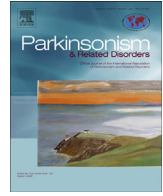




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Effects of augmented visual feedback during balance training in Parkinson's disease: A pilot randomized clinical trial



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ABSTRACT

Background: Balance training has been demonstrated to improve postural control in patients with Parkinson's disease (PD). The objective of this pilot randomized clinical trial was to investigate whether a balance training program using augmented visual feedback is feasible, safe, and more effective than conventional balance training in improving postural control in patients with PD.

Methods: Thirty-three patients with idiopathic PD participated in a five-week training program consisting of ten group treatment sessions of 60 min. Participants were randomly allocated to (1) an experimental group who trained on workstations consisting of interactive balance games with explicit augmented visual feedback (VFT), or (2) a control group receiving conventional training. Standing balance, gait, and health status were assessed at entry, at six weeks, and at twelve weeks follow-up.

Results: Sixteen patients were allocated to the control group and seventeen to the experimental group. The program was feasible to apply and took place without adverse events. Change scores for all balance measures favored VFT, but the change in the primary outcome measure, i.e. the Functional Reach test, did not differ between groups ($t(28) = -0.116, p = .908$). No other differences between groups were statistically significant.

Conclusions: VFT proved to be a feasible and safe approach to balance therapy for patients with PD. In this proof-of-concept study VFT was not superior over conventional balance training although observed trends mostly favored VFT. These trends approached clinical relevance only in few cases: increasing the training load and further optimization of VFT may strengthen this effect.

Trial registration: Controlled Trials, ISRCTN47046299.

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1. Introduction

Individuals suffering from Parkinson's disease (PD) will, over time, typically be confronted with increasing difficulties with walking, balance, and making transfers [1]. This is important as mobility-related quality of life is closely linked to social participation [2] while impaired postural control contributes significantly to falls [3]. Balance and gait-related symptoms tend to be largely

resistant to pharmacological treatment [4]. Allied health therapies such as exercise programs are therefore often implemented to improve mobility [5,6]. A recent meta-analysis suggests that balance-oriented training programs can address mobility-related deficits in patients with PD, but stresses that current evidence is inconclusive [6].

Biofeedback appears to be a promising means to deliver balance therapy [7]. Recent technological developments in the gaming industry have seen integration of players' own physical movements with virtual environments, furnishing new opportunities to provide explicit augmented visual feedback that engages the patient in cognitive and motor activities simultaneously [8]. For PD patients *serious games* may be particularly valuable

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considering the beneficial effects of external stimuli on motor function [9]. Commercially available game consoles with games that target balance control and other forms of physical capacity (e.g. Nintendo Wii™ Fit) are increasingly used in rehabilitation [10]. Pilot studies suggest that (home-based) exercise using Wii Fit is feasible in patients with mild PD and may improve measures of balance and gait, activities of daily living, and self-confidence [11,12]. However, a single randomized clinical trial (RCT) that compared Wii-based training with conventional balance therapy for PD patients found no additional benefits over control treatment in improving daily activities, balance, and cognitive performance [13]. A systematic review by Barry et al. concluded that the safety and clinical effectiveness of exercise-based computer games in general has not been established sufficiently [10]. In addition, the games and equipment may not be optimized for use with patients with PD, compromising user experience and safety [10]. The clinical utility of Wii Fit for instance, appears to be limited by the extent to which therapists can adjust parameters such as exercise complexity, speed, and workload [10]. Progressively modifying exercises in terms of dose and intensity is a key aspect of adequate physical training [14]. These shortcomings can be addressed by employing equipment that is designed for use in a clinical setting, with special attention for patients who experience severe mobility-related difficulties. This might improve effectiveness and applicability of visual feedback techniques in balance training.

In the present pilot RCT we investigated the feasibility of visual feedback-based balance training (VFT) specifically designed for clinical therapeutic settings in terms of applicability and safety. In addition, we compared the effects of the training program with conventional balance training in patients with PD. We hypothesized that VFT can be applied safely and more effectively than conventional training to improve standing balance performance.

2. Methods

2.1. Design

We compared two parallel treatment groups of PD patients. A detailed description of the study protocol was reported previously [15]. This study was registered as an International Standard Randomised Controlled Trial under ISRCTN47046299.

Assessments took place at entry prior to randomization (T0), at six weeks (T1), and at 12 weeks (T2) follow-up. A five-week training program was conducted between T0 and T1. All assessments and training sessions were performed in the ON-phase of levodopa medication.

2.2. Participants

A total of 33 patients with idiopathic PD were recruited from patient databases of the Department of Rehabilitation Medicine of VU University Medical Center (VUmc). Inclusion criteria were (i) a diagnosis of idiopathic PD according to the UK Brain Bank criteria [16], mild to moderate stage (i.e. Hoehn & Yahr stages II and III), (ii) able to participate in either training program, and (iii) written and verbal informed consent. Exclusion criteria were the (i) presence of (other) neurological, orthopedic, or cardiopulmonary problems that could impair participation, (ii) Mini Mental State Examination (MMSE) score below 24, (iii) a recent change in dopaminergic medication, and (iv) cognitive, visual, and/or language problems impeding participation. Participants did not receive other physical therapy treatments during the study period.

2.3. Intervention

Both groups received two treatment sessions per week for a period of five weeks in the outpatient clinic of VUmc. Each session lasted 60 min of which 45 min were dedicated to a series of workstations aimed to improve standing balance performance. In both intervention groups the dynamic balance exercises focused on controlling body posture in the forward, backward and sideward directions, exploring limits of stability, shifting weight from one foot to another, sit-to-stand movements, and included dual-task exercises. Patients worked in pairs, taking turns performing the exercise while the other person rested. Two senior therapists supervised training sessions, defined training goals, and monitored training intensity to ensure progressive overload throughout the training period. Participants kept a training log for the duration of the training program.

2.4. Visual feedback training

The experimental group received VFT, which was explicitly integrated in each workstation. Workstations consisted of a flat-panel LCD monitor connected to a PC containing a total of six, commercially available, interactive dynamic balance exercises (Motek Medical, Amsterdam, The Netherlands; see Fig. 1). Movement registration using a force plate (Forcelink, Culemborg, The Netherlands) or inertial sensors (Xsens, Enschede, The Netherlands) served to convert body movements to motion of an object ('avatar') displayed on the monitor, allowing patients to move within a virtual environment. Four exercises challenged control of body lean. They varied with respect to the coupling between lean and avatar motion. For instance, leaning forward would be associated with an increase in velocity of the avatar in some exercises, with downward movement in another, and with upward movement of the avatar in yet another exercise. The two remaining exercises were related to more functional tasks associated with standing balance, namely taking a step and performing a sit-to-stand movement. During the stepping exercise visual feedback referred to foot placement, whereas during the sit-to-stand movement feedback was related to upper body orientation while sitting, and related to upper leg orientation while coming to stance. Each game allowed a number of parameters to be adjusted so as to increase the difficulty (sensitivity to movement along each axis, speed, duration).

2.5. Conventional balance training

For the control group the workstations consisted of balance exercises recommended by the present Dutch guidelines for physical therapy in PD [14]. These workstations focused on training standing balance and included exercises while standing on one leg or with eyes closed, stepping exercises, dual-task exercises, sit-

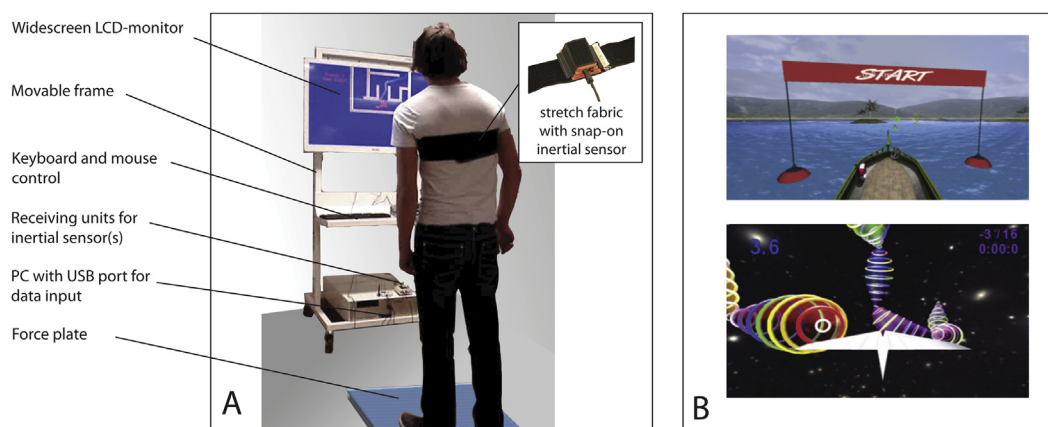


Fig. 1. Illustration of the intervention in the experimental group. A: Setup of mobile workstation with force plate and/or inertial sensor. B: Screenshots of examples of balance games. (Reproduced from Ref. [15]).

to-stand exercises, and exercises on the balancing beam or other challenging support surfaces.

2.6. Measurements and procedures

Assessments took place in a motion laboratory at the Faculty of Human Movement Sciences of the VU University Amsterdam. Besides the clinimetric assessments described in this report, combined posturographic and electroencephalographic recordings were performed (not reported here [15]). The clinimetric test battery was carried out according to current guidelines [14] and validated in a previous study [17].

2.7. Outcomes

2.7.1. Primary outcome measure

The functional reach test (FRT), which measures the limits of stability as perceived by the subject by assessing the difference between the length of the arm and the maximal forward reach distance. The FRT provides a reliable and valid assessment of standing balance [18] and, as far as the authors know, the only established quantitative measure that addresses body lean.

2.7.2. Secondary outcome measures

- Balance and gait:** the Berg Balance Scale [19], the single leg stance test [20], and the 10 m walk test [21].
- Health status and level of activity and participation:** Hoehn and Yahr stage, Unified Parkinson Disease Rating Scale, parts I, II, III, and IV [22], the Falls Efficacy Scale [14,23], the Parkinson's Disease Questionnaire-39 [24], the Hospital Anxiety and Depression [25], and the Multidimensional Fatigue Inventory [26].

2.7.3. Descriptor variables

Age, disease duration, MMSE [27], fall status, and medication as recorded during the first assessment. A patient was categorized as a faller if he or she scored > 0 on

item 13 of the UPDRS. Patients were asked at each subsequent visit whether their medication had changed during the previous six weeks.

In their training log participants recorded each session's training load, rate of perceived exertion, as well as any (near-) falls.

2.8. Randomization and blinding

Potential participants were selected from a local outpatient database and contacted in order of waiting time. Participants were grouped in sets of six. Each set of participants was allocated to either VFT or conventional therapy by drawing an opaque sealed envelope from a pre-compiled random collection by an independent investigator not involved in the present study.

Assessors were blinded for group allocation. Patients were instructed to refrain from revealing treatment allocation to the assessors.

2.9. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 20 (IBM Corp.). All outcomes were tested for group differences at baseline. Categorical outcome measures were tested using Fisher's exact test if contingency tables were of size 2×2 , and the Fisher–Freeman–Halton test if tables were of larger size. Continuous outcome measures were assessed for normality using the Shapiro–Wilk test and for equality of variance using Levene's test and analyzed by parametric or nonparametric tests for independent samples, as appropriate. Nonparametric tests were used for all other outcomes. The family-wise error rate was set at 0.05 by means of the Bonferroni correction, requiring the individual two-tailed tests to be evaluated at $\alpha = 0.05/30 = 0.0017$ as threshold for significance.

Differences in outcome measures between groups were assessed using change scores for each interval (i.e. T1–T0, and T2–T1). These scores were subjected to a Mann–Whitney *U* test (non-parametric case) or an independent samples *t*-test (parametric case), with *group* as between-subjects factor. Cohen's *d* is reported as effect size for independent *t*-tests, while effect size for Mann–Whitney *U*-tests was calculated by dividing the obtained *U* value by the product of the two sample sizes [28]. Data were assessed using an available-case analysis as well as intention-to-

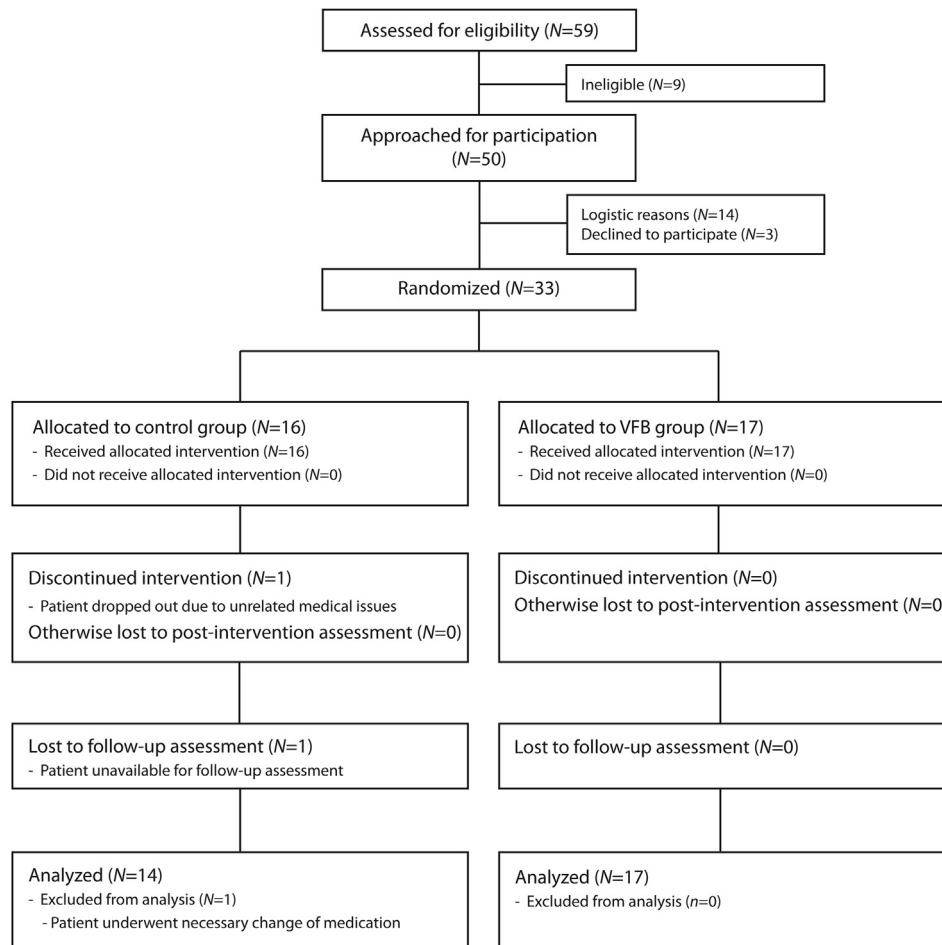


Fig. 2. Flowchart of trial.

treat analyses using the baseline value carried forward to impute missing values in the worst-case scenario and the mean group change to do so in the best-case scenario. The number of available cases was evaluated separately for each individual outcome. In keeping with intention-to-treat analyses, subjects were entered into the final analyses irrespective of the number of attended sessions.

2.10. Ethical approval and informed consent

The protocol was approved by the Medical Ethics Committee of VUmc Amsterdam and all patients signed informed consent.

3. Results

3.1. Trial profile

A total of 33 patients were included in the trial (Fig. 2). Sixteen patients received the control intervention and seventeen patients received the VFT intervention. Both groups included one patient who was treated using chronic deep brain stimulation. One patient in the VFT group received intestinal levodopa infusion. One patient in the VFT-group received an acetylcholinesterase inhibitor; no patients received atypical antipsychotic drugs.

The median (interquartile range) number of attended sessions was 9.0 (8.0–9.75) in the control group and 9.0 (8.0–10.0) in the VFT-group. In the control group no subjects attended fewer than seven training sessions. In the VFT group three subjects attended fewer than seven sessions.

No falls or other adverse events were reported to have taken place during the training sessions. One patient in the control group dropped out because of health problems unrelated to PD; another was excluded due to a change in medication prescription. One subject was lost to follow-up as she could no longer be contacted,

but was included in the analyses covering the intervention period. Fourteen participants from the control group and seventeen from the VFT group entered the final analyses.

The average rating of perceived exertion during the training sessions was 10.7 ± 2.4 ('fairly light') for the control group and 9.7 ± 2.2 for the VFT group ('light') and was not statistically significant different between groups ($t(25) = 1.446, p = .161$).

3.2. Baseline demographics

Baseline characteristics for randomized subjects are summarized in Table 1. No significant differences between the two groups were observed at baseline (all p -values > 0.05).

3.3. Primary outcome

Table 2 shows the median change scores for the intervention (T1–T0) and follow-up periods (T2–T1), for the available cases. Change of the primary outcome measure FRT did not differ significantly between the groups ($t(28) = -0.116, p = .908, d = 0.043$; adjusted $\alpha = 0.0017$). Results for the intention-to-treat analysis were similar.

3.4. Secondary outcomes

There were no statistically significant differences in change scores for any of the outcome measures (all p -values > 0.0017), neither during intervention, nor during follow-up. For the balance-related outcomes the non-significant trends all favored VFT. Similar results were obtained in the intention-to-treat analysis.

Table 1

Baseline comparison between groups for descriptor variables of all randomized patients. Values indicate either the mean (\pm standard deviation); the median (first quartile – third quartile); or number of patients per category. MMSE: Mini Mental State Examination; HY: Hoehn–Yahr stage; UPDRS: Unified Parkinson's Disease Rating Scale; PG: posture and gait subscore; FRT: functional reach test; BBS: Berg balance scale; FES: falls efficacy scale; PDQ-39: Parkinson's disease questionnaire; HADS: hospital anxiety and depression scale; MFI: multidimensional fatigue inventory.

	Control center	Dispersion	VFT center	Dispersion	Statistic	p
Gender [m/f]	8/8		12/5		n/a	0.296
Age [yrs]	68.8	± 9.68	66.3	± 6.39	1.414 (29)	0.168
Disease duration [yrs]	8.8	(2.50, 11.50)	9.0	(4.00, 13.25)	98.5	0.415
L-dopa equivalence [mg/day]	722.8	± 441.25	716.9	± 453.46	0.435 (29)	0.667
MMSE	28.0	(26.00, 30.00)	29.0	(28.00, 30.00)	92.0	0.271
HY						
score	2.5	(2.00, 3.00)	2.5	(2.00, 2.50)	111.0	0.734
1.5/2/2.5/3/3.5/4	0/5/5/6/0/0		0/6/8/3/0/0		1.737	0.469
Fallers [no/yes]	12/4		8/9		n/a	0.157
UPDRS						
Total [0–199]	52.0	(35.25, 63.75)	46.0	(32.25, 62.00)	88.5	0.678
I [0–16]	1.0	(1.00, 2.50)	2.0	(1.00, 3.00)	68.5	0.168
II [0–52]	13.0	(9.00, 15.50)	12.0	(6.50, 17.50)	94.0	0.871
III [0–112]	30.8	(19.00, 40.50)	28.0	(17.75, 35.63)	113.5	0.827
IV [0–23]	6.0	(4.00, 7.50)	4.0	(2.75, 6.50)	97.0	0.378
PG [0–20]	5.0	(3.00, 7.75)	4.0	(3.00, 6.00)	93.5	0.852
FRT [cm]	27.14	± 9.61	26.38	± 6.72	0.233 (28)	0.817
BBS [0–56]	51.5	(47.50, 56.00)	53	(49.75, 55.00)	111.0	0.749
Single leg stance [s]						
Preferred	20.64	(5.79, 47.26)	41.30	(13.75, 60.00)	96.5	0.366
Non, preferred	10.70	(4.17, 35.20)	18.86	(8.56, 41.36)	105	0.578
10 m walk test						
Walk speed [m/s]	1.21	± 0.26	1.15	± 0.28	0.352 (29)	0.727
Step length [m]	0.67	± 0.12	0.66	± 0.09	0.179 (29)	0.859
FES [0–30]	8.0	(2.00, 15.75)	4.0	(1.00, 8.75)	76.0	0.319
PDQ-39 [0–100]	45.00	(18.13, 59.38)	23.75	(10.00, 35.00)	68.0	0.114
HADS						
Anxiety [0–21]	5.0	(3.25, 7.75)	4.0	(1.50, 7.50)	87.0	0.453
Depression [0–21]	5.0	(3.50, 7.50)	3.5	(2.50, 6.00)	72.5	0.163
MFI						
General [4–20]	13.0	(11.25, 16.50)	11.5	(8.50, 15.00)	84.5	0.390
Physical [4–20]	12.0	(11.00, 15.75)	11.0	(8.00, 14.50)	77.5	0.243

Table 2

Change scores between T0 and T1, and between T1 and T2, for the control group and the VFT group for the available cases. Reported are the number of patients per group that were included in the analysis, the median, interquartile range and Mann–Whitney *U* test statistics when outcomes were tested using nonparametric tests, and mean, standard deviation and *t*-values when outcomes were tested using parametric tests; and their associated *p*-, and *z*-values. Upward arrows indicate median changes that represent clinical improvements, downward arrows denote clinical deterioration. ES: effect size.

	Change at post-intervention						Change at follow-up					
	Control			VFT			Control			VFT		
	N	Center (dispersion)	Statistic	N	Center (dispersion)	Statistic	N	Center (dispersion)	Statistic	N	Center (dispersion)	Statistic
FRT [cm]	14	-0.05 (±4.62)	↑	16	0.18 (±6.04)	↑	13	-1.04 (±5.87)	↓	16	1.31 (±6.10)	↑
BBS [0–56]	14	-1.00 (-2.00, 2.00)	↑	17	1.00 (-0.25, 2.00)	↑	13	0.00 (-1.25, 1.25)	–	17	0.00 (-1.00, 1.00)	–
Single leg [s]	14	0.00 (-1.84, 2.17)	–	17	0.90 (0.00, 6.07)	↑	13	0.01 (-0.54, 3.61)	↑	17	0.00 (-1.28, 1.90)	–
Preferred	14	-0.53 (-6.74, 0.41)	↓	17	0.13 (-1.97, 12.59)	↑	13	0.00 (-0.53, 4.15)	–	17	0.00 (-0.62, 1.15)	–
Non-preferred	14	0.001 (±0.174)	↑	17	0.145 (±0.357)	↑	13	0.031 (±0.165)	↑	17	0.021 (±0.241)	↑
10 m Walk test	14	0.003 (±0.072)	↑	17	0.050 (±0.110)	↑	13	0.008 (±0.092)	↑	17	-0.016 (±0.125)	↓
UPDRS												
Total [0–199]	11	5.00 (-0.50, 10.75)	↓	15	2.00 (-4.00, 4.75)	↓	11	-1.00 (-4.00, 6.00)	↑	17	-3.00 (-9.00, 4.25)	↑
Motor [0–112]	13	4.50 (2.38, 7.87)	↓	17	1.00 (-4.38, 6.63)	↓	12	-4.00 (-9.50, 2.00)	↑	17	-4.00 (-8.13, 3.13)	↑
Posture & gait [0–20]	11	1.00 (-0.75, 2.00)	↓	15	0.00 (-1.00, 1.00)	–	11	1.00 (-1.00, 1.75)	↓	17	0.00 (-1.00, 1.00)	–
FES [0–30]	12	0.50 (-3.00, 2.00)	↓	15	0.00 (-1.00, 0.00)	–	12	1.50 (0.00, 2.50)	↓	17	0.00 (-1.00, 1.00)	–
PDQ-39 mobility [0–100]	12	0.00 (-5.00, 2.50)	–	16	2.50 (-8.75, 10.00)	↓	12	8.75 (-5.00, 22.50)	↓	17	0.00 (-10.63, 2.50)	–
HADS												
Anxiety [0–21]	12	0.00 (-1.50, 1.50)	–	16	1.00 (0.00, 1.00)	↓	12	0.50 (-1.00, 2.50)	↓	17	0.00 (-2.25, 0.25)	–
Depression [0–21]	12	0.00 (-1.00, 0.00)	–	16	1.00 (0.50, 2.00)	↓	12	1.50 (-1.00, 3.00)	↓	17	-1.00 (-2.25, 0.25)	↑
MFI												
General [4–20]	12	0.00 (-1.00, 0.50)	–	16	-0.50 (-2.00, 1.00)	↑	12	1.50 (-0.50, 3.00)	↓	17	0.00 (-2.00, 2.25)	–
Physical [4–20]	12	0.00 (-2.50, 1.50)	–	16	-0.50 (-2.00, 1.00)	↑	12	1.50 (-2.50, 4.00)	↓	17	0.00 (-1.25, 2.25)	–

4. Discussion

The present pilot RCT is, as far as we know, the first to investigate the feasibility, safety and effectiveness of a balance training program based on augmented visual feedback specifically designed for patients with PD. Our results show that VFT is feasible for individuals with PD, safe to use and applicable in a group setting.

Adherence was comparable between groups, with all but three subjects attending seven sessions or more. No adverse events were reported throughout the trial and the two forms of training were comparable in terms of perceived exertion. The therapists involved in the training reported that VFT was well received by most participants, with the element of scoring being particularly appreciated. They also observed that mildly-affected patients could operate the workstations independently, while more severely-affected patients required some assistance and/or supervision. All in all, the equipment was considered suitable for use in a (group) setting where continuous one-on-one supervision is not required. Use of the equipment in a home setting is, although technically feasible, at present associated with substantial financial costs.

Change scores related to balance outcomes all favored VFT, but statistically significant differences between groups could neither be established for the primary outcome measure functional reach distance, nor for any other measure. Hence, our findings do not support the hypothesis that visual feedback-based balance training is superior to conventional balance training in improving standing balance performance as measured with the FRT.

VFT was not found to be superior to conventional training, but, importantly, neither was it found to be inferior. These results are in line with those reported for Wii-based training [13]. Equivalence of treatments is an important consideration as VFT and other types of game-based exercise could be associated with lower costs, greater accessibility, and increased patient motivation [10].

As the trends for most outcomes favored VFT (Table 2), the question arises whether this pilot RCT was powerful enough to detect statistically significant effects. Furthermore, only for the outcome walking speed did the difference in change score approach the minimal detectable change [21]. A power analysis for this outcome revealed that in order to find a significant difference between groups with a power of 0.8, each group should include at least 61 subjects. Sample size was thus a limitation of this study. For all other outcomes the magnitude of the improvements did not appear to be clinically relevant, regardless of the type of intervention. An ancillary analysis of within-group effects failed to show a significant treatment effect over time for either intervention. This suggests that the ten-session training volume implemented in this pilot study may have been insufficient to elicit substantial training-related improvements. Increasing treatment intensity by increasing the number of sessions is hence the most likely option for improving the interventions' effectiveness. In addition, the exercises may need to be intensified in terms of adequate dose and level of difficulty [6]. Participants from both groups rated their level of exertion on average as 'light', indicating that there is room for an increase in exercise intensity. Also, patients worked in pairs at each workstation, which in the case of VFT meant a great reduction in time spent practicing. In future forms of VFT this issue may be resolved by the development of multiplayer games.

As indicated above, an important notion for future studies will be to reconsider the choice of (primary) outcome measures. In previous reports the FRT was shown to be responsive to treatment and detect differences between groups of patients with PD [29,30], but in hindsight the FRT measure, reflecting static leaning balance, may be less suitable for changes induced by dynamic VFT. Alternatively, effects induced by the intervention may have been too subtle to be identified by functional measures of balance. Though

outside the scope of the present report, future analyses of combined posturographic and EEG recordings that were part of the study protocol may help reveal differential effects of training for both groups [15].

To conclude, the results of our proof-of-principle study support the notion that VFT in a group setting is safe and feasible for providing therapeutic balance training to PD patients, albeit not more effective than conventional therapy. While all trends in change scores favored VFT, these differences did not reach statistical significance and were clinically meaningful only for a single outcome measure. Though improved patient motivation may suffice to warrant the application of an equipment-intensive approach such as VFT, future efforts should first focus on improving the intervention in order to strengthen its effects. This may be realized by increasing the training load and by optimization of the technology.

Conflict of interest

The authors declare no competing interests.

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Financial disclosures of all authors

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Authors' roles

EvW and GK obtained funding for the study. All authors contributed to the research design. Intervention and clinimetric, posturographic and EEG assessments were outlined by EvW, AD and MvdH. MvdH is principally responsible for the assessments, data-analysis, and drafting of the manuscript. All authors critically reviewed the manuscript and approved the submitted version.

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