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The laser shoes

A new ambulatory device to alleviate freezing of gait in Parkinson disease

Claudia Barthel, MSc, Jorik Nonnekes, MD, PhD, Milou van Helvert, MSc, Renée Haan, MSc, Arno Janssen, PhD, Arnaud Delval, MD, PhD, Vivian Weerdesteyn, PhD, Bettina Debû, PhD, Richard van Wezel, PhD, Bastiaan R. Bloem, MD, PhD, and Murielle U. Ferraye, PhD

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Correspondence
Dr. Ferraye
m.u.ferraye@utwente.nl
or
murielle.ferraye@gmail.com

Abstract

Objective

To assess, in a cross-sectional study, the feasibility and immediate efficacy of laser shoes, a new ambulatory visual cueing device with practical applicability for use in daily life, on freezing of gait (FOG) and gait measures in Parkinson disease (PD).

Methods

We tested 21 patients with PD and FOG, both "off" and "on" medication. In a controlled gait laboratory, we measured the number of FOG episodes and the percent time frozen occurring during a standardized walking protocol that included FOG provoking circumstances. Participants performed 10 trials with and 10 trials without cueing. FOG was assessed using offline video analysis by an independent rater. Gait measures were recorded in between FOG episodes with the use of accelerometry.

Results

Cueing using laser shoes was associated with a significant reduction in the number of FOG episodes, both "off" (45.9%) and "on" (37.7%) medication. Moreover, laser shoes significantly reduced the percent time frozen by 56.5% (95% confidence interval [CI] 32.5–85.8; $p = 0.004$) when "off" medication. The reduction while "on" medication was slightly smaller (51.4%, 95% CI −41.8 to 91.5; $p = 0.075$). These effects were paralleled by patients' positive subjective experience on laser shoes' efficacy. There were no clinically meaningful changes in the gait measures.

Conclusions

These findings demonstrate the immediate efficacy of laser shoes in a controlled gait laboratory, and offer a promising intervention with potential to deliver in-home cueing for patients with FOG.

Classification of evidence

This study provides Class III evidence that for patients with PD, laser shoes significantly reduce FOG severity (both number and duration of FOG episodes).

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From the Departments of Neurology (C.B., M.v.H., R.H., B.R.B., M.U.F.), Rehabilitation (J.N., V.W.), and Otorhinolaryngology (A.J.), Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, and Department of Biophysics (R.v.W.), Radboud University, Nijmegen, the Netherlands; Department of Clinical Neurophysiology (A. D.), Lille University Medical Center, France; Sint Maartenskliniek Research, Development & Education (V.W.), Nijmegen, the Netherlands; Grenoble Alpes University (B.D.); Grenoble Institute of Neurosciences (B.D.), INSERM U1216, France; and Biomedical Signal and Systems Group (J.N., R.v.W., M.U.F.), MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, the Netherlands.

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Glossary

CI = confidence interval; **FAB** = Frontal Assessment Battery; **FOG** = freezing of gait; **GABS** = Gait and Balance Questionnaire; **MDS-UPDRS Part III** = Movement Disorder Society–Unified Parkinson's Disease Rating Scale motor part III; **NFOGQ** = New Freezing of Gait Questionnaire; **PD** = Parkinson disease; **PTF** = percent time frozen; **VCD** = visual cueing devices.

Freezing of gait (FOG) is a common episodic symptom in Parkinson disease (PD).[1] Associated gait abnormalities affect step scaling, step symmetry, and step time consistency just prior and in-between FOG episodes.[2–4] FOG increases the risk of falls and related injuries, severely compromising patients' quality of life.[1,5,6] FOG remains a great therapeutic challenge in clinical practice.[7] Nonpharmaceutical approaches appear helpful to complement dopaminergic treatment effects.[8]

External cueing encompasses a wide range of means to increase perceptual sensations by providing an explicit temporal or spatial motor target.[9] Visual cueing might be the preferred cueing modality for FOG.[10] Stepping over transverse lines regularly drawn on the floor has an immediate and powerful effect. However, translating this trick into efficient visual cueing devices (VCD) proves difficult.[11–16]

Recently, we developed laser shoes as a new VCD able to reduce FOG (figure 1),[17] with 2 major advantages. First, it represents a closed-loop VCD, likely more efficient than open-loop devices.[18] Closed-loop VCD provide individuals with sensory signals tuned to their own motion and stepping frequency, while assuring constant regularity.[19,20] Several other devices, manually controlled, did not feature this requirement, resulting in disappointing outcomes.[11,15,21] Second, laser shoes have the potential to be used in daily life. Until now, most existing devices lacked ease of application.[22,23] While theoretically attractive, implementing virtual reality glasses in daily life poses great challenges on the patients' compliance in wearing such cumbersome devices.[19,20] For true clinical utility of any ambulatory intervention that can assist patients, regardless of where they are, it is crucial to deliver cueing continuously and automatically in a user-friendly manner, without need to perform additional movements to obtain cueing.

We aimed to objectively test the immediate efficacy of laser shoes on FOG in the laboratory. We hypothesized that laser shoes would deliver efficient immediate visual cueing able to reduce FOG.

Methods

Participants

We included 21 patients with PD according to the UK Brain Bank Criteria.[24] All patients had a recent history of regular and disabling FOG, defined as presence of FOG several times a day in the last month (score of 1 "Yes" on question 1: "Have you experienced FOG in the past month?" and score of 3 "Very often, more than once a day" on question 2: "How often do you experience FOG?" of the New Freezing of Gait Questionnaire [NFOGQ]).[25] Exclusion criteria were other neurologic disorders, uncorrected visual impairment, or physical inability. The sample size is based on comparable experiments.[11]

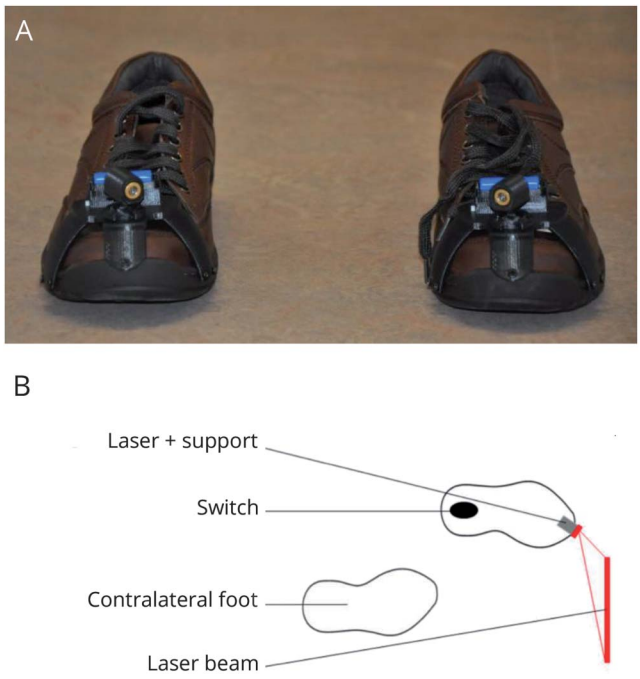
Standard protocol approvals, registrations, and patient consents

The study was approved by the local ethics committee. All participants gave written informed consent prior to participation. The experiment was performed in accordance with the Declaration of Helsinki and with local ethical guidelines.

Laser shoes

We described the basic laser shoes concept previously.[17] Briefly, laser shoes incorporate a transverse line-generating

Figure 1 Photograph and working mechanism of laser shoes



(A) The photograph shows the men's model of laser shoes. (B) The laser is activated during heel strike by a switch located under the sole of the contralateral foot, and appears orthogonally to the contralateral foot.

laser attached to a normal shoe (figure 1A). The laser is activated during heel strike by a switch located under the sole of the contralateral foot. The laser line appears orthogonally in front of the contralateral foot that is about to enter the swing phase. When the body weight is removed from the heel, the laser is deactivated. This cycle repeats itself step after step, delivering the cues alternately to each foot. This way, the cues are tuned exactly to the patient's motion.

Assessment procedure

The study consisted of 2 laboratory assessments, "off" and "on" medication, on 2 separate mornings. Their order was randomized and counterbalanced across patients. The "off" medication assessment took place at least 8 hours following withdrawal of dopaminergic medication.[26] For the "on" medication condition, patients took their own first morning medication upon arrival at the laboratory. Breakfast was provided and assessments were conducted when participants reported a subjectively good "on" state, about 45 minutes after medication intake. Both laboratory assessments included questionnaires and clinical measures, and a gait test to record the efficacy of laser shoes using a combination of objective, clinical, and subjective measures (see below).

Clinical characteristics

On both days, global motor and executive functioning were assessed using the Movement Disorder Society–Unified Parkinson's Disease Rating Scale motor part III (MDS-UPDRS Part III)[27] and the Frontal Assessment Battery (FAB).[28] Quality of life was determined using the 39-item Parkinson's Disease Questionnaire[29] and subjective severity of FOG using the NFOGQ.[25]

FOG assessment

On both days, isolated FOG-provoking tasks were used to objectify FOG, including stepping in place for 30 seconds, 3 rapid full turns from standstill on the spot in both directions, and taking short, rapid steps over a 10-meter course.[30] These FOG triggers were not included in the gait protocol because they naturally interfere with the adequate use of cues. Statistical analyses were restricted to patients in whom FOG could be objectified, either during the gait protocol (described below) or during these FOG-provoking tasks. Participants wore a safety harness.[30]

Experimental design

The efficacy of laser shoes was assessed using a gait protocol with 5 trials: (1) walking back and forth over 10 meters (undisturbed trial); (2) walking back and forth over 10 meters while counting down from 100 in steps of 7 or 3 (dual-task); (3) turning on command while walking, including 180° and 360° right and left turns (total of 4 turns); (4) walking to pick up a cone at 7 meters and then back carrying the cone; (5) walking around obstacles placed on the walkway according to a predefined route. Patients wore the laser shoes continuously. A switch allowed us to turn the visual cueing "off" or "on." Patients performed all trials with and without cueing. The order of the 10 trials was randomized. For trials with cueing, participants were instructed to use the cue whenever necessary, e.g., when experiencing FOG. They could either "step in the direction of" or "step over" the laser beam, as most convenient. To minimize practice effects, participants received 5–10 minutes to get familiar with the laser shoes prior to testing. The distance between the laser beam and the shoe was adapted to each patient's needs, i.e., step length.

Outcomes

Objective measures

Patient performance on the gait protocol was videotaped for offline rating of FOG by an independent rater (J.N.) blinded for medication condition but not to the laser shoes condition (Class III evidence for all measures). For each patient and for each of the 2 cueing conditions, we computed the percent time frozen (PTF) (Class III evidence), our primary outcome measure and gold standard for FOG assessment, as the cumulative time spent frozen over all performed trials, as a function of total walking duration.[31] The total number of FOG episodes was also recorded. In addition, during walking, a triaxial accelerometer sensor (MoveTest, McRoberts, the Hague, the Netherlands) was placed on the participant's lower back to objectively measure spatiotemporal gait measures. For this analysis, gait segments that included FOG episodes, voluntary stops (e.g., to talk), and turns during walking were excluded from analyses, as done previously.[2] This allowed distinguishing the effects of cueing on FOG per se from general effects of cueing on gait measures. The sensor had a sampling frequency of 100 Hz and was synchronized offline with the video recording using ELAN (Max Planck Institute for Psycholinguistics; tla.mpi.nl/tools/tla-tools/elan/). Velocity (m/s), step length (meters), cadence (steps/min), step time asymmetry (relative difference between left and right step duration), step time variability (or coefficient of variation = SD×100), and double limb support were calculated.

Clinical and subjective measures (Class III evidence)

The Gait and Balance Questionnaire (GABS) is a validated questionnaire in PD.[32] However, rather than using the entire scale, we used a modified version that only extracted the relevant gait items, considering gait and FOG separately. The composite gait score was computed from the sum of items 3.10, "Gait," from the MDS-UPDRS Part III, and items 16, "Half-turn while walking," 17, "Full turn," and 24, "Modified Performance Oriented Gait Assessment Scale" from the GABS (maximum score of 26). The composite FOG score was computed as the sum of items 3.11, "Freezing of gait" from the MDS-UPDRS Part III, and item 22, "Test freezing" from the GABS (maximum score of 9).

Following completion of day 2, a 7-point Likert scale was used to investigate the subjective experience of patients on laser shoes' efficacy (from 1 = large improvement to 7 = large

worsening). Finally, patients were asked about their potential interest (yes, no, maybe) in acquiring laser shoes.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 20 (SPSS Inc., Chicago, IL). Medication ("off" vs "on") and cueing (with-cueing vs without-cueing) were processed as within-subject factors. Kolmogorov-Smirnov analysis tests evaluated data distributions. In case of abnormal distributions, we used the nonparametric Friedman tests. Post hoc Wilcoxon signed-ranked tests were performed focusing on the comparison between the with-cueing and without-cueing conditions, both "off" and "on" medication. This concerned all dependent variables except for the composite gait score, velocity, and step time asymmetry, the distributions of which were normal and homogeneous (Levene test p value >0.05). These latter variables were analyzed using repeated-measures analyses of variance and post hoc Tukey honestly significant different test. The level of significance was set at 0.05 for all tests. We also provide the percentage improvement and confidence intervals (CIs) for the PTF, our primary outcome measure. These were calculated based on the individual percentage improvements, excluding those patients who did not show FOG during the gait protocol. Given the interplay between FOG and executive functioning, we performed Pearson correlation tests between the difference in time frozen with-cueing and without-cueing "off" medication and the FAB score. We further tested whether different baseline clinical measures could predict the therapeutic response. We considered the patients' age, disease duration, MDS-UPDRS III total score "off" and "on" medication, and NFOGQ score as potential predictors, and performed Pearson correlation tests between these measures and the absolute difference in PTF "off" medication.

Results

Participant characteristics

One patient was excluded due to inability to properly see the laser. Of the remaining 20 participants, 17 demonstrated FOG during both the FOG provocative tasks and the gait protocol, 2 participants demonstrated FOG during the provocative tasks only, while in 1 patient, FOG remained nonobjectified. The latter "subjective" freezer was excluded from analyses because the intervention effect depended on the occurrence of FOG. Identical statistical results were observed for the 19 objective freezers and the 17 patients who froze both during the gait protocol and during the FOG provocative tasks. We therefore report the results for the 19 patients. Their clinical characteristics are reported in table 1.

Table 1 Participant characteristics (n = 19)

	Mean ± SD or n (%)
Age, y	68.68 ± 11.15
Men	16 (84.2)
Body mass index	25.60 ± 3.51
Disease duration, y	11.21 ± 6.68
Hoehn & Yahr score	
"On" medication	2.21 ± 0.42
"Off" medication	2.37 ± 0.60
NFOGQ	
NFOGQ part 2	16.21 ± 1.78
NFOGQ part 3	7.26 ± 2.38
NFOGQ total score	23.16 ± 2.85
MDS-UPDRS III total score	
"On" medication	36.21 ± 12.80
"Off" medication	45.68 ± 10.30
FAB total score	
"On" medication	15.53 ± 2.82
"Off" medication	15.32 ± 1.92
PDQ-39	
PDQ-39 mobility subscore	60.59 ± 14.58
PDQ-39 ADL subscore	52.74 ± 22.14
PDQ-39 total score	42.46 ± 12.88

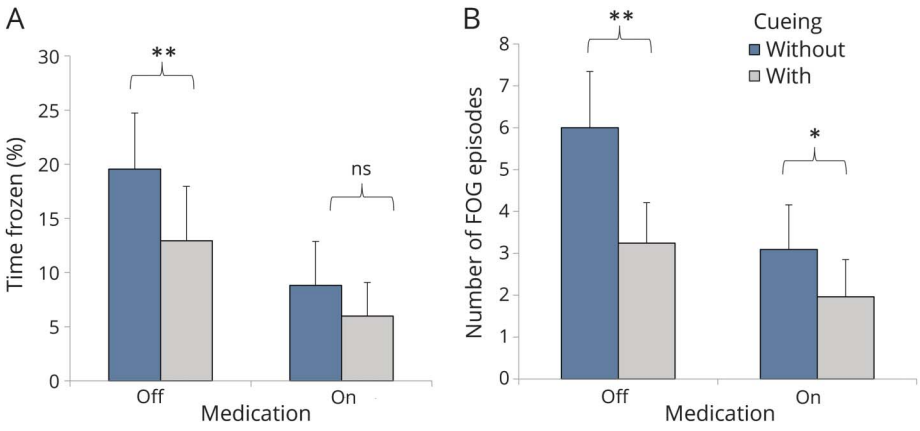
Abbreviations: FAB = Frontal Assessment Battery (score/18); MDS-UPDRS = Movement Disorder Society–Unified Parkinson's Disease Rating Scale (score/132); NFOGQ = New Freezing of Gait Questionnaire (score/29); PDQ-39 = 39-item Parkinson's Disease Questionnaire.
For MDS-UPDRS, PDQ-39, and NFOGQ, higher scores indicate worse functioning. For FAB, lower scores indicate worse functioning.

Percent time frozen and number of FOG episodes

Friedman tests were significant both for the PTF ($\chi^2 = 11.64$, $p = 0.009$) and for the number of FOG episodes ($\chi^2 = 15.12$, $p = 0.002$). Cueing was associated with a significant reduction in the PTF "off" medication (without-cueing: 19.6% ± 5.2%; with-cueing: 12.9% ± 5.0%, percentage improvement 56.5%, 95% CI 32.5–85.8; $p = 0.004$). "On" medication, the reduction in the PTF fell short of significance (without-cueing: 8.8% ± 4.1%; with-cueing: 6.0% ± 3.1%, percentage improvement 51.4%, 95% CI −41.8 to 91.5; $p = 0.075$) (figure 2A). There was no significant correlation between the difference in PTF with-cueing and without-cueing and the FAB score, both "off" ($p = 0.084$) and "on" medication ($p = 0.21$), nor was there any significant correlation between baseline clinical measures and amount of improvement offered by laser shoes "off" medication (age, $p = 0.35$; disease duration, $p = 0.43$; MDS-UPDRS III total score "off" medication, $p = 0.38$; MDRS-UDPRS III total score "on" medication, $p = 0.63$; NFOGQ, $p = 0.12$).

Cueing was associated with a significant reduction in number of FOG episodes, both "off" (without-cueing: 6.0 ± 1.3; with-cueing: 3.3 ± 1.0, $p = 0.007$) and "on" medication (without-cueing: 3.1 ± 1.1; with-cueing: 2.0 ± 0.9, $p = 0.028$) (figure

Figure 2 Objective outcomes from the gait protocol



(A) Percent time frozen with-cueing and without-cueing, both "off" and "on" medication. (B) Number of freezing of gait (FOG) episodes with-cueing and without-cueing, both "off" and "on" medication. **Significance at $p < 0.001$; *significance at $p < 0.05$; ns = nonsignificant.

2B). "Off" medication, 16 out of 19 patients experienced a total of 114 FOG episodes without-cueing, vs 62 in 12 patients with-cueing (45.9% reduction with-cueing). "On" medication, 11 patients experienced 61 FOG episodes without-cueing, vs 38 in 8 patients with-cueing (37.7% reduction with-cueing).

Gait measures

The results are shown in table 2. There was a slight increase in step length with-cueing compared to without-cueing when "off" medication but this difference was not significant. "On" medication, cueing resulted in a small increase in double limb support time. No other variables showed significant differences.

Composite FOG and composite gait score

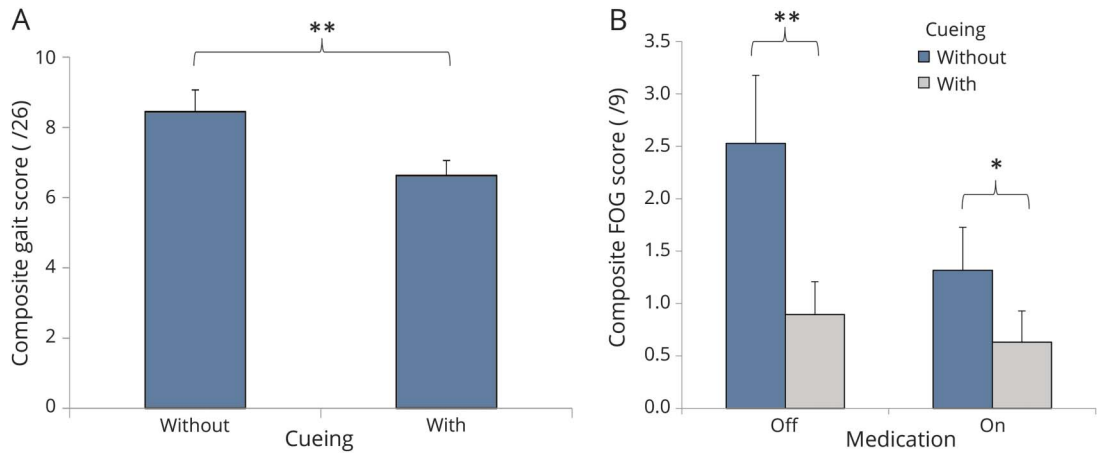
There was a significant main effect of cueing on the composite gait score, with lower scores (better performances) with-cueing (without-cueing: 8.45 ± 0.62; with-cueing: 6.63 ± 0.42, $F_{1,18} = 21.55$, $p = 0.000$) (figure 3A). The interaction between cueing and medication was not significant ($F_{1,18} = 3.30$, $p = 0.086$). Friedman test was significant for the composite FOG score ($\chi^2 = 11.72$, $p = 0.008$). Specifically, the FOG score significantly improved with-cueing, both "off" (without-

Table 2 Gait measures

Variables	"Off" state			"On" state			*p* Values (Friedman test or ANOVA)[a]
	Without-cueing	With-cueing	*p* Values (without vs with-cueing)	Without-cueing	With-cueing	*p* Values (without vs with-cueing)	
Velocity, m/s	0.95 ± 0.29	0.97 ± 0.29	NA	1.18 ± 0.29	1.11 ± 0.28	NA	0.348
							0.087
Step length, m	0.47, 0.26–0.57	0.49, 0.28–0.59	0.070	0.56, 0.20–0.67	0.55, 0.28–0.65	0.286	0.010[b]
Cadence	105.79, 55.90–129.05	103.11, 60.06–121.52	NA	109.12, 79.82–125.00	104.70, 69.42–125.45	NA	0.313
Step time asymmetry	0.12 ± 0.07	0.12 ± 0.06	NA	0.11 ± 0.05	0.12 ± 0.09	NA	0.601
							0.629
Step time variability	13.62, 4.89–27.95	13.72, 7.71–39.80	NA	13.62, 5.67–41.75	12.91, 4.28–34.47	NA	0.615
Double limb support	0.37, 0.34–0.40	0.37, 0.35–0.39	0.876	0.34, 0.33–0.38	0.36, 0.33–0.40	0.025[b]	0.008[b]

Abbreviations: ANOVA = analysis of variance; NA = not applicable (whenever Friedman test >0.05).
Values represent mean ± SEM for variables for which parametric tests could be used (velocity and step time asymmetry); for the rest, values represent the median and interquartile range.
[a] For velocity and step time asymmetry for which an ANOVA was performed, *p* values for the simple main effect of cueing (upper value) and for the medication × cueing interaction (lower value) are reported.
[b] Level of significance was set at $p < 0.05$.

Figure 3 Clinical outcomes



(A) Composite gait score with-cueing and without-cueing. (B) Composite freezing of gait (FOG) score with-cueing and without-cueing, both "off" and "on" medication. **Significance at $p < 0.001$; *significance at $p < 0.05$.

cueing: 2.53 ± 0.65; with-cueing: 0.89 ± 0.31, $p = 0.002$) and "on" medication (without-cueing: 1.32 ± 0.41; with-cueing: 0.63 ± 0.29, $p = 0.038$) (figure 3B). Cueing reduced FOG occurrence by 64.5% "off" and 52.0% "on" medication.

Subjective measures

When asked about their impression about laser shoes on the Likert scale, 12 out of 19 patients reported a moderate to large improvement, 4 a small improvement, and 3 no effect. No patient reported a negative impression. Furthermore, 12 out of 19 patients expressed interest in acquiring laser shoes, 6 were unsure, and 1 not interested.

Discussion

We developed laser shoes as a new closed-loop visual cueing solution for FOG. Here, we evaluated their feasibility and efficacy in a controlled laboratory experiment. We report a marked and significant reduction in FOG occurrence (2-fold reduction in number of FOG episodes during the "off" phase) and FOG duration (56.5% reduction during the "off" phase). None of the patients reported worsening of their gait. These objective effects were paralleled by the patients' positive subjective experiences. We discuss these results, the limitations of our study, and the future perspectives for possible domestic application.

FOG is complex and difficult to trigger in a controlled setting. Therefore, assessing FOG in the laboratory usually introduces clear biases with respect to the actual severity, and precludes definite conclusions on an intervention efficacy.[30] In our study, we increased the odds of observing FOG by (1) using a gait protocol with established FOG triggering circumstances; (2) selecting patients with disabling FOG, occurring multiple times a day; and (3) testing them both "off" medication (when FOG is more likely to occur) and "on" medication. Only 2 of the 19 patients failed to show FOG. This high proportion of objective freezers, while not excluding greater FOG severity in the home setting, supports the reliability of our laboratory findings. In addition, as recommended recently,[30] we used a comprehensive assessment approach combining objective methods (blinded videos ratings), clinical methods (validated scales), and subjective methods (patient experience).

We did not select patients for their familiarity with visual cueing. Yet most of them showed a clear response to the visual cues provided by laser shoes, in contrast with the disparate intrastudy outcomes often reported in cueing studies before.[13,33] It is possible that these heterogeneous results on visual cueing pertained to the impracticality of the used devices, which might have interfered with an otherwise more positive outcome, in particular among patients with executive dysfunction.[34] Interestingly, we found no correlation between degree of improvement afforded by laser shoes and frontal cognitive functioning, suggesting that (at least in this controlled laboratory setting) patients showed immediate benefits from laser shoes, regardless of their frontal cognitive abilities. This underscores their user-friendliness, and highlights their potential for a possibly broader applicability in a large group of patients with FOG. Future work remains needed to study whether these results will actually translate to the home setting.

Unlike what was reported previously,[35] the observed improvement in step length with laser shoes was not clinically meaningful, as the reduction remained far below normative values.[35,36] However, we did not impose any spatial constraints to increase step length. We reasoned that imposing a non-natural step length (aiming to reduce gait hypokinesia)

might overload the patients' resources, potentially masking the effect on FOG.

Implementing cueing in daily life raises several issues that laser shoes might resolve. First, implementation could be hampered by learning problems in patients with cognitive dysfunction.[34,37,38] Here, we show that poor cognitive functioning (assessed using the FAB) does not preclude benefits from laser shoes. Second, lack of consistent immediate effects of cueing has thus far prevented researchers from investigating any possible learning or retention effects after the initial training. In one study, the immediate effects of cueing were already small, likely explaining why sustained long-term effects were absent.[39] The present study shows large immediate beneficial effects of laser shoes. It will be interesting to see whether (and for how long) these can survive cueing discontinuation. Also, laser shoes are a closed-loop VCD, more likely to produce residual effects.[18] Third, cued training in the home can only be effective when patients are compliant. We expect that laser shoes might offer a practically acceptable VCD for domestic use.

This study has some limitations. We used a passive condition as control, where patients walked with the same shoes but with the laser beams turned off. Future work should include an active control condition, comparing laser shoes to another VCD, to study their pure added value. In addition, for laser shoes to be effective, participants must look down to the ground while walking, and this may have affected their gait. Projection of visual cues into the frontal visual field (e.g., using smart glasses) might be an attractive alternative, but the results so far are not very encouraging,[40] perhaps because smart glasses are more distracting than laser shoes, or because they hamper peripheral vision. We suspect that the effect of looking down may have been limited, for 2 reasons. First, patients with PD typically present with a stooped posture, with an inevitable tendency to look downwards. In that regard, laser shoes would provide cues in accordance with this natural tendency. Second, all patients were instructed to only look down whenever necessary, e.g., when experiencing FOG. Such brief glances at the cues were often sufficient to keep gait going, perhaps because the availability of cues created increased confidence and less stress. Other limitations were the uncorrected post hoc analyses for multiple comparisons, due to the pilot character of this study, and the lack of assessor blinding to the cueing condition. Finally, we did not take into account prior past experience of patients with cueing. Some patients were familiar with cueing strategies, possibly making it easier for them to respond positively.

Taken together, these results suggest that laser shoes are an interesting practical and efficient device that, beyond any immediate effect on FOG, may possess the appropriate features for successful cueing training. Future studies will need to examine predictors of good therapeutic response, and assess whether these results transfer to the home setting.

Author contributions

C.B. participated in the design the study, testing of the patients, analysis of the data, writing of the first draft of the paper, and revising the different versions of the manuscript. J.N. analyzed the video data of the study and critically revised the different versions of the manuscript. M.v.H. and R.H. participated in patient testing, analysis of the data, and revision of the manuscript. A.J. participated in data analysis and revised the manuscript. A.D. and R.v.W. critically revised the manuscript. V.W., B.D., and B.R.B. participated in the design of the study and critically revised the manuscript. M.U.F. conceived and developed the laser shoes, designed and supervised the conduct of the study, and participated in the testing of the patients, analysis of the data, and writing and revising the manuscript.

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Disclosure

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