dr. Simon from the National Parkinson Foundation. The U-Step Walking Stabilizers and Lasercanes used for this study were provided by In-Step Mobility Products Corp. (www.ustep.com). None of the authors have any financial ties to In-Step Mobility Products. Other than providing the Walking Stabilizers and lasercanes, In-Step Mobility Products had no involvement in the conduct of this study, data interpretation, or preparation and publication of this manuscript.

References

[1] Nieuwboer A, Feys P, de Weerdt W, Dom R. Is using a cue the clue to the treatment of freezing in Parkinson's disease? Physiother Res Int 1997;2:125–32. discussion 133–134.

[2] Wielinski CL, Erickson-Davis C, Wichmann R, Walde-Douglas M, Parashos SA. Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. Mov Disord 2005;20:410–5.

[3] Grimbergen YA, Munneke M, Bloem BR. Falls in Parkinson's disease. Curr Opin Neurol 2004;17:405–15.

[4] Gray P, Hildebrand K. Fall risk factors in Parkinson's disease. J Neurosci Nurs 2000;32:222–8.

[5] Bloem BR, Hausdorff JM, Visser JE, Giladi N. Falls and freezing of gait in Parkinson's disease: a review of two interconnected, episodic phenomena. Mov Disord 2004;19:871–84.

[6] Latt MD, Lord SR, Morris JG, Fung VS. Clinical and physiological assessments for elucidating falls risk in Parkinson's disease. Mov Disord 2009;24:1280–9.

[7] Robinson K, Dennison A, Roalf D, Noorigian J, Cianci H, Bunting-Perry L, et al. Falling risk factors in Parkinson's disease. NeuroRehabilitation 2005;20:169–82.

[8] Giladi N, McMahon D, Przedborski S, Flaster E, Guillory S, Kostic V, et al. Motor blocks in Parkinson's disease. Neurology 1992;42:333–9.

[9] Lamberti P, Armenise S, Castaldo V, de Mari M, Iliceto G, Tronci P, et al. Freezing gait in Parkinson's disease. Eur Neurol 1997;38:297–301.

[10] Cubo E, Moore CG, Leurgans S, Goetz CG. Wheeled and standard walkers in Parkinson's disease patients with gait freezing. Parkinsonism Relat Disord 2003;10:9–14.

[11] Morris ME, Iansek R, Galna B. Gait festination and freezing in Parkinson's disease: pathogenesis and rehabilitation. Mov Disord 2008;23(Suppl. 2):S451–60.

[12] Nieuwboer A. Cueing for freezing of gait in patients with Parkinson's disease: a rehabilitation perspective. Mov Disord 2008;23(Suppl. 2):S475–81.

[13] Morris ME, Iansek R, Kirkwood B. A randomized controlled trial of movement strategies compared with exercise for people with Parkinson's disease. Mov Disord 2009;24:64–71.

[14] Giladi N. Freezing of gait. Clinical overview. Adv Neurol 2001;87:191–7.

[15] Kompoliti K, Goetz CG, Leurgans S, Morrissey M, Siegel IM. "On" freezing in Parkinson's disease: resistance to visual cue walking devices. Mov Disord 2000;15:309–12.

[16] Frazzitta G, Maestri R, Uccellini D, Bertotti G, Abelli P. Rehabilitation treatment of gait in patients with Parkinson's disease with freezing: a comparison between two physical therapy protocols using visual and auditory cues with or without treadmill training. Mov Disord 2009;24:1139–43.

[17] Jiang Y, Norman KE. Effects of visual and auditory cues on gait initiation in people with Parkinson's disease. Clin Rehabil 2006;20:36–45.

[18] Ferrarin M, Brambilla M, Garavello L, Di Candia A, Pedotti A, Rabuffetti M. Microprocessor-controlled optical stimulating device to improve the gait of patients with Parkinson's disease. Med Biol Eng Comput 2004;42:328–32.

[19] McAuley J, Daly P, Curtis C. A preliminary investigation of a novel design of visual cue glasses that aid gait in Parkinson's disease. Clin Rehabil 2009;23:687–95.

[20] Nieuwboer A, Kwakkel G, Rochester L, Jones D, van Wegen E, Willems AM, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. J Neurol Neurosurg Psychiatry 2007;78:134–40.

[21] Giladi N, Shabtai H, Simon ES, Biran S, Tal J, Korczyn AD. Construction of freezing of gait questionnaire for patients with Parkinsonism. Parkinsonism Relat Disord 2000;6:165–70.

[22] Giladi N, Tal J, Azulay T, Rascol O, Brooks DJ, Melamed E, et al. Validation of the freezing of gait questionnaire in patients with Parkinson's disease. Mov Disord 2009;24:655–61.

[23] Giladi N, Huber-Mahlin V, Herman T, Hausdorff JM. Freezing of gait in older adults with high level gait disorders: association with impaired executive function. J Neural Transm 2007;114:1349–53.