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Parkinson's Disease: Postural Instability Interventions

The effectiveness of physiotherapy treatment on balance dysfunction and postural instability in persons with Parkinson's disease: a systematic review and meta-analysis

Abstract

Background: Balance dysfunction and postural instability in Parkinson's disease are among the most relevant determinants of an impaired quality of life. Physiotherapy interventions are essential to reduce the level of disability by treating balance dysfunction and postural instability. The aim of this systematic review with meta-analysis was to test the effectiveness of conventional physiotherapy interventions in the management of balance dysfunction and postural instability in Persons with idiopathic Parkinson's disease.

Method: A systematic literature search of the Cochrane Library, PubMed/Medline, PEDro, Rehadat, and Rehab Trials were performed by 2 reviewers (AY and AT) independently. Eligible randomised controlled trials published from September 2005 to June 2015 were included. The selected RCTs, which investigated the effects of conventional physiotherapy treatments in the management of postural instability and balance dysfunction in Persons with Parkinson's disease, were assessed on a methodological quality rating scale. Included studies differed clearly from each other with regard to patient characteristics, intervention protocol, and outcome measures. Important characteristics and outcomes were extracted, summarized and analyzed.

Results: Eight trials with a total of 483 participants were eligible for inclusion of which 5 trials provide data for meta-analysis. Benefits from conventional physiotherapy treatment were reported for all of the outcomes assessed. The pooled estimates of effects showed significantly improved berg balance scale (SMD, 0.23; 95 % CI, 0.10–0.36; $P < 0.001$) after exercise therapy, in comparison with no exercise or sham treatment. Exercise interventions specifically addressing components of balance dysfunction demonstrated the largest efficacy with moderate effect size (SMD, 5.98; 95 % CI, 2.29–9.66; $P < 0.001$). Little effects were observed for interventions that specifically targeted Falls efficacy scale. The pooled data indicated that physiotherapy exercises decreased the incidence of falling by 6.73 (95 % CI: −14.00, 0.54, $p = 0.07$) with the overall effect of $Z = 1.81$.

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Conclusion: Physiotherapy interventions like balance training combined with muscle strengthening, the range of movement and walking training exercise is effective in improving balance in patients with Parkinson's disease and more effective than balance exercises alone. Highly challenging balance training and incremental speed-dependent treadmill training can also be part of a rehabilitation program for management of balance dysfunction and Postural instability in patients with idiopathic Parkinson's disease.

Keywords: Randomized controlled trials, Parkinson's disease, Physiotherapy, Postural instability, Balance dysfunction, Exercise, Equilibrium, Postural control, Rehabilitation

Background

Parkinson's disease (PD) is a debilitating chronic neurodegenerative illness resulting in motor dysfunction, which leads to weakness, pain, and tightness, difficulty in walking, rising from chairs, clumsy movements and a decline in physical activity. It is the second most common neurological disease in the world that affects neurophysiologic function, movement abilities, and quality of life (QOL) [1–5].

Balance dysfunction (BD) and Postural instability (PI) are the common incapacitating symptoms of PD. Untreated BD and PI can lead to increased frequency of falls and injuries which in turn increases the chance of developing Comorbidity and disability by causing alterations in postural control strategies during standing tasks and when performing voluntary movements [5–7]. Balance dysfunction and PI are also associated with a loss of equilibrium, sudden falls, progressive loss of independence and immobility [8–10].

Balance dysfunction and PI usually occur in the middle-later stages of the disease and became a clinical concern since they are not easily amenable to treatment with medication [11, 12]. Although Patients with PD get the best available medications, they still experience a declining of body function, daily activities, participation and weakening in mobility [13].

Recently, a number of systematic reviews assessed the effect of physiotherapy treatments or exercises in the management of balance dysfunction and postural instability among patients with idiopathic PD [14–18]. Although the results seem promising,most studies included in the systematic review have a small number of patients enrolled in their included studies and methodological limitations such as limited quality and a limited set of relevant outcome measures. This makes their result inconclusive about the use of physiotherapy treatments in the management of BD and PI bias [12, 19, 20].

Therefore, this systematic review aimed to evaluate the effectiveness of conventional physiotherapy treatments in improving balance and postural stability among persons with idiopathic PD.

Method

Protocol and registration

The systematic review was done using the preferred reporting items for systematic reviews and Meta-analysis (PRISMA) checklist.

There was no registration done either for the protocol or the systematic review.

Eligibility criteria

A study was included if it met the following criteria:

a) Randomized controlled trial methodology (level 1b evidence according to Oxfords level of evidence criteria [21] (see Table 1).
b) Quality rating of greater than or equal to 5 by PEDro score;
c) The target population was individuals with idiopathic PD of any time duration;
d) The effects of different conventional physiotherapy treatment techniques or exercise interventions were compared with control or comparison groups,
e) The primary outcomes included at least one of the following: postural instability, deficits in balance demanding activities, or risk of falling
f) The article was available in English.

A study was excluded: –If the effects of non-exercise interventions were evaluated (like behavioral interventions), If other study designs than RCT were used and If quality rating was 4 or less as determined by PEDro score.

Data sources and search strategy

Five databases (Cochrane Library, PubMed/Medline, PEDro, Rehadat, and Rehab Trials) were used during article selection process from February 2015 to September 2015. An electronic database search for relevant Randomized controlled trials (RCTs) which examined physiotherapy techniques used to treat, BD and PI among people with PD of any duration and published in international medical journals in the English language from 2005 to June 2015was conducted. We(AY,

Table 1 Hierarchies of evidence for questions of therapy, prevention, aetiology or harm [CEBM]

Level 1a:	Systematic reviews (with homogeneity) of randomized controlled trials (RCTs)
Level 1b:	Individual RCTs (with narrow confidence interval)
Level 1c:	All or none studies
Level 2a:	Systematic reviews (with homogeneity) of cohort studies
Level 2b:	Individual cohort study or low quality RCTs (e.g. <80 % follow-up)
Level 2c:	"Outcomes" Research; ecological studies
Level 3a:	Systematic review (with homogeneity) of case-control studies
Level 3b:	Individual case-control study
Level 4:	Case-series (and poor quality cohort and case-control studies)
Level 5:	Expert opinion without explicit critical appraisal, or based on physiology, bench research or 'first principles'

AT) searched articles using keywords of *RCTs, Parkinson's disease, physiotherapy, postural instability, balance dysfunction, Exercise, equilibrium, postural control, and rehabilitation.*

The relevance of the reviewed studies was checked based on their topic, objectives, and methodology. Preliminary assessments have been made and some articles were excluded at the first step just by looking at the topic. On the second step, abstracts have been seen and were excluded if they did not match to the current study objectives. For the rest, the whole content of the articles was accessed and selected based on the independent and dependent variables under review.

Type of intervention

The intervention was chosen if the RCTs used one of the following conventional physiotherapy treatment techniques: stretching, aerobic training, relaxation and muscle activation, strengthening exercises and treadmill walking.

Type of outcomes

The primary outcomes of this study were changes in berg balance scale and falls efficacy scale among the intervention and control group at the end of the follow-up. However, there are some other secondary outcome measures used in this systematic review with Meta-analysis (Table 2).

Data extraction and analysis

Two reviewers (AY, AT)extracted data from the selected RCT studies using pre-designed forms independently. Any conflict between these two reviewers was resolved by consensus. From the selected studies, the following parameters were extracted; demographic variables (mean age, sample size), Initial and Final results of used outcome measures, and the type of intervention given along with the duration of follow-up (Table 2).

Data which are suitable to meta-analysis were entered and analyzed using RevMan 5.3 software. The difference in percentage in each treatment was recorded. When there is no documented difference, it was calculated by extracting the mean change in the experimental and control group.

Quality assessment

The selected RCTs were critically appraised with 11 items of PEDro scale scores extracted from the Physiotherapy Evidence Database (www.pedro.org.au), 10 of which were scored using explicit decision rules. The PEDro scale assesses the methodological quality of a study based on important criteria, such as concealed allocation, intention-to-treat analysis, and adequacy of follow-up.

These characteristics make the PEDro scale a useful tool to assess the methodological quality of physical therapy and rehabilitation trials. The PEDro scale is based on a Delphi list [22] and consists of 11 items. Items 2–9 refer to the internal validity of a paper, and items 10 and 11 refer to the statistical analysis, ensuring sufficient data to enable appropriate interpretation of the results [23].

Item 1 is related to the external validity and therefore not included in the total PEDro score Item 4 (baseline similarity) was considered to be fulfilled if there were no significance ($p > 0.05$) difference between groups at baseline for one key outcome measure. Only one outcome had to achieve baseline similarity, in the case of more than one outcome is measured by the trials to fulfill item 4 criteria. The trials were rated independently by two investigators. Studies were excluded in the subsequent analysis if the cut-off of 5 points was not reached on PEDro scale score.

The following data were extracted from the included trials: study design, subject information, and description of interventions between the control and experimental group, outcome measures, outcome data, follow-up period. These data were then compiled into a prepared table. The two reviewers who selected the appropriate studies also extracted the data and evaluated the risk of bias. Data at baseline, post-treatment and follow-ups were extracted for interested outcomes.

Data analysis

Qualitative analysis

The necessary information was extracted from each original study by using a format prepared in Microsoft Excel Spreadsheet.

Table 2 Characteristics of included randomized controlled trials

Authors	Participant characteristics	Intervention types and intensity for experiment and control groups	Outcomes
(Ashburn et al. 2007) [7]	• *n* = 142 (Exp = 70, Control = 72).	Exp group: muscle strengthening, range of movement, balance training, walking training and Strategies for falls prevention, movement initiation and compensation.	• Rates of Falling
	• Sex :male = ____female = ____	Con group: visited by nurse For 6 months	• Functional reach
	• Mean Age of expt. =72.7(9.6)		• BBS timed up and go test
	• Mean Age of control. =71.6(8.8)		
	• Baseline UPDRS: Exp = 19.8(8.3) and Control = 22.2(11.9)		
(Smania et al. 2010) [8]	• *n* = 64 (Exp = 33, control = 31)	Exp group: Exercises of self-destabilization of the COBM, Inducing destabilization of COBM externally and coordination between leg and arm movements during walking &locomotor dexterity over an obstacle course	• BBS
	• Mean Age of expt. =67.64 (7.41)	Cont.group:- active joint mobilization, muscle stretching, and motor coordination exercises.	• ABC
	• Mean Age of control = 67.26(7.18)	21 treatment sessions of 50 min each for one month.	• UPDRS
	• idiopathic PD and PI (Hoehn and Yahr [H&Y] stage 3–4)		• modified Hoehn and Yahr scale
(Protas et al., 2005) [24]	*n* = 18(Expt. = 9, Control = 9)	Exp group I: Gait training(walking on a treadmill at a speed greater than over ground walking speed)	Gait parameters
	Mean age of exp. = 71.3(7.4)	Exp group II [PNF]: Basic and Gait PNF, movement guidance, support & resistance for 1 h/day, three times per week for 8 weeks	5-step test report of falls
	Mean age of contrl. = 73.7 (8.5)		
(Schlenstedt et al. 2015) [27]	*n* = 32(Res. Training : *n* =17, balance training: *n* = 15;	2x/week for 7 weeks, Each session lasted 60 min.	Fullerton Advanced Balance (FAB) scale
	Mean age of exp. = 75.7 ± 5.5	Resistance training group: strengthening exercise was given to lower limb muscles	Timed-up-and-go-test (TUG)
	Mean age of contl. = 75.7 ± 7.2	Balance training group : stance- and gait tasks which require feed forward and feedback postural control	UPDRS
(Conradsson et al. 2015) [25]	(*n* = 100), experimental group = 51	Expt: reactive postural adjustments to control their balance during single-tasking(a 10-week Hi Balance program)	• Mini BESTest,
	Control group =49.	Control: normal physical activities and participation in ongoing rehabilitation program.	• gait velocity
	Mean Age of expt. =72.9 (6.0)		• Falls Efficacy Scale
	Mean Age of control. =73.6 (5.3)		
(Shen and Mak 2014) [29]	*n* = 51, (Expt., = 26) and (Contrl, = 25).	Expt : technology assisted balance + gait training	• falls rate
	Mean Age of expt. =63.3 (8.0)	Control :- strengthening exercises (3 sessions/week, separated by 4 weeks of selfsupervised home-based training at a frequency of 5 sessions/week	• single-leg-stance time,
	Mean Age of control. =65.3 (8.5)		• stride length
(Allen et al. 2010) [26]	*n* = 45 (Expt. =21 and Contrl. = 24)	Exp't: Multi component exercise program (home-based)	• falls risk score
	Mean Age of expt. =66 (10)	3 sessions/week/40-60 min/session/week for 30 days for 72 sessions	• timed sit-to-stand
	Mean Age of control. =68 (7)	Control: Usual care (no exercise)	• falls rate
(Cakit et al. 2007) [28]	*n* = 31 (expt. = 21, control = 10), mean age =71.8 ± 6.4	Experimental group: Incremental speed-dependent treadmill training for 8 weeks.	• UPDRS
	baseline UPDRS 18.14 _ 9.32	control group: not really mentioned	• BBS
			• Dynamic Gait Index
			• FES

Quantitative analysis (Meta-Analysis)

Meta-analysis was performed using the Review manager (RevMan5.3) software. The post-intervention data were used to obtain the pooled estimate of the immediate effect of physiotherapy interventions and effects beyond intervention period. Heterogeneity between trials was assessed using the I^2 statistic. Heterogeneity was considered substantial if I^2 was greater than 50 % and a random effects model applied; otherwise, a fixed effects model was used for the analysis. The pooled data for each outcome were reported as weighted mean differences (MD) with a 95%CI.

Results

Search yield

A total of 346 records were identified from electronic search and additional records but 131 were duplicates. After screening title, abstracts, and references 119 papers were removed. The full-text article was obtained for 33 papers of which 25 papers were eliminated as they did not meet inclusion criteria and therefore, 8Studies included in the qualitative synthesis and 5 of them included in quantitative synthesis (see Fig. 1).

Characteristics of included trials

All 8 trials involved a total of 483 participants and investigated the effectiveness of physiotherapy treatment and Exercise on improving postural stability and balance in Persons with Parkinson's disease. All trials were conducted in between September 2005 and June 2015 (see Table 2).

Quality

The mean PEDro scores of the included trials were 7. Three studies [8, 24, 25] blinded participants, two studies [8, 24] blinded therapists and the other five trials did not, due to innate difficulties. Concealed allocations of participants were stated clearly in only two studies [25, 26] and the intention to treat analysis was considered by only three studies [25–27]. The quality assessment scores and

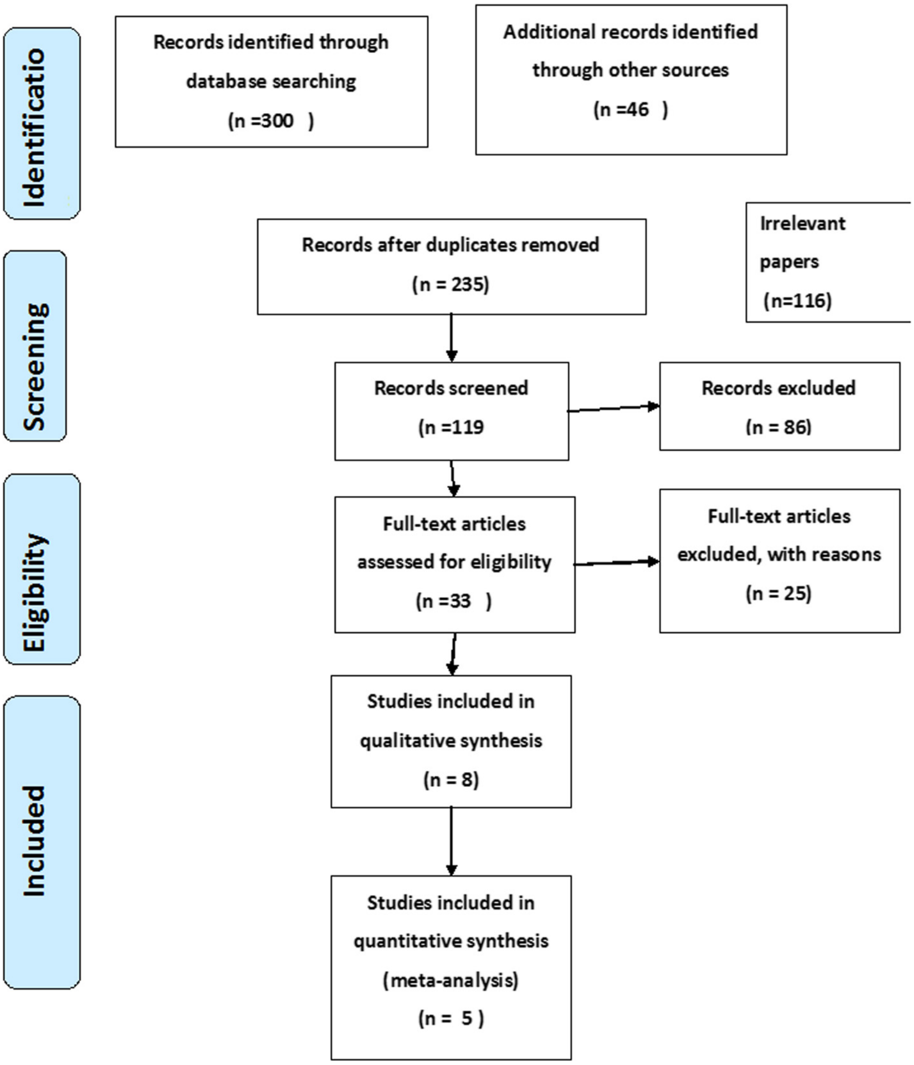


Fig. 1 PRISMA Flow diagram showing the flow of information in the procedure of including studies in systematic review, 2015, Ethopia

the decisions of each item for the included trials are shown in Table 3.

Participants

There were 248 patients (ranged from 9 to 70 patients per study) in the experimental group and 235 patients (ranged from 9 to 72 patients per study) in the control group. Three of the trails [7, 25, 26] recruited community-dwelling participants, two trials recruited their outpatient study participants from medical educational and research centers [24, 28] and the other three trials [8, 27, 29] recruited their study participants from hospitals. The mean age range of the participants was 63.3 ± 8.0 to 75.7 ± 5.5 in the experimental group and 65.3 ± 8.5 to 75.7 ± 7.2 in the control group. In seven of the included articles, the disease severity of their study participants was recorded using the Hoehn and Yahr[H&Y] Scale and Patients with idiopathic PD with a baseline stage between 2 and 4 were recruited as a study participant [7, 8, 24, 25, 27–29].

Interventions

The experimental groups were treated with different treatment approaches. Five studies used postural adjustment and falls prevention strategies and balance training [7, 8, 25–27, 29],three studies used strengthening exercises [7, 26, 27], three studies applied gait training through overground walking and treadmill training [26, 28, 29] only one study [24] used PNF exercise and coordination training has been given for another one study [8].

Balance training was performed in the form of static, dynamic and functional balance training [7], in the form of exercises aimed at improving both feed forward and feedback postural reactions [8], in the form of highly challenging balance training (HiBT) that incorporates both dual-tasking and PD-specific balance components [25],in the form of stance- and gait tasks which require feedforward and feedback postural control [27] and in the form of technology-assisted balance training [29].

Strengthening exercises were performed with the aim to improve hip flexors, hip extensors and abductors, knee flexors and extensors, ankle dorsiflexors and plantar flexors [27], in the form of progressive lower limb strengthening [26], knee and hip extensors and hip abductors muscle strengthening [7].

Participants undertook training for 30 to 60 min per session for 7 to 24 weeks. Participants of the control group received no intervention in two studies [24, 28], visited by nurses [7], given joint mobilization and stretching exercises [8], asked to do physical activities [25], took medication and usual care [26] and provided strengthening exercise in two studies [27, 29].

Outcome measures

Three trails used berg's balance scale of 0–56 scale range to measure the effect of training on balance outcome [7, 8, 28]. Three trials [25, 26, 28] used falls efficacy scale to assess balance and risk of falling. Falls risk in one study [26], UPDRS [27, 28], Fullerton Advanced balance scale [8, 27] and falls rate [8, 29] were also used as outcome measures to assess the level of balance dysfunction, postural instability, and risk of falling among patients with Parkinson's disease (See Table 4).

Table 3 PEDro criteria and summary of quality assessment scores of Included studies ($n = 8$)

Criteria	(Ashburn et al., 2007) [7]	(Smania et al., 2010) [8]	(Protas et al., 2005) [24]	(Schlenstedt et al., 2015) [27]	(Conradsson et al., 2015) [25]	(Shen and Mak, 2014) [29]	(Allen et al., 2010) [26]	(Cakit et al., 2007) [28]
Eligibility criteria	✓	✓	✓	✓	✓	✓	✓	✓
Random allocation	1 Block	1 block	1	1	1	1	1	1
Allocation concealed	1	0	0	0	1	0	1	0
Baseline similarity	1	1	1	1	1	1	1	1
Patient blinding	0	1	1	0	1	0	0	0
Therapist blinding	0	1	1	0	0	0	0	0
Assessor blinding	1	1	1	1	0	1	1	1
<15 % drop outs	1	1	1	0	1	0	1	0
ITT analysis	1	0	0	1	1	0	1	0
Between group comparison reported	1	1	1	1	1	1	1	1
Post intervention point & variability measures	1	1	1	1	1	1	1	1
Total	8/10	8/10	8/10	6/10	8/10	5/10	8/10	5/10

Table 4 Summary of results of included randomized controlled trials (*n* = 8)

Reference	Results
(Ashburn et al. 2007) [7]	1. Functional reach test(cm): – Experimental group at (start/8 weeks/6 months) = 23.2/23.6/23.8 Control group at (start/8 weeks/6months) = 25.0/24.0/22.5 2. Berg balance scale(BBS) (o-56) : the higher the score, the risk of falling decreases Experimental group at (start/8 weeks/6 months) = 44.3/45.8/45.3 Control group at (start/8weeks/6months) = 43.6./45.2/44.6
(Smania et al. 2010) [8]	1. BBS(0–56):- Experimental group (before/after/1 month) =44.5/49.8/49.9 Control group (before/after/1 month) = 41.8/41.0/40.85 2. Activities-Specific Balance Confidence Scale ABC(0–100):- Experimental group (before/after/1 month) = 54.3/61.3./62.3 Control group (before/after/1 month) = 49.5/48.2/47.0 3. Number of falls : Experimental group (before/after/1 month) = 4.3/1.3/1.3 Control group (before/after/1 month) = 4.6/4.1/4.1
(Protas et al. 2005) [24]	Gait and step perturbation training resulted in a reduction in falls and improvements in gait and dynamic balance.
(Schlenstedt et al. 2015) [27]	1. FAB scale :- resistance group 22.2 ± 4.8 Balance group 24.5 ± 4.6,(*P* value = 0.123)
(Conradsson et al. 2015) [25]	1. Falls Efficacy scale score:- Experimental group (baseline/post test = 30.1(/27.3 Control group (baseline/post test = 28.8/26.5
(Shen and Mak 2014) [29]	There were fewer fallers in the expt. than in the Cont. group at Post 3 m, Post 6 m, and Post 12 m (P < .05). In addition, the expt. group had lower fall rate than the Cont. group at Post 3 m, 6 m and 15 m
(Allen et al. 2010) [26]	1. PD falls risk score: Experimental group (baseline(SD)/post test(SD) =34(25)/23(22) Control group (baseline(SD)/post test(SD) = 39(34)/38(31) 2. Falls Efficacy scale score :- Experimental groups(baseline/post test = 28.1(12.1)/25.8(7.9) Control groups baseline/post test =29.1(10.3)/30.4(10.8)
(Cakit et al. 2007) [28]	1. BBS : Experimental group (baseline/8 weeks = 37.0 ± 9.41/44.09 ± 7.11 Control Group (baseline/8 weeks = 42.6 ± 9.37/41.4 ± 10.65 2. Falls Efficacy Scale : expt. group(baseline/8 weeks. = 37.72 ± 9.29/25.45 ± 7.46 Control group(baseline/8 weeks. = 26.8 ± 8.06/29.2 ± 9.87

Qualitative analysis of the effect of physiotherapy interventions on different outcomes

The effects of postural adjustment, fall prevention strategies, and balance training exercises on near falls and quality of life have been done by a study done in Southampton. The results showed that there was a tendency towards a reduction in fall events and injurious falls [7].

An RCT conducted in Italy brought that balance training showed significant improvements in declining PI and improving balance in patients with PD [8].

Another study conducted in the USA showed that Gait and step perturbation training can result in a reduction in falls and improvements in gait and dynamic balance for patients with PD [24].

According to a RCT conducted in Sweden, a HiBT regimen that incorporated both dual-tasking and PD-specific balance components (walking tasks on varying surfaces with or without visual constraints and voluntary arm/leg/trunk movements) significantly benefited balance and gait abilities when compared with usual care and showed promising transfer effects to everyday living [25].

Another comparative RCT done in Germany found that it is effective to use both coordinated resistance and balance training to improve balance and postural control for patients with PD [27].

A study done in china on the effectiveness of technology-Assisted Balance and Gait training found that the balance and gait training program assisted by technological devices reduced the number of fallers and the fall rate compared with the strength training program. It supported the clinical use of balance and gait training for reducing fall events in people with PD [29].

The effects of an exercise program on reduction of fall risk factors in People with PD were determined by a study done in Australia. It found that there were trends towards improvement in the exercise group for measures of muscle strength, walking, and fear of falling, but there was a lack of improvement in balance outcomes [26].

A study done in turkey on the effects of incremental speed-dependent treadmill training on postural instability and fear of falling found that specific exercise programs using incremental speed-dependent treadmill training may improve mobility, reduce postural instability and fear of falling in patients with Parkinson's disease [28].

The effects of physiotherapy interventions on different outcome measures are summarized in Table 4.

Meta- analysis on effects of physiotherapy interventions on berg balance scale

The effects of muscle strengthening, range of movement, balance training, walking training, Exercises of self-destabilization of the center of body mass and incremental speed-dependent treadmill training on berg balance scale(BBS)immediately after intervention period was examined by pooling data from three trials involving 239 participants. The pooled data indicated that physiotherapy exercises increased BBS by 5.98 (95 % CI-2.29 to 9.66,$p = 0.001$) than the control group (Fig. 2).

Meta- analysis on effects of physiotherapy interventions on falls efficacy scale

The effects of muscle strength, balance training, freezing and reactive postural adjustments in controlling balance during single-tasking compared with normal physical activities and participation in ongoing rehabilitation program was examined by pooling data from three studies involving 167participants. The pooled data indicated that these physiotherapy exercises decreased the incidence of falling by 6.73: (95 % CI: −14.00, 0.54, $p = 0.07$) with the overall effect of $Z = 1.81$. However, it was not significant. There was heterogeneity between the studies ($I^2 = 99$ %) (See Fig. 3).

Discussion

The objective of this systematic review was to evaluate the current evidence for benefits of physiotherapy treatments for treating balance impairment, postural instability and reducing the tendency and frequency of falling for patients with idiopathic Parkinson's disease.

The overall result of this systematic review of RCTs indicates that multifactorial physiotherapy interventions like muscle strengthening, range of movement, balance training and walking training exercises were found to have a positive effect on treating BD and PI among idiopathic patients with PD. But the effect of training intensity, duration, and modality is variable and inconsistent.

In this systematic review, different balance training techniques were found to be effective in improving balance and they were administered in the form of static, dynamic and functional training [7]. Exercises aimed at improving both feed forward and feedback postural reactions [8], HiBT that incorporates both dual-tasking and PD-specific balance components [25], stance- and gait tasks which require feed forward and feedback postural control [27] and technology assisted balance training exercises [29] also demonstrated a very promising outcome of balance improvement. This finding is supported by a meta-analysis which found that exercises and motor training can improve the performance of balance-related activities in people with PD [12].

Physiotherapy interventions targeted at preventing falls and Exercises of self-destabilization of the Center of body mass during walking and locomotor dexterity have an impact on reinforcing the need to focus attention on maintaining balance when performing mobility tasks in a standing position [7, 8]. This result was found by two studies which have the following limitations: Increasing numbers of control subjects who accessed rehabilitation outside of the trial by 6 months [7], lack of a follow-up assessment at 3 or more months after training and lack of assessment of some important parameters related to balance and PI [8].

This systematic review showed that repetitive exercises, HiBT, and incremental speed-dependent treadmill training will help to improve range of motion, endurance, gait parameters, functional reaching activities and postural stability in particular and balance at large. It also showed that those exercises help to decrease fall rate and fear of falling which could have the direct or indirect contribution in improving balance [7, 24–26, 28]. However, the results of a study done on the effects of HiBT [25] can only be generalized to elderly, specifically community-dwelling individuals with mild- to moderate-stage PD without known cognitive impairments.

Other limitations of these studies include a majority of the participants were recruited by advertisement, a method that can lead to a convenience sample of individuals

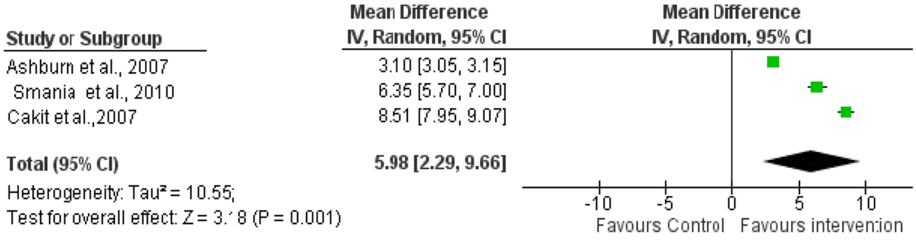


Fig. 2 Comparison of physiotherapy interventions with controls in relation to the Berg balance scale

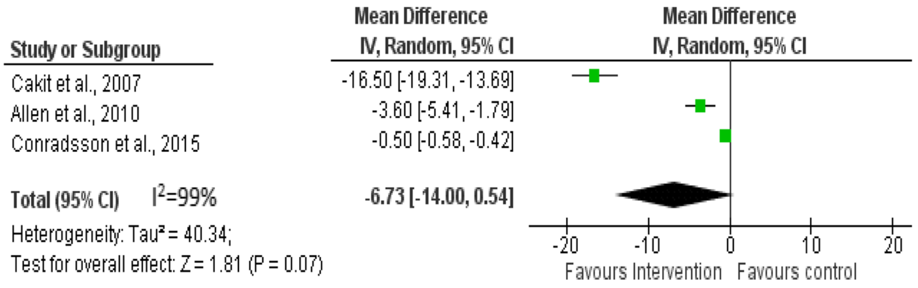


Fig. 3 Comparison of physiotherapy interventions with controls in relation to falls efficacy scale

interested in training and improving balance abilities [25], did not attempt to prevent participants from changing their medications during the study period for ethical reasons [26], relatively small sample size and unable to address the intensity, frequency, and duration of the training intervention [24] and having small sample size [28].

The difference between resistance and balance training to improve postural control and balance in people with PD have also been analyzed in this systematic review and weak evidence was found that freely coordinated resistance training might be more effective than balance training [27]. Nevertheless, the major limitation of this RCT is that training frequency was low and probably under-dosed to detect significant differences between these two competing training types. Second, it had a 20 % drop-out rate which might have been underpowered to detect significant differences. Furthermore, they did not assess fall rates which would be of interest as strength and balance performance are independent risk factors for falls. Finally, they did not include any control group without any intervention which would allow to further interpret the effects of both training types [27].

Technology assisted balance and gait training have been found significant in reducing the number of fallers at Post 3 month, 6 months, and 12 months. In addition, it also showed that a lower fall rate than the Control group was registered [29]. However, the included study has several limitations. First, the sample size and statistical power were not adequate to detect group differences. Second, there was a possible placebo effect since subjects were not blinded to group assignment. Third, all of the subjects were community-dwelling people with a mild to moderate disease level. Fourth, they used monthly phone follow-up registration of fall incidence instead of using a fall diary because most of the subjects did not have education beyond the elementary level and some were even illiterate. Fifth, the dropout rate of 31 % was relatively high. Therefore, the results cannot be generalized to patients with advanced-stage PD or those who have been institutionalized and educated [29].

This meta-analysis indicated that a significant difference was obtained on physiotherapy intervention for improving balance. However, there was not a significant difference was obtained on physiotherapy intervention for improving postural stability.

A meta-analysis of the effects of exercise and motor training on balance and falls in PD supported our finding. It concluded that there was a significant but small benefit of physiotherapy interventions on balance-related performance measures. However, there was no beneficial effect on falls in PD [30].

Limitation of this systematic review

Addressing all important outcome measures was not possible. No attempts were made to source unpublished studies, nor studies published in languages other than English. The authors suggestively agreed that unpublished trials may have poor methodology over the published ones. The review had feasibility constraint over translation for other language trails.

Conclusion

The results of this systematic review with meta-analysis concluded that physiotherapy interventions like balance training combined with muscle strengthening, the range of movement, walking training exercise is effective in improving balance in patients with PD and more effective than balance exercises alone.

HiBT and incremental speed-dependent treadmill training can also be part of a rehabilitation program for management of balance and Postural instability in patients with idiopathic PD.

Clinical application

This review suggests that physiotherapy techniques, exercises, and balance training appear to result in comparable outcomes for balance, postural stability, and reduction in falls. Consequently, prescription of balance and walking training exercise, repetitive exercises, HiBT and incremental speed-dependent treadmill training for idiopathic PD may pledge substantial improvement. Therefore, balance training exercises should be incorporated into a plan of care in conjunction with other necessary interventions to make the patient independent as much as possible.

Effects of a sensory-motor orthotic on postural instability rehabilitation in Parkinson's disease: a pilot study

Abstract

Background: Proprioceptive deficits have been largely documented in PD patients, thus external sensory signals (peripheral sensory feedback) are often used to compensate the abnormalities of proprioceptive integration.
This pilot study aims to evaluate the feasibility and the effectiveness of a rehabilitation-training program, combined with the use of a sensory-motor orthotic in improving balance in a small sample of PD patients.

Methods: Twenty PD patients were randomly allocated into two groups: (i) *the Experimental group*, where participants were asked to wear a sensory-motor orthotic during the balance training program and (ii) *the Control group*, where subjects performed an identical training program without wearing any kind of orthotics. In all, the training program lasted 10 sessions (5 days a week for 2 weeks) and the clinical and instrumental assessments were performed at baseline, immediately after the end of the training and 4 weeks after the rehabilitative program was stopped.

Results: All clinical outcome measures tested improved significantly at post and follow-up evaluations in both groups. Interestingly, at the end of the training, only the experimental group obtained a significant improvement in the functional reaching test (sway area - eyes closed) measured by means of stabilometric platform and this result was maintained in the follow-up evaluation.

Conclusions: Our preliminary results suggested that the use of a sensory-motor orthotic, in combination with a tailored balance training, is feasible and it seems to positively impact on balance performance in Parkinson's disease.

Trial registration: EudraCT N. 003020–36 - 2013.

Keywords: Parkinson's disease, Sensory-motor orthotic, Postural instability, Rehabilitation

Background

Parkinson's disease (PD) is a neurological progressive disorder characterized by balance dysfunctions, often associated with the high risk of falling [1] that negatively impacts on the quality of life [2]. In PD, most of the falls occur during a sudden change of posture or during walking [3] in various circumstances (i.e., gait initiation, dual task conditions). Balance problems, in PD patients, are probably due to the overlapping of different factors, such as stopped posture, deficits in postural responses [4], reduced limit of stability [5] and impaired executive function (i.e., deficit in selective attention) [6]. Although much is known about the multifactorial nature of gait disturbances and falls in PD, the pathophysiology of postural instability is still unclear. It seems to depend on a complex interactions between the impairment caused by the disease at different levels of the nervous system and compensatory strategies [7, 8]. It is well- known that postural control in PD patients mainly relies on visual information, which is possibly used for compensating proprioceptive impairments [9, 10]. Indeed, PD patients seem to have somatosensory abnormalities with abnormal proprioceptive (kinesthetic) processing that produces a reduced perception of passive motion limb position [11, 12] and space orientation [13]. Therefore, abnormalities in sensory processing have been suggested to play a major role in the pathogenesis of sensory dysfunctions in PD [14]. Some authors demonstrated that in a gravity environment, healthy subjects mainly rely on somatosensory information in order to maintain an upright posture [15] and that artificially impairing proprioception worsens postural stability, particularly reducing the COP displacements in response to external perturbations during visual deprivation [16]. In fact, in PD, a defective scaling and habituation of postural reactions during either neck or leg vibration has been revealed [17, 18].

Beside the poor effect of dopaminergic treatment in improving balance problems, the effects of physical activity and exercise programs on improving balance [19–21] and quality of life [21] have been extensively proven in patients with PD. However, the possibility of enhancing training effects, by combining intervention with proprioceptive orthotic, has never been tested.

Proprioceptive rehabilitation aims to improve or enhance the perception of proprioceptive signals and their central integration, thus possibly compensating the impaired "gating" function of the basal ganglia [22]. Furthermore, external sensory signals (peripheral sensory feedback) can be used to compensate the abnormal sensorimotor integration in PD patients [23]. Moreover, muscle spindle endings respond to proprioceptive stimulations with an increased muscular activation, thus producing a tonic contraction on the stimulated muscle [24, 25].

In detail, the sensory-motor (SM) orthotic [Fig. 1] used in this study, combines biomechanical and sensory-motor input on the plantar surface of the feet by modulating through function activation of specific muscle groups. In fact, it has been demonstrated that tendon stimulation has an influence on muscular tone with increased voluntary activation and improved muscle velocity and strength [26, 27]. The proposed novel orthotic is composed of four spots, which through muscle tendon stimulation exerts a compression which activates anticipated muscle contractions: a) the medial spot which activates the medial muscular kinetic chain (tibia, adductor, paraspinal muscles); b) the lateral spot which activates the lateral muscular kinetic chain (peroneal, abductor, iliotibial, paraspinal muscles muscles); c) the metatarsal and under digital spots which stimulate the extensor muscular kinetic chain (fingers flexors, triceps, femoris biceps s, gluteus and paraspinal muscles). No prior study of SM orthosis on balance dysfunctions in PD has been published before. We have no evidence to support this hypothetical mechanism of function.

The present study aims (i) to explore the feasibility and the safety of using a Sensory-Motor orthotic as a tool of increasing plantar proprioceptive information and (ii) investigating if the combination of the SM orthotic, with a balance training, might enhance postural control, balance and gait in a small group of PD patients.

Methods

Participants

A total of 30 patients with idiopathic PD, according to the United Kingdom Parkinson's Disease Society Brain Bank criteria [28], were recruited from the Department of Neurorehabilitation in Villa Margherita, Arcugnano (Vicenza), Italy.

Participants were enrolled in the study if they met the following inclusion criteria: stage 3 of the Hoehn and Yahr (H&Y) scale, Mini Mental State Examination (MMSE) [29] with score > 24, ability to walk independently without a walking aid and to attend a physiotherapy venue, the absence of serious co-morbidities (cardiac, pulmonary or orthopaedic diseases) that could impact gait or balance. Patients were excluded if they suffered from major depression (diagnosed by means of a Diagnostic and Statistical Manual of Mental Disorders - DSM V criteria), had Deep

Fig. 1 Example of the sensory-motor orthotic

Brain Stimulation implants, were medically unstable or had medication induced (dyskinesias), had an history of other conditions affecting stability (e.g., poor visual acuity or vestibular dysfunction, neuropathy or sensory ataxia). In this pilot study, we recruited patients in stage 3 of H&Y scale exclusively. Thus, all patients were in a moderate stage of PD and had balance problems probably due to abnormal sensory motor integration. In addition, as this was a pilot study, we selected only PD in H&Y = 3 because we wanted to limit, as much as possible, the heterogeneity amongst the patients recruited. At the end of the screening phase, twenty patients with PD were enrolled in the study and ten patients were excluded because six participants did not meet the inclusion criteria (*n* = 1 had MMSE > 24; *n* = 2 needed assistance during walking; *n* = 2 had DBS and *n* = 1 had severe dyskinesia) and four patients were unable to attend the physiotherapy program due to personal reasons.

Study design (Fig. 2)

In this pilot study, after the initial screening procedures, participants were randomly allocated into two groups: (i) *The Experimental group*, in which participants were asked to wear a SM orthotic before and after the training program or (ii) *The Control group*, where subjects performed an identical training program without wearing any kind of orthotics.

All the clinical and instrumental assessments were performed at baseline (PRE - within 1 week before the beginning of the intervention), after the end of the training (POST - within two days after the last training session) and 4 weeks after the completion of the rehabilitative program (FU - follow-up assessment). Randomization procedure, conducted by a third party, was used to allocate participants to one of the two treatment groups (i.e., experimental or control groups). The assessors were blinded to the group allocation during the whole duration of the study. The study coordinator responsible for the SM orthotics supervision was not blinded to the group allocation, but he was not involved in rehabilitation procedures or outcome assessments. The physiotherapists providing the training program were blinded and not involved in other aspects of the trial (i.e., aims, hypothesis or predictions of the study were not disclosed).

Interventions

All PD subjects underwent a training balance program composed by 10 sessions (5 days a week for 2 weeks). Each session lasted 50 min and the exercises were identical for both groups. Table 1 details the type of daily balance training program provided by the hospital physiotherapists in accordance to the Koninklijk Nederlands Genootschap voor Fysiotherapie - KNGF Guidelines for Physiotherapy. At the beginning of each session, participants were

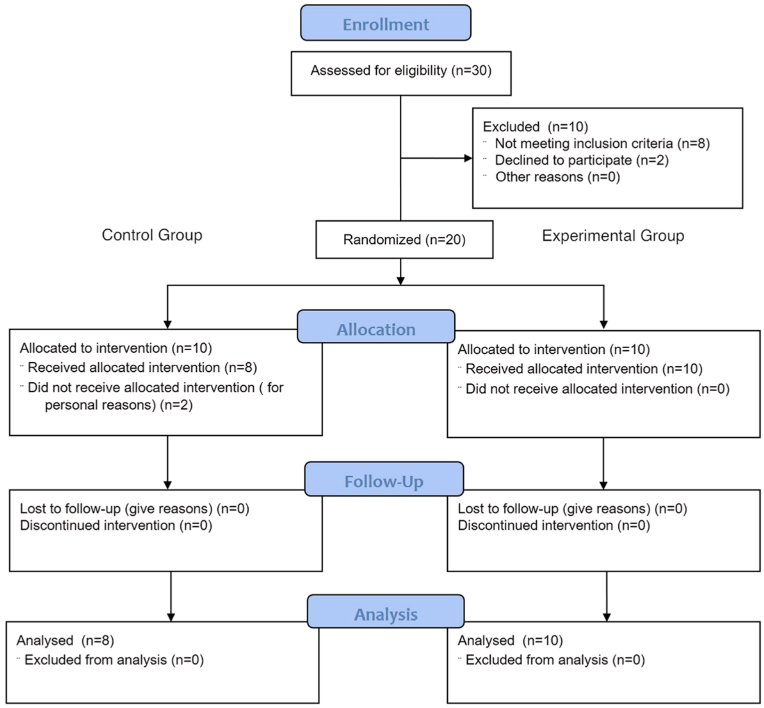


Fig. 2 CONSORT 2010 Flow Diagram. Effects of a Sensori-Motor Orthotic on Rehabilitation of Postural Instability in Parkinson's disease: a Phase II Randomized Pilot Study

Table 1 KNGF Guidelines: physiotherapy program for balance training

Improvement of physical capacity	To maintain or to improve physical capacity with training of aerobic muscle strength (with the emphasis on the muscles of the trunk and legs), joint mobility (among others, axial) and muscle length (among others, muscles of the calf and the hamstrings, flexor and extensor of the knee)
Improvement of the transfers	To train transfers by applying cognitive improvement strategies and cues to initiate and continue movements
Normalizing body posture	To prevent or treat postural deformities with exercises for postural alignment and coordinated movements
Training balance	To optimize balance during the performance of activities in static and dynamic conditions with exercises for training strength and perturbation-based balance training with emphasis of functional reaching test in protected condition and how to activate postural responses to perturbation. Falls prevention strategies.
Gait training	To walk safely and to increase (comfortable) walking speed with exercise walking with the use of cues and cognitive movement strategies and to train muscle strength and mobility of the trunk and upper and lower limbs.

required to sign a form in order to attest their attendance. The physiotherapy protocol included 30 min of exercises designed to improve balance. Precisely, intervention included a perturbation-based balance-training program, where patients were asked to voluntarily reach their limit of stability. During these exercises, participants were required to concentrate and activate the appropriate postural responses in order to react to the external perturbations. Balance training was preceded by warming up and stretching exercises and followed by a cooling down period. Each phase lasted approximately 10 min. Subjects who enrolled in the Experimental group were required for the entire duration of the study (2 weeks) to wear the SM orthotics all day long except during the training balance sessions.

Clinical and instrumental tests

Clinical assessments

Motor impairment was assessed during the III section (motor examination) of the Unified Parkinson's disease Rating Scale (UPDRS) [30], the Berg Balance Scale (BBS) [31], the Timed Up and Go (TUG) [32], and the Six-minute Walking Test (6mWT) [33]. We also quantified the health-related quality of life in all participants using the Parkinson's Disease Questionnaire (PDQ-39) [34]. All adverse events such as injuries, distress and hospital admissions were verified by phone interviews and recordings taken during the pilot study period.

Posturography assessments

Static posturography was assessed in keeping with current guidelines [35]. The Center of Pressure (CoP) excursion was recorded by means of a force platform (Milletrix model 2.0–Rome, Italy). All data were collected with a 50 Hz sampling frequency. The CoP was recorded during an upright stance in a quiet room. Participants were instructed to stand erect, with their arms alongside their body. Their feet were kept at an angle of about 30° opened to the front and with the heels approximately 3 cm apart. Furthermore, an instrumental version of the functional reaching test (FRT) [36] was executed by asking the subject to elevate their arm to shoulder's height and then to perform a maximum forward reach, while maintaining the heel on the platform with their feet planted in a standing position.

In all the tasks, data was collected for 51.2 s, in both eyes opened (EO) and eyes closed (EC) conditions. The following parameters were taken into account: the sway area (mm^2), measured as the 95th percentile of an ellipse fitted to the overall CoP trace; COP velocity (mm/s) and the Romberg index. These parameters were chosen as a tool to evaluate CoM displacement during sway as a response to perturbation.

Statistical analysis

Demographic and clinical characteristics between the two intervention groups of PD (Experimental and Control) were tested by means of Chi-square (χ^2) test (gender) and *t*-test (age, UPDRS - Part III Motor, and disease duration) statistics. All clinical and instrumental variables were examined for normality (Shapiro-Wilk W test), and mean and standard deviation (SD) were calculated. For the analysis a Repeated Measures (RM) Analysis of Variance (ANOVA) was used with Group (Experimental, Control) as between-subjects factor and Time (Baseline, Post and Follow-up) as within-subjects factor. The pre-defined level of significance was set at $p < 0.05$. Post hoc analysis of significant interactions was performed by means of -tests applying the Bonferroni correction for multiple comparisons when necessary. All statistical analyses were performed with SPSS 22.0.

Results

At the end of the study, two patients were excluded from the analysis because they dropped out from the training protocol due to personal reasons. Patients with PD enrolled into two groups, did not differ for demographic, clinical characteristics (Table 2) and clinical assessment (p always > 0.05) recorded at the baseline. For the sample as a whole, 100% of intervention sessions were delivered across study arms. No major adverse event or death was recorded during the study period.

Table 2 Baseline demographic and clinical variables of the two groups enrolled in the study

	EXP Group mean ± SD	CTRL Group mean ± SD	Statistics Baseline
Gender (M/F)	7/3	5/3	
Age (yr)	69.18 ± 7.61	63.37 ± 6.89	$p = 0.24$
Height (cm)	160.91 ± 9.58	160.62 ± 14.74	$p = 0.96$
Weight (kg)	69.54 ± 13.33	67.62 ± 8.31	$p = 0.72$
Disease duration (yr)	7.82 ± 4.00	8.12 ± 2.90	$p = 0.86$
Falls (n)	1.45 ± 2.16	0.87 ± 0.99	$p = 0.07$
Levodopa (mg/day)	455.32 ± 355.49	409.19 ± 340.68	$p = 0.74$
• *Dopamine agonist (LEDD mg)*			
Pramipexole E.R.	$n = 2$	$n = 3$	N.A.
Ropirinole E.R.	$n = 3$	$n = 3$	N.A.
Rotigotine ($n = 1$)	$n = 1$	$n = 1$	N.A.
Rasagiline ($n = 1$)	$n = 2$	$n = 1$	N.A.
• *Other drugs (LEDD mg)*			
Entacapone	$n = 1$	$n = 2$	N.A.
Selegiline	$n = 1$	$n = 2$	N.A.
Amantadine	$n = 2$	$n = 2$	N.A.

Exp, Experimental; CTRL, Control; M, Male; F, Female; Yr, Years; Cm, centimeters; Kg, Kilograms; Mg = Milligrams; N, number; ER = Extended Released; N.A., Not Applicable

Clinical assessments

All data [mean ± standard deviation (SD)] collected at baseline, post and follow-up examinations are reported in Table 3. Statistical analysis showed a positive effect of the balance-training program with no differences between groups in all the variables considered. Precisely, the mean score of UPDRS-III was significantly reduced in the Experimental as well as in the Control groups. RM-ANOVA revealed a significant effect of TIME ($p < 0.01$), without any significant Time X Group interaction ($p = 0.41$). Interestingly, improvements were seen both immediately after the training and at the FU examination (p always < 0.01).

For the tests assessing dynamic balance performance (BBS and TUG), RM-ANOVA showed a main effect of TIME (BBS: $p < 0.01$ and TUG: $p < 0.01$) with no Time X Group interaction. In details, for BBS a significant increase of the total score was seen at Post ($p < 0.01$) and at the FU ($p < 0.01$) evaluations as well as for TUG, where a significant decrease of time in performing the test was seen immediately after the training ($p = 0.01$) and 1 month later (FU: $p < 0.01$). No Time X Group interaction was revealed by the statistical analysis. Similar results were also found in gait resistance performance. Indeed, the analysis of 6MWT data showed a significant effect of Time ($p = 0.02$) with no differences between the two groups. Thus, an overall improvement was seen immediately after the training (Post: $p = 0.03$) and it was maintained at the FU examination ($p = 0.01$). Balance and gait improvements were also confirmed by a significant decrease of fall rate. Indeed, RM-ANOVA showed a main effect of Time ($p < 0.01$) with an improvement at post ($p = 0.01$). However, no significant Time X Interaction was recorded by the statistical analysis ($p = 0.55$). Finally, positive changes on participants' QoL recorded by means of PDQ-39 questionnaire were seen at the end of the training (Post: $p = 0.03$) as well as the following testing time (FU: $p = 0.02$). Indeed, RM-ANOVA revealed a significant effect of TIME ($p = 0.02$) with no significant Time X Group interaction.

Posturography

Statistical analysis did not reveal significant changes for sway area recorded in the quiet stance test (p always >0.05) in both conditions (EC and EO). However, RM ANOVA showed a significant main effect of Group ($p = 0.04$) and a significant Group x Time interaction ($p = 0.03$) for 95% confidence ellipse area data obtained during the FRT test in the EC condition. Furthermore, post-hoc analysis revealed that only the experimental group obtained a significant improvement at the end of the training period ($p = 0.02$) and this result was maintained at the follow-up examination (Fig. 3). Similar results were also found for the values obtained for the Romberg index. Indeed, statistical analysis (RM-ANOVA) revealed a significance of the factor Group ($p = 0.04$) as well as a significant Group x Time interaction. Post-hoc analysis showed that only in the experimental group, velocity increased at the end of the training ($p = 0.03$) and at the follow-up evaluation ($p = 0.04$) (Fig. 4). No significant changes were detected during static and dynamic (FRT) evaluation under EO condition. Finally, no significant changes were found for CoP velocity in any experimental condition (EC and EO).

Discussion

The aim of the present study was to explore the feasibility and the safety of using a Sensory-Motor orthotic as a tool for increasing plantar proprioceptive information. Furthermore, it was carried out to verify if the combination of the SM orthotic, with a rehabilitative intervention, could enhance postural control, balance and gait in a group of subjects with PD.

The rehabilitative program was delivered successfully, with a good level of adherence rate confirmed by the patient's participation and involvement. On the whole, our results demonstrated that combining balance training with a sensory-motor orthotics in a rehabilitation setting is feasible and might lead to some clinically meaningful effect in PD patients with postural instability. However, only subjects enrolled in the experimental protocol

Table 3 Clinical variables of the two groups enrolled in the study and their comparisons at each time point

	PSM Group	CTRL Group	Statistic post-hoc TIME
Motor UPDRS section III at T0-Baseline	40.87 ± 6.01	39.00 ± 11.89	
Motor UPDRS section III at T1-Discharge	37.12 ± 6.66	36.90 ± 12.02	$p < 0.01$
Motor UPDRS section III at T2-Follow up	35.55 ± 6.57	36.80 ± 11.80	$p < 0.01$
Berg Balance Scale T0-Baseline	45.63 ± 5.92	45.12 ± 4.58	
Berg Balance Scale T1-Discharge	49.3 ± 3.15	47.12 ± 5.05	$p < 0.01$
Berg Balance Scale T2-Follow up	50.1 ± 2.72	49.37 ± 5.35	$p < 0.01$
Falls T0-Baseline	1.45 ± 2.16	0.87 ± 0.99	
Falls T1-Discharge	0.45 ± 1.03	0.12 ± 0.31	$p < 0.01$
Falls T2-Follow up	0.00 ± 0.00	0.00 ± 0.00	N.A.
Timed Up and Go T0-Baseline	13.08 ± 2.17	13.8 ± 3.43	
Timed Up and Go T1-Discharge	12.13 ± 1.35	12.8 ± 2.81	$p = 0.01$
Timed Up and Go T2-Follow up	10.81 ± 1.07	13.2 ± 2.75	$p < 0.01$
6MWT T0-Baseline	305.64 ± 48.89	319.8 ± 48.59	
6MWT T1-Discharge	335.64 ± 44.09	332.5 ± 66.00	$p = 0.03$
6MWT T2-Follow up	342.2 ± 59.99	328.38 ± 70.18	$p = 0.01$
PDQ-39 T0-Baseline	57.7 ± 22.93	59 ± 14.38	
PDQ-39 T1-Discharge	54.36 ± 24.47	49.5 ± 20.52	$p = 0.03$
PDQ-39 T2-Follow up	52.1 ± 27.44	51.25 ± 19.46	$p = 0.02$

Exp, Experimental, *CTRL* Control, *UPDRS* Unified Parkinson Disease Rating Scale, *6MWT* Six Meters Walking Test, *PDQ-39* Parkinson's Disease Questionnaire-39 items. N.A., not applicable

P values represent the post hoc analysis (T0 vs T1 and T0 vs T2) when a main effect of TIME was detected with Repeated Measures ANOVA

significantly improved their limit of stability measured by a stabilometric platform. Precisely, an increase of sway area values, obtained during the instrumental functional reaching test, and an improvement of the Romberg index were seen only in the experimental group immediately after the training and follow-up evaluation. As stated in the introduction, PD-related abnormality in proprioception might manifest itself as alteration of kinesthesia (for a review see [13]. Indeed, PD patients have an impaired sense of the timing [37] and discrimination [38] of proprioceptive inputs, which can also lead to deficient compensation of mechanical perturbations, especially during the activation of anticipatory postural adjustments [39]. The enhancement of the proprioceptive inflow, as that induced by the sensory-motor orthotic used in this study, might overcome the subtle impairment in kinesthesia, as previously argued [37]. PD patients used to have a reduced limit of stability particularly during dynamic conditions, thus pointing to dynamic posturography as a better instrument of capturing improvements in

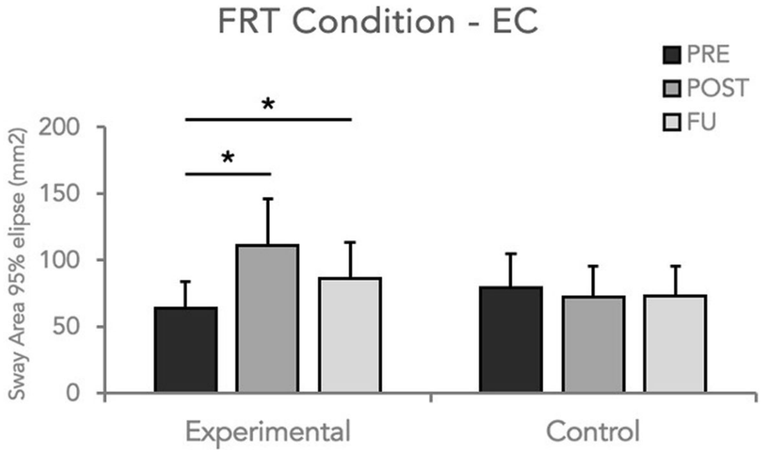


Fig. 3 Sway area values during instrumental FRT-EC condition of the two groups enrolled in the study at each time point

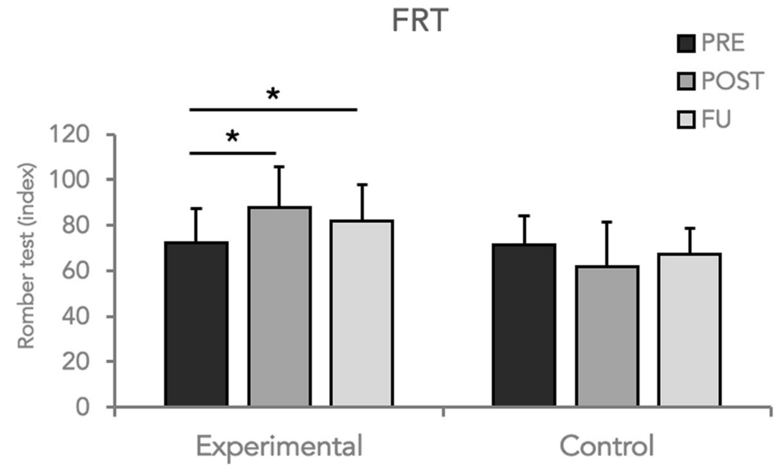


Fig. 4 Romberg index values during FRT condition of the two groups enrolled in the study at each time point

balance [5, 35]. It is well-known that anticipatory postural adjustments and reactive postural reactions in PD are compromised, in the sense that they are reduced in amplitude and velocity [39]. So another possible mechanism of action could be related to the influence on muscles of proprioceptive stimulation exerted by the SM orthotic, since tendon stimulation [40, 41] seems to increase muscular tone and velocity promoting the activation of anticipatory postural adjustments and reactive postural reactions. Finally, it is important to notice that significant changes in the posturographic data during the FRT in the experimental group were seen only when patients were required to execute the test with their eyes closed, a set-up relying on proprioceptive information. This fact might suggest an improvement of proprioceptive signals derived from the effect of the SM orthotic.

This pilot study has a number of limitations. Firstly, even if testing occurred at the peak dose of the morning medications, we cannot rule out the bias introduced by fluctuations in levodopa plasmatic concentration. Secondly, even though the sample size allowed the detection of significant changes, here we reported results obtained in a small group of patients, thus our results have to be replicated by larger trials. Thirdly, due to the shortness of training and the follow-up examination, we did not evaluate changes in fall rates. Further study should have to include episode supervision of falls. Fourthly, even if the physiotherapy program for balance training was conducted in accordance with published guidelines, the execution of exercises were influenced by therapists expertise and patients' motivation, meaning that our protocol does not necessarily reflect the clinical practice in other parts of the world. Fifthly, we did not include in this pilot study, an aged matched control group for evaluating changes in balance related to basal ganglia dysfunction, so we cannot conclusively ascribe our findings to basal ganglia malfunction in PD.

Finally, we want to underline that postural control measured by dynamic posturography might give more information about mechanisms of postural instability in PD than static posturography. Performing the FRT might not be as good as a test measured by dynamic posturography.

Conclusions

This pilot study shows that a tailored balance training, in association with the sensory-motor orthotic, appears to be safe and feasible and is able to positively impact on mobility, balance, gait and quality of life. This preliminary study provides promising data on the feasibility and safety of our protocol, thus supporting the development of a large scale Randomized Control Trial. Future studies are certainly needed and will expand our knowledge on the mechanisms of action of SM orthotic, on the time needed to achieve a meaningful improvement and its long-term duration.

Effects of a balance-based exergaming intervention using the Kinect sensor on posture stability in individuals with Parkinson’s disease: a single-blinded randomized controlled trial

Abstract

Background: The present study examined the effects of a balance-based exergaming intervention using the Kinect sensor on postural stability and balance in people with Parkinson’s disease (PD).

Methods: We conducted a subject-blinded, randomized controlled study. Twenty people with PD (Hoehn and Yahr stages I through III) were recruited and randomly assigned to either a balance-based exergaming group ($N = 10$) or a balance training group ($N = 10$) for an 8-week balance training period. Postural stability was assessed using the limits of stability (LOS) and one-leg stance (OLS) tests. Balance was assessed using the Berg Balance Scale (BBS) and the timed up and go (TUG) test. Participants were assessed pre- and post-training.

Results: After training, participants in the balance-based exergaming group showed significant improvements in LOS performance, and in the eyes-closed condition of the OLS test. Both training programs led to improvements in BBS and TUG performance. Furthermore, balance-based exergaming training resulted in significantly better performance in directional control in the LOS test (78.9 ± 7.65 %) compared with conventional balance training (70.6 ± 9.37 %).

Conclusions: Balance-based exergaming training resulted in a greater improvement in postural stability compared with conventional balance training. Our results support the therapeutic use of exergaming aided by the Kinect sensor in people with PD.

Trial registration: ClinicalTrials.gov.NCT02671396

Keywords: Balance training, Exergaming, Postural stability, Parkinson’s disease

Abbreviations: BBS, Berg Balance Scale; BE, Balance-based exergaming; BT, Balance training; COG, Center of gravity; LOS, Limits of stability; OLS, One-leg stance; PD, Parkinson's disease; TUG, Timed up and go; VR, Virtual reality

Background

People with idiopathic Parkinson's disease (PD) commonly exhibit postural instability during daily activities [1]. PD-related balance impairment is associated with a loss of mobility and increased likelihood of falls, and can cause marked disability [2, 3]. To ameliorate postural instability, techniques using external feedback with cueing or sensory stimuli have been investigated [4, 5]. Several studies suggest that external feedback may initiate other neural pathways and play a significant role in the volitional control of movements for people with PD [6, 7].

Virtual reality (VR) technologies such as exergaming may have therapeutic value in the treatment of postural instability [8–10]. VR is a technology that allows the user to interact directly with a computer-simulated environment [11]. Exergames are computer games that are controlled by body movements. VR and exergaming can provide augmented feedback in real time, while a person performs specific motor tasks [12]. Opportunities for repeated accurate performance can be incorporated into VR and exergaming to enhance motor learning [7, 13]. Moreover, VR games can be effective for retaining participants' interest and motivation.

A recent meta-analysis suggested that exergaming may provide an appropriate training approach to improve balance and functional mobility in healthy older people [14]. These findings raise the possibility that exergaming might also provide an approach for improving postural instability for people with PD. A previous study examined the effects a 6-week home-based balance training program using the Wii Fit game for a total of 18 training sessions on balance and functional abilities in people with PD, compared with a group of paired healthy participants [15]. Another study investigated the effects of Wii-based training compared with conventional balance training for 7 weeks (a total of 14 training sessions) on activities of daily living in people with PD [16]. Both studies revealed positive effects of exergaming on balance, functional abilities and activities of daily living among people with PD. However, positive effects were found only within groups, with no between-group differences observed in a comparison with the control group. The absence of between-group differences may have resulted from an inability to capture the full-body motion involved in postural control, or the lack of a sufficiently sensitive sensor to accurately measure motion. The shortcomings of the Wii system's sensors may limit its potential as an effective intervention [17].

A new exergaming system was recently developed using the Kinect sensor. The Kinect sensor is a low-cost device that can provide measurements for most of the main human joints. Previous studies reported that a kinematic measurement method using the Kinect sensor was accurate and reliable for measuring postural control [18, 19]. These findings suggest that the Kinect sensor could provide a useful tool for therapeutic use. However, there has been little research into the therapeutic use of the Kinect sensor to date.

The present study sought to test a therapeutic application of exergaming using the Kinect sensor. We examined the effects of an 8-week balance-based exergaming program developed in our lab, compared with an 8-week period of conventional balance training (16 training sessions), on postural stability and balance in people with PD. We hypothesized that participants who underwent an 8-week balance-based exergaming intervention would demonstrate superior performance on measures of postural stability and balance, compared with those who received balance training.

Methods

Participants

Participants were recruited from Mackay Memorial Hospital in Taipei. Outpatients with PD were informed about the study by a neurologist. Eligibility required a diagnosis of idiopathic PD according to the United Kingdom Brain Bank Criteria [20] by the same neurologist. Information on age, gender, the more affected side, and disease duration were obtained through patient interviews and from medical charts. All participants met the following inclusion criteria: (1) Hoehn and Yahr stages I through III, (2) a score of ≥ 24 on the mini-mental state examination, (3) stable medication usage and (4) standing unaided to perform the measurement and training. The exclusion criteria were as follows: (1) histories of other neurological, cardiovascular, or orthopedic diseases affecting postural stability and (2) uncontrolled chronic diseases. In total, 48 individuals were identified as potential participants for this study. Of these, 22 participants gave informed consent and participated in the study.

Study design

This study was a subject-blinded, randomized controlled trial. The study protocol was approved by the Institutional Review Board of Mackay Memorial Hospital (reference number: 13MMHIS120) and was explained to all participants before their participation. The study was performed in accordance with the Declaration of Helsinki. Block randomization was used to assign participants to either the balance-based exergaming (BE) or the conventional balance training (BT) group. Assignment was performed by an independent person who selected one of a set of sealed envelopes 30 min before the intervention began. Participants in the BE and BT groups received an 8-week balance-based exergaming intervention, and conventional balance training, respectively. Measures of postural stability and functional balance were measured pre- and post-training. The measurement and intervention were conducted with participants in the “on” state, when they were moving freely and easily without dystonia, excessive rigidity or tremor. The data were collected in a university laboratory.

Intervention

Participants in both groups underwent balance training for 50 min per session, two sessions every week, for 8 weeks. Each training session began with a 10-min warm-up and ended with a 10-min cool-down. Both the warm-up and cool-down periods focused on stretching exercises of the trunk and extremities.

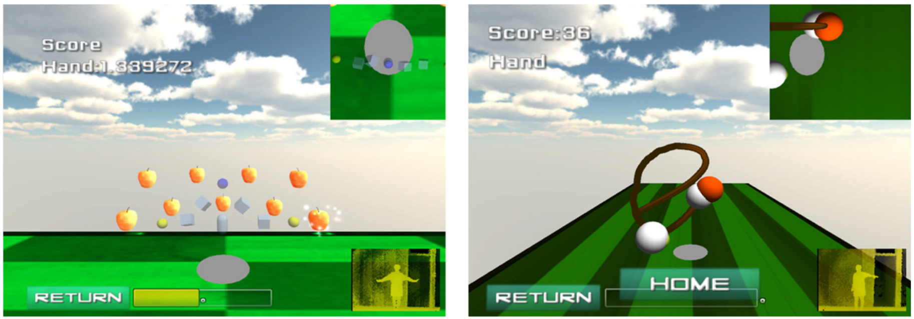
Participants in the BE group received a 30-min balance-based exergaming intervention using the Kinect sensor (Microsoft Corporation, Redmond, WA, USA). The Kinect sensor incorporates infrared light and a video camera, which creates a 3D map of the area in front of it. This device provides full-body 3D motion capture. Four exergaming programs were used for training (Fig. 1), designed to incorporate an appropriate level of challenge to match the ability and fitness of people with PD. The first program was called Reaching task 1. In this task, participants were asked to reach toward a stationary target at a given location. The second program was called Reaching task 2. Participants were asked to track a moving object by lengthening the arm and immersing the hand into the object as it flew in 3D space. The third program was called Obstacle avoidance. Participants were instructed to avoid upcoming obstacles that approached from varying directions at random, by moving the body right/left or up/down. The final task was called Marching. Participants were instructed to step alternately without going forward or backward while following dynamic bars that were automatically rising and falling at a predetermined speed and frequency. During the training duration, the challenge level was increased progressively by adjusting the amplitude, frequency, speed, complexity and number of hints. The details of the exergaming programs are shown in Table 1.

Participants in the BT group underwent a 30-min conventional balance training session. The training program included reaching activities, weight-shifting activities and marching activities. The general training protocols used for the BT group were the same as those used for the BE group. The challenge level was increased progressively by changing the base of support, speed, complexity and deprivation of sensory inputs.

Outcome measures

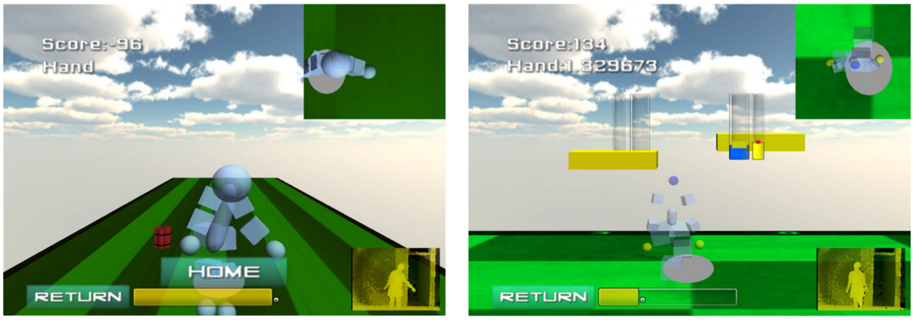
Postural stability

The limits of stability (LOS) and one-leg stance (OLS) tests were used to assess postural stability in this study. Participants were harnessed into a suspension system to prevent falls when performing the tasks. LOS performance



a Reaching task 1 (stationary object)

b Reaching task 2 (moving object)



c Obstacle avoidance

d Marching

Fig. 1 Screen shots of interaction with the exergaming program. Four exergaming programs, Reaching task 1 (**a**), Reaching task 2 (**b**), Obstacle avoidance (**c**) and Marching (**d**), were designed and used for training

Table 1 Program of balance-based exergaming intervention

Program	Action	Progression	Motor demand
Reaching task 1	Standing in a given area and reaching toward a stationary target at different heights, depths and in different directions	• Reaching length • Number of targets • Range of distribution • Amount of repetition	• Weight shifting • Challenging limits of stability • Functional transitions
Reaching task 2	Standing in a given area and tracking a moving object while extending arm and immersing the hand into the object as it flew in 3D space	• Speed • Moving range • Pathway pattern • Remembered sequence or course of trajectory	• Weight shifting • Arm coordination • Advance motor planning
Obstacle avoidance	Standing in a given area and preparing to avoid upcoming obstacles that randomly approached from varying directions by moving body sideways or up/down	• Obstacle hitting ratio • Speed • Dual task • Hitting direction	• Quick change strategy • Movement adaption • Agility
Marching	Alternating steps without going forward while following dynamic bars that automatically rose and fell at a predetermined speed and frequency	• Frequency • Gap between steps	• Functional stepping • Leg coordination • Single limb support

was measured using the Smart Balance Master (NeuroCom International Inc., Clackamas, OR, USA) instrument to extract quantitative data [21–24]. The LOS test provides an assessment of the ability to intentionally displace the center of gravity (COG) to the participant's stability limits without losing balance. In this task, participants were asked to quickly transfer their COG, while standing on stable force plates, toward eight targets spaced at 45° intervals around the COG, represented on a computer monitor. All participants underwent one practice trial followed by one test trial. In the LOS test, we measured reaction time (the time from the presentation of a start cue to the onset of the voluntary shifting of the participant's COG toward the target position), movement velocity (average speed of COG movement based on the middle 90 % of the distance, measured in degrees per second), end point excursion (percentage of the distance achieved toward a target on the initial movement) and directional control (100 % being a straight line from the center of pressure to the intended target). The validity and reliability of the LOS test in people with neurological disease has been well established [25–27].

The OLS test is an assessment of postural steadiness [15, 28–31]. Participants were asked to cross their arms over the chest, and to stand on either the less or more affected leg, with the other leg raised so that the raised foot was near but not touching the ankle of the stance leg. The assessor timed the OLS test until participants either: (1) uncrossed the arms, (2) moved the stance leg, (3) moved the raised leg touching the floor or the stance leg, (4) opened the eyes on eyes-closed trials or (5) reached a maximum of 30 s. Each participant performed three trials with the eyes open, and three trials with the eyes closed. Data were averaged from the three trials. A previous study found a high degree of reliability (ICC = 0.87) in the OLS test in older adults [32].

Functional balance

The Berg Balance Scale (BBS) and the timed up and go (TUG) test were used to assess functional balance. The BBS comprises a set of 14 balance-related tasks, ranging from standing up from a sitting position, to standing on one foot. The degree of success in each task is given a score from zero (unable) to four (independent), and the final measure is the sum of all scores. The highest possible score on the BBS is 56, which indicates excellent balance. The validity and reliability (ICC > 0.95) of BBS scores in people with PD has been established in several studies [33–35]. The TUG test is a mobility test requiring both static and dynamic balance. During the test, the assessors measured the time participants took to rise from a chair, walk 3 meters, turn around, walk back to the chair, and sit down. Each participant performed three trials of the TUG test. Data were averaged from the three trials. The TUG test has previously been found to have high validity and reliability (ICC > 0.87) for assessing balance in people with PD [36, 37].

Sample size

The sample size calculation was based on a pilot study that tested eight participants at Hoehn and Yahr stages 1 and 2, indicating a difference of 0.2 s between pre- and post-training on reaction time in the LOS test. Based on this difference, a sample size calculation indicated that 20 participants would be sufficient for 85 % power ($\alpha = 0.05$).

Statistical analysis

All analyses were performed using the SPSS 20.0 statistical package (SPSS Inc., Chicago, IL, USA). Descriptive statistics were generated for all variables, and distributions of variables were expressed as the mean ± standard deviation. Because of the relatively small number of participants included in the current study ($N < 30$) and since the results of a Shapiro-Wilk test did not allow us to assume that the data were normally distributed, nonparametric tests were employed. Comparison of two groups for general characteristics was made using chi-square or Mann-Whitney *U* test for categorical or continuous variables, respectively. The Friedman test, followed by a post hoc test, was used to determine differences in each dependent variable. The Wilcoxon signed-rank post hoc test was performed for within-group comparisons and the Mann-Whitney U post hoc test was performed for between-group comparisons. The statistical significance was set at $P \leq 0.05$.

Results

A total of 48 individuals were screened and 22 enrolled between 2013 and 2014. Of these, 11 were assigned to the BT group, and 11 were assigned to the BE group. Of 22 participants, two did not complete the intervention (one in the BT group and one in the BE group). A flow diagram of the study protocol is shown in Fig. 2. The 20 participants who completed the intervention attended all intervention sessions. None of the participants reported any adverse events.

The demographic characteristics of participants in both groups are presented in Table 2. Demographic differences between the two groups were not significant. Moreover, differences in all pre-intervention-selected outcome measures in the two groups were not significant (Table 3).

The results of the interventions are presented in Table 3. Analysis of selected outcomes using the Friedman test revealed a significant effect of intervention type on reaction time, endpoint excursion and directional control in the LOS test, and in the less affected leg in the eyes-closed condition in the OLS test, the BBS and the TUG test. Within-group post hoc analysis revealed that balance-based exergaming training significantly improved LOS performance (improving reaction time from 0.96 ± 0.33 to 0.74 ± 0.24 s, end point excursion from 75.2 ± 12.48 to 84 ± 12.04 % and directional control from 75.7 ± 8.78 to 78.9 ± 7.65 %) and OLS on the less affected leg in the eyes-closed condition (from 3.35 ± 2.85 to 6.1 ± 8.65 s). Compared with the BT group (70.6 ± 9.37 %), the BE group (78.9 ± 7.65 %) exhibited better performance in directional control of LOS post-training. Functional balance in both groups, as measured by the BBS and the TUG test, was improved significantly post-training compared with pre-training. However, no significant differences were found between groups.

Discussion

This study produced two main findings: (1) balance-based exergaming training had a greater effect on postural stability compared with conventional balance training; and (2) both training programs improved functional balance in people with PD.

The current study tested two balance training programs with similar training protocols. A recent meta-

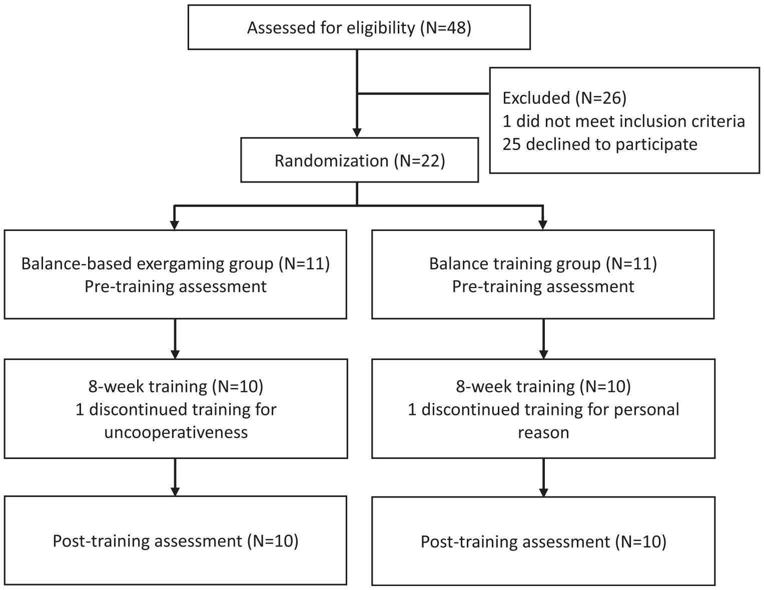


Fig. 2 Flowchart of the experimental design

Table 2 Baseline demographics and clinical characteristics of the subjects

	Balance-based exergaming group (*N* = 10)	Balance training group (*N* = 10)	*P*
Age (years)	67.5 ± 9.96	68.8 ± 9.67	0.67
Sex (male/female)	9/1	7/3	0.58
Disease duration (years)	4.03 ± 3.74	5.22 ± 4.85	0.34
Hoehn and Yahr stage	1.6 ± 0.84	1.4 ± 0.52	0.73
Mini-Mental State Examination	27.4 ± 2.59	28.2 ± 1.99	0.40
More affected side (right/left)	8/2	5/5	0.35

Data are presented as the mean ± standard deviation or proportion

analysis examined the BBS, postural sway, TUG, and Functional Reach test as measures of postural stability, reporting that exercise therapy is an important treatment option for improving postural stability in people with PD [38]. The findings suggested that exercises containing a balance component were most beneficial in improving postural stability in people with PD [38]. In the current study, we used the LOS and OLS tests to measure postural stability, and the BBS and TUG tests to measure functional balance. The current findings were in line with the findings of Klamroth et al., who reported that balance training was beneficial for performance in the BBS and TUG tests [38]. Our findings revealed that only balance-based exergaming training produced positive effects on LOS and OLS, with particularly strong effects on directional control in LOS. These findings suggest that exergaming training using the Kinect sensor contributed to the beneficial gains we observed. As a therapeutic tool, the Kinect sensor can provide specific motor practice using full-body motion capture, which offers precise real-time information to guide performance and monitor body movement. Previous clinical trials indicated that exergaming programs using the Kinect sensor resulted in accurate capture of movement components [39, 40].

Our results revealed within-group improvements on most measures of postural stability during the exergaming intervention training period. Our exergaming programs involved various balance challenges. This may have contributed to our positive findings, involving actions focused on agility, challenging postural or locomotor-like skills, and reaching away from the base of support. All of these are involved in whole-body movements. In addition, the repetitive, real-time feedback and graded complexity in our exergaming programs may have contributed to the positive effects of training reflected in LOS performance. However, the movement velocity of LOS remained unchanged after exergaming training. Persistent bradykinesia [41] and a choice to focus on improving accuracy rather than faster motor performance among people with PD are possible reasons for our movement velocity findings [21]. The current results also revealed better OLS performance in the eyes-closed condition after exergaming training. A previous study using a Wii-based system reported similar results [15]. Because participants needed to focus on

Table 3 Outcome measures for each group

	Balance-based exergaming group (*N* = 10)		Balance training group (*N* = 10)		Friedman test
	Pre-training	Post-training	Pre-training	Post-training	*P*
Limits of stability					
Reaction time (sec)	0.96 ± 0.33	0.74 ± 0.24*	0.88 ± 0.24	0.79 ± 0.18	<0.001
Movement velocity (deg/sec)	3.37 ± 1.35	3.83 ± 0.97	4.19 ± 1.54	4.57 ± 1.41	0.07
Endpoint excursion (%)	75.2 ± 12.48	84 ± 12.04*	79.7 ± 13.84	81.8 ± 11.37	0.04
Directional control (%)	75.7 ± 8.78	78.9 ± 7.65*,†	70.9 ± 10.85	70.6 ± 9.37	0.02
One-leg stance					
Less affected with eyes open (sec)	17.39 ± 12.87	15.16 ± 10.53	9.14 ± 9.63	12.98 ± 11.08	0.47
More affected with eyes open (sec)	15.06 ± 11.23	15.58 ± 11.58	13.72 ± 12.43	14.54 ± 9.65	0.09
Less affected with eyes closed (sec)	3.35 ± 2.85	6.1 ± 8.65*	2.71 ± 2.54	5.31 ± 7.68	0.002
More affected with eyes closed (sec)	3.06 ± 2.55	4.13 ± 2.74	5.88 ± 7.56	6.66 ± 8.41	0.16
Berg Balance Scale	50.9 ± 5.32	53.2 ± 2.86*	50.4 ± 4.79	53 ± 1.89*	0.001
Timed up and go (sec)	9.5 ± 2.45	8.71 ± 1.8*	10.05 ± 4.66	9.18 ± 3.42*	0.007

Data are presented as mean ± standard deviation

*and †are $P \leq 0.05$ for within-group and between-group comparisons, respectively each joint position while carrying out the fine motor plan necessary for many of the tasks in the exergaming training, stimulation of proprioceptive feedback or an improvement in the internal representation of balance may have enhanced OLS performance.

Little evidence is available regarding the minimal clinically important differences in postural stability and balance outcomes in people with PD. Evidence of minimal clinically important differences for LOS and OLS test in PD is lacking. Steffen and Seney reported a minimal detectable change of 5 points on the BBS for people with PD [34]. In the current study, we recorded a 2.45-point improvement after balance training for BBS. The minimally detectable change in TUG performance in people with PD has previously been reported to be 3.5 s [42], which is greater than the 0.83-second improvement observed in the present study. The small but significant changes observed in this study support the therapeutic use of exergaming interventions. However, a greater evidence base is required to support the clinical significance of these results.

Several important characteristics have been identified for useful interventions in PD, suggesting that interventions should be task-specific, progressive, variable in terms of practice, and highly challenging [43, 44]. The exergaming programs designed for the current study involved each of these components. For specificity, the full-body motion capture method can be tailored for the needs of balance strategies. To create an appropriate practice resource and construct the progression and variability of program, we implemented enriched setting parameters by increasing speed, repetition and the addition of tasks. Additionally, the novel motor training gave participants more experience and an opportunity to explore or learn to negotiate the new challenges. Although only directional control in the LOS test showed a significant between-group difference, exergaming training using the Kinect system may provide additional benefits. Participants are able to practice free motions without wearing a sensor that could cause discomfort and inconvenience. Reduced staff intervention and the affordability of the device are important economic benefits of the system. Finally, considering the clinical implications of our findings, the current results suggest that the Kinect system can provide an assistive modality with therapeutic potential as a training tool under the supervision of a therapist.

The current study involved several limitations. First, the sample size was small, limiting the strength to interpret our results. Second, calibration variability was observed during the preparation of each exergaming session. This issue may have influenced the effect of training because calibration was used to normalize each participant's body information. This formed the basis of the exergaming programs that were tailored for individuals with varying levels of ability. Third, most participants in this study exhibited only mild impairment, and performance at baseline was relatively high. This may have limited the benefits received from training, and the generalizability of our findings to the target population. Finally, the absence of kinematic data meant we were unable to examine spatio-temporal changes in detailed movements.

Conclusion

The current study revealed that an 8-week period of balance-based exergaming training using the Kinect sensor resulted in a greater improvement of postural stability than conventional balance training. Both exergaming and conventional balance training had positive effects on functional balance. This trial supports the potential therapeutic use of exergaming aided by the Kinect sensor for people with PD. Importantly, the significant changes in BBS and TUG performance observed after both the exergaming and conventional balance training did not reach the minimal detectable change in patients with PD. Further studies on the use of exergaming are needed to verify the clinical implications of these results.

Immediate effects of physical therapy on postural instability and frontal lobe dysfunction, as indicated by Frontal Assessment Battery score, in Parkinson's disease

Abstract

Background: The association between the immediate effects of physical therapy on motor symptoms and frontal lobe dysfunction has not been clarified in patients with Parkinson's disease. This study examined the immediate effects of physical therapy on postural instability in patients with Parkinson's disease and whether the improvement in postural instability was associated with Frontal Assessment Battery (FAB) score, as an indicator of frontal lobe dysfunction.

Methods: Twelve patients with idiopathic Parkinson's disease (Hoehn–Yahr classification range 3–4), independent ambulation, and no dementia were divided into FAB high-score (score ≥ 13, $n = 6$) and low-score (score ≤ 12, $n=6$) groups. Postural parameter data was acquired using a three-dimensional motion analysis system and a three-dimensional inclination and horizontal stimulation system before and after a 30-min physical therapy program. Measurements were obtained for total displacement of the center of gravity (COG), total anterior-posterior (AP) displacement of the spinous process of the 7th cervical vertebra (C7) marker, maximum AP displacement of the C7 marker, maximum anterior speed of the C7 marker, and maximum posterior speed of the C7 marker.

Results: The high-score group showed significant decreases in total displacement of the COG and total AP displacement, maximum AP displacement, maximum anterior speed, and maximum posterior speed of the C7 marker. The low-score group showed no significant changes. FAB score was significantly correlated with change in maximum AP displacement of the C7 marker. Multivariate logistic regression analysis showed FAB score was the only predictor of improvement in total AP displacement and maximum AP displacement of the C7 marker.

Conclusions: There may be an association between the immediate effects of physical therapy on PI and FAB score in Parkinson's disease. Thus, FAB score could be useful for predicting which the patients with Parkinson's disease would be more likely to show the immediate effects of physical therapy on postural instability.

Keywords: Frontal Assessment Battery, immediate effects, Parkinson's disease, physical therapy, three-dimensional motion analysis, three-dimensional inclination and horizontal stimulation system, postural instability

Introduction

Postural instability (PI) and gait disturbance are common symptoms in the late stage of Parkinson's disease (PD), where PI is due to the loss of postural reflexes. Although not common in the early stages of the disease, PI is one of the most common factors that cause distress in the later stages [1]. PI, alongside gait disturbance, hypokinesia, and rigidity, can result in falls, fractures, and fear of fall and ultimately to reductions in daily activities and functional independence [2].

As PD progresses, various complex non-motor symptoms [3] tend to occur more often. Among them, frontal lobe dysfunction (FLD), which is associated with motor learning and executive disorder, modifies the motor symptoms. The presence and severity of dysexecutive syndrome can be assessed using the Frontal Assessment Battery (FAB), a simple bedside battery that evaluates such skills as motor programming, inhibitory control, and environmental autonomy [4].

The efficacy of physical activity such as physical therapy and treadmill training has been reported for PD [5-7]. The effects of physical therapy can be shown by the analysis of detailed kinematics data to determine PI by, for example, using a three-dimensional motion analysis system (3D-MAS) and a three-dimensional inclination and horizontal stimulation system (3D-IHSS). We previously reported an association between the immediate effects of physical therapy on gait disturbance and FAB score [8], but there have been no reports to date on whether there is an association between the immediate effects of physical therapy on PI and FAB score, as a potential predictor of improvements in PI.

The aim of this study was to investigate whether the immediate effects of physical therapy on PI in PD patients was associated with FAB score by employing 3D-MAS and 3D-IHSS, and FAB score could be a predictor of improvement in PI by using multivariate logistic regression analysis.

Methods

The study was approved by the Ethics Committee of Gunma University Hospital, Japan and all participants provided written consent before the study commenced.

Participants

Twelve PD outpatients with PI at our hospital were recruited consecutively for this study. In line with the methods of our previous study evaluating the immediate effects of physical therapy on gait disturbance and on FAB score [8], a diagnosis of idiopathic PD was confirmed in all participants by general and neurological examination conducted according to the UK Brain Bank criteria by two neurologists with a special interest in movement disorders [9]. All participants were classified as Hoehn–Yahr 3–4. All were receiving stable pharmacological treatment, with the total dose of antiparkinsonian medication calculated as levodopa equivalent dose (LED) [10]. As in our previous study [8], participants simultaneously underwent the following evaluations before kinematics measurement: Unified PD Rating Scale (UPDRS) assessment [11], Mini-Mental State Examination (MMSE) [12], and FAB. To exclude other diseases except PD, magnetic resonance imaging (MRI) and technetium-99m ethyl cysteinate dimer single photon emission computed tomography (ECD-SPECT) were performed. ECD-SPECT was evaluated using an easy Z-score imaging system (eZIS) and quantitative analysis of global and regional cerebral blood flow (CBF) in 14 regions of interest [13].

Exclusion criteria were as follows; (1) Patient had any other neuromuscular, cardiopulmonary, osteoarticular or psychiatric disorders. (2) Patient could not walk independently without an assistive device such as a cane or walker. (3) Medication for PD was modified within one month prior to the study. (4) Patient had manifested the on-off phenomenon. (5) Patient had participated in PT or any rehabilitation program in the previous 2 weeks. (6) Patient with an MMSE score ≤25. (7) Patient with specific abnormalities except for mild atrophic change by MRI or significant difference in global or regional CBF by ECD-SPECT (**Table 1**).

FAB

FAB score correlates with scores on other evaluation tools, namely, the Wisconsin card sorting test and symbol search [14]. The FAB domains of conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy are graded using a 4-point scale (0–3) for a total score of 18 [4]. Patient with frontal lobe dysfunction has a low FAB score [4]. Based on the median FAB score of 13, patients were assigned to a high-score group (n = 6; score: ≥13) or a low-score group (n = 6; score: ≤12).

Physical therapy session

One 30-min physical therapy protocol was administered by experienced, licensed physical therapists (**Table 2**).

Trunk movement analysis

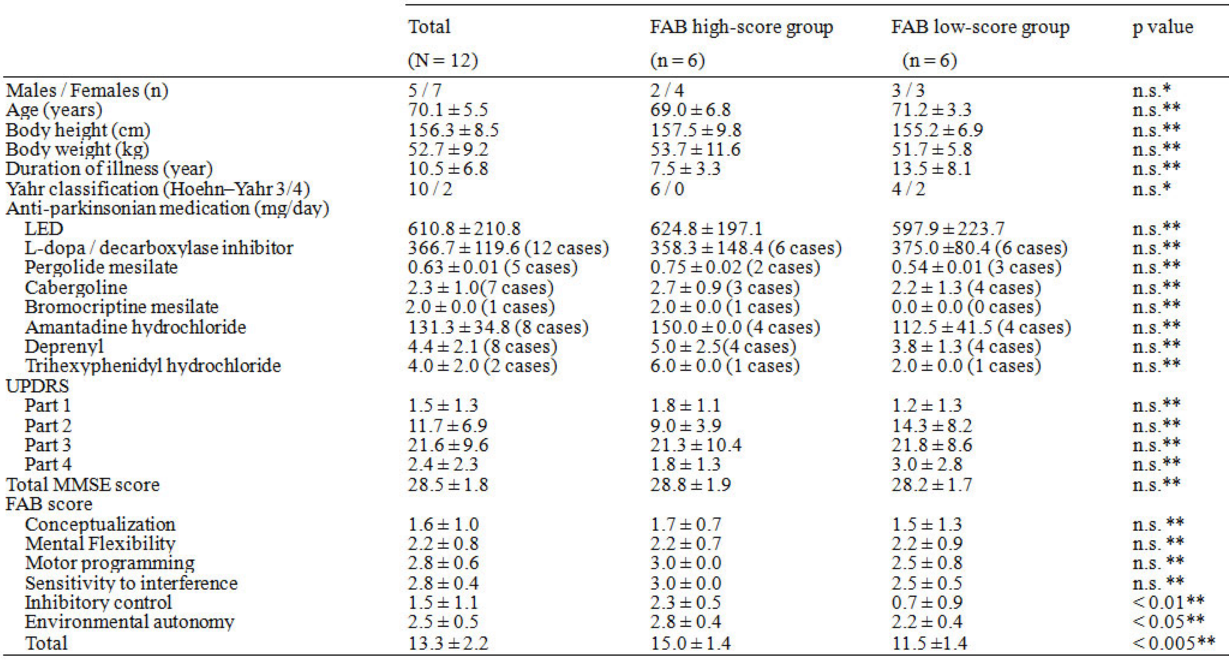
A combined system comprised of 10-camera 3D-MAS (Vicon612®, Oxford Metrics, Oxford, UK) and 3D-IHSS (GS-6900B®, Anima Corp, Tokyo, Japan) was used to acquire kinematic data on trunk movement before and after the physical therapy session. Analysis of postural movement was performed at the university hospital before and after the intervention.

3D-IHSS can measure the center of gravity (COG) and has the platform that can give stimulations in an anterior–posterior or oblique direction (**Figure 1**). The system also can set the protocol of platform movement (movement distance, duration of a cycle, frequency). While giving patients the stimulations on the moveable platform, 3D-IHSS collects the data of the COG. The data is total displacement of the COG. Mean values of 3 trials were calculated for each examination and were used for analysis.

The test-retest reliability of total COG displacement provided by 3D-IHSS has been investigated. The reliability coefficients before and after intervention were 0.811 and 0.857, respectively.

All patients were asked to stand without any standing aids on the 3D-IHSS moveable platform in the rehabilitation unit. A safety harness was fitted to avoid falls. 3D-IHSS provided

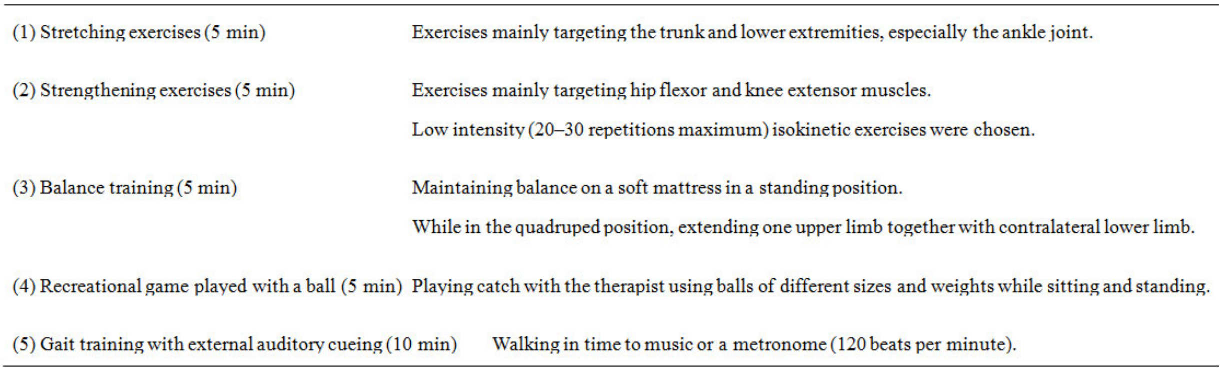
Table 1. Clinical characteristics of patients with Parkinson's disease and FAB scores.



	Total (N = 12)	FAB high-score group (n = 6)	FAB low-score group (n = 6)	p value
Males / Females (n)	5 / 7	2 / 4	3 / 3	n.s.*
Age (years)	70.1 ± 5.5	69.0 ± 6.8	71.2 ± 3.3	n.s.**
Body height (cm)	156.3 ± 8.5	157.5 ± 9.8	155.2 ± 6.9	n.s.**
Body weight (kg)	52.7 ± 9.2	53.7 ± 11.6	51.7 ± 5.8	n.s.**
Duration of illness (year)	10.5 ± 6.8	7.5 ± 3.3	13.5 ± 8.1	n.s.**
Yahr classification (Hoehn–Yahr 3/4)	10 / 2	6 / 0	4 / 2	n.s.*
Anti-parkinsonian medication (mg/day)				
LED	610.8 ± 210.8	624.8 ± 197.1	597.9 ± 223.7	n.s.**
L-dopa / decarboxylase inhibitor	366.7 ± 119.6 (12 cases)	358.3 ± 148.4 (6 cases)	375.0 ±80.4 (6 cases)	n.s.**
Pergolide mesilate	0.63 ± 0.01 (5 cases)	0.75 ± 0.02 (2 cases)	0.54 ± 0.01 (3 cases)	n.s.**
Cabergoline	2.3 ± 1.0(7 cases)	2.7 ± 0.9 (3 cases)	2.2 ± 1.3 (4 cases)	n.s.**
Bromocriptine mesilate	2.0 ± 0.0 (1 cases)	2.0 ± 0.0 (1 cases)	0.0 ± 0.0 (0 cases)	n.s.**
Amantadine hydrochloride	131.3 ± 34.8 (8 cases)	150.0 ± 0.0 (4 cases)	112.5 ± 41.5 (4 cases)	n.s.**
Deprenyl	4.4 ± 2.1 (8 cases)	5.0 ± 2.5(4 cases)	3.8 ± 1.3 (4 cases)	n.s.**
Trihexyphenidyl hydrochloride	4.0 ± 2.0 (2 cases)	6.0 ± 0.0 (1 cases)	2.0 ± 0.0 (1 cases)	n.s.**
UPDRS				
Part 1	1.5 ± 1.3	1.8 ± 1.1	1.2 ± 1.3	n.s.**
Part 2	11.7 ± 6.9	9.0 ± 3.9	14.3 ± 8.2	n.s.**
Part 3	21.6 ± 9.6	21.3 ± 10.4	21.8 ± 8.6	n.s.**
Part 4	2.4 ± 2.3	1.8 ± 1.3	3.0 ± 2.8	n.s.**
Total MMSE score	28.5 ± 1.8	28.8 ± 1.9	28.2 ± 1.7	n.s.**
FAB score				
Conceptualization	1.6 ± 1.0	1.7 ± 0.7	1.5 ± 1.3	n.s. **
Mental Flexibility	2.2 ± 0.8	2.2 ± 0.7	2.2 ± 0.9	n.s. **
Motor programming	2.8 ± 0.6	3.0 ± 0.0	2.5 ± 0.8	n.s. **
Sensitivity to interference	2.8 ± 0.4	3.0 ± 0.0	2.5 ± 0.5	n.s. **
Inhibitory control	1.5 ± 1.1	2.3 ± 0.5	0.7 ± 0.9	< 0.01**
Environmental autonomy	2.5 ± 0.5	2.8 ± 0.4	2.2 ± 0.4	< 0.05**
Total	13.3 ± 2.2	15.0 ± 1.4	11.5 ± 1.4	< 0.005**

FAB: Frontal Assessment Battery, LED: levodopa equivalent dose, UPDRS: Unified Parkinson's disease Rating Scale, MMSE: Mini-Mental State Examination, Mean ± SD, n.s. = not significant, statistical analysis: * Chi-square test, ** Mann–Whitney U-test.

Table 2. Physical therapy protocol.



(1) Stretching exercises (5 min)	Exercises mainly targeting the trunk and lower extremities, especially the ankle joint.
(2) Strengthening exercises (5 min)	Exercises mainly targeting hip flexor and knee extensor muscles. Low intensity (20–30 repetitions maximum) isokinetic exercises were chosen.
(3) Balance training (5 min)	Maintaining balance on a soft mattress in a standing position. While in the quadruped position, extending one upper limb together with contralateral lower limb.
(4) Recreational game played with a ball (5 min)	Playing catch with the therapist using balls of different sizes and weights while sitting and standing.
(5) Gait training with external auditory cueing (10 min)	Walking in time to music or a metronome (120 beats per minute).

stimulation in an anterior–posterior direction (movement distance, 10 cm; duration of 1 anterior–posterior cycle, 2 s; 6 cycles), and the combined 3D-MAS and 3D-IHSS system simultaneously acquired kinematic data on trunk movement.

A spherical retro-reflective surface marker was fixed to the patient's skin over the spinous process of the 7th cervical vertebra (C7). To ensure accuracy, 3D-MAS was calibrated prior to data collection. Using C7 as a positional marker [8], 3D-MAS measured the following parameters on the horizontal plane: total anterior-posterior (AP) displacement of the C7 marker, maximum AP displacement of the marker, maximum anterior speed of the marker, and maximum posterior speed of the marker. Mean values of 3 trials were calculated for each examination and were used for analysis. All data were acquired by an assessor blinded to patient data.

We previously reported the reliability and accuracy of this system for recording three-dimensional kinematic data [8]. Interclass correlation coefficients ranged from 0.870 to 0.994 for intra-rater reliability and from 0.906 to 0.999 for inter-rater reliability.

Statistical analysis

Statistical analysis was performed using SPSS software Version 25.0 (IBM, Chicago, IL). As in our previous study [8], significant differences between the FAB high- and low-score groups were determined using the Mann–Whitney U test or

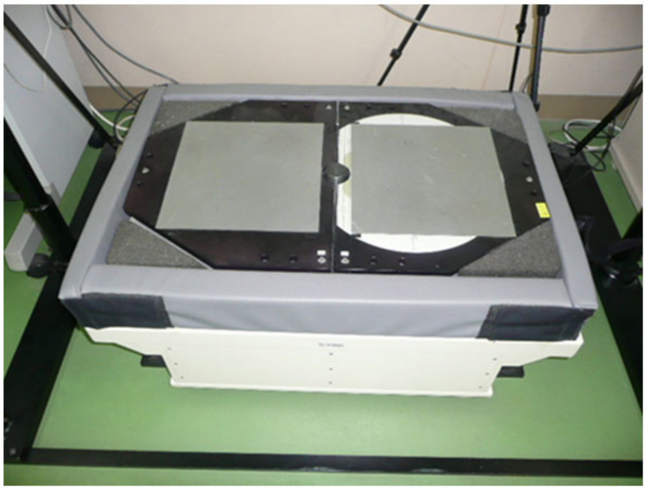


Figure 1. Three-dimensional inclination and horizontal stimulation system (3D-IHSS).

Chi-squared test. Pre- and post-measurements were compared with Wilcoxon's matched-pair signed-rank test. Correlations between variables were evaluated using Spearman's rank-order correlation coefficients. To predict the immediate effects of physical therapy, a multivariable logistic regression model controlling for possible confounding covariates was fitted by stepwise forward selection of variables: age, duration of illness, Hoehn–Yahr classification, LED, all four parts of the UPDRS, total MMSE score, and FAB score. Variables that were statistically significant were then included in multivariate logistic regression analysis. Because of the sample size and number of variables, the entry probability for logistic analysis was set at the 0.10 level of significance rather than the 0.05 level in an effort to avoid type II error. Associations between the clinical characteristics and the independent variables were determined by odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was set at *P*<0.05. Descriptive statistics are reported as mean ± SD.

Results

Comparisons between the FAB high-and low-score groups before physical therapy intervention revealed no significant differences in sex, age, duration of illness, Hoehn–Yahr classification, antiparkinsonian medication, LED, all four parts of the UPDRS, or total MMSE score. The FAB low-score group showed significant decreases in inhibitory control, environmental autonomy, and total scores compared with the high-score group (**Table 1**). MRI revealed no specific abnormalities except for mild atrophic change. Quantitative analysis by ECD-SPECT showed no significant difference in global or regional CBF between the two groups.

Comparisons before and after physical therapy revealed the following results (**Table 3**). The high-score group showed significant decreases in total displacement of the COG, total AP displacement of the C7 marker, maximum AP displacement of the marker, maximum anterior speed of the marker, and maximum posterior speed of the marker. The low-score group showed no significant differences. FAB score correlated significantly with changes in maximum AP displacement of the C7 marker and maximum anterior speed of the C7 marker (**Table 4**, **Figure 2**).

Multivariate logistic regression analysis revealed that FAB score was the only predictor of improvement in total AP displacement of the C7 marker and maximum AP displacement of the C7 marker. In addition to FAB score, analysis showed MMSE score, UPDRS part 3 (which involves the evaluation of

Table 3. Changes in postural stability parameters between before and after physical therapy.

	FAB high-score group (n = 6)	p value	FAB low-score group (n = 6)	p value
Total displacement of COG (cm)				
	58.4 ± 83.7	< 0.05	5.0 ± 28.5	n.s.
Total AP displacement of C7 marker (cm)				
	158.5 ± 299.3	< 0.05	4.2 ± 98.0	n.s.
Maximum AP displacement of C7 marker (cm)				
	17.2 ± 19.0	< 0.005	-4.0 ± 24.8	n.s.
Maximum anterior speed of C7 marker (cm/s)				
	23.8 ± 40.1	< 0.05	-6.8 ± 37.2	n.s.
Maximum posterior speed of C7 marker (cm/s)				
	32.5 ± 42.1	< 0.01	17.5 ± 44.7	n.s.

FAB: Frontal Assessment Battery, COG: Center of gravity, AP: anterior–posterior, C7: spinous process of the 7th cervical vertebra Mean ± SD, n.s.: not significant, statistical analysis: Wilcoxon matched pairs signed rank Test

Table 4. Correlation between FAB score and changes in postural stability parameters between before and after physical therapy.

	Correlation coefficient	p value
Total displacement of COG (cm)	0.094	n.s.
Total AP displacement of C7 marker (cm)	0.305	n.s.
Maximum AP displacement of C7 marker (cm)	0.462	< 0.01
Maximum anterior speed of C7 marker (cm/s)	0.390	< 0.05
Maximum posterior speed of C7 marker (cm/s)	0.268	n.s.

FAB: Frontal Assessment Battery, COG: Center of gravity, AP: anterior–posterior, C7: spinous process of the 7th cervical vertebra Mean ± SD, n.s.: not significant, statistical analysis: Spearman's rank order correlation coefficient.

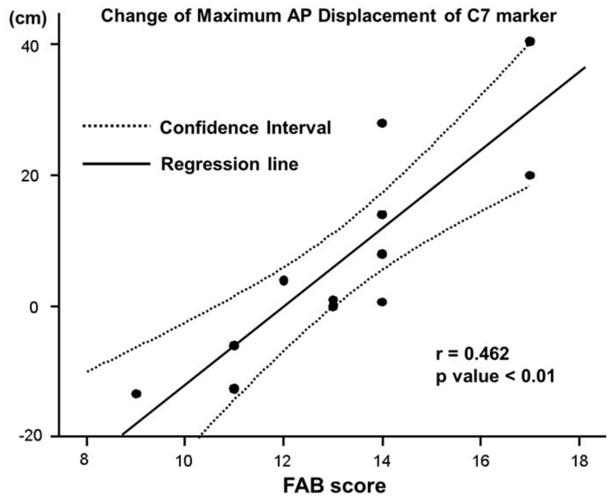


Figure 2. Frontal Assessment Battery score and change in maximum anterior–posterior displacement of the marker of the spinous process of the 7th cervical vertebra.
AP: anterior–posterior, C7: spinous process of the 7th cervical vertebra, statistical analysis: Spearman's rank order correlation coefficient.

posture and postural stability), and LED were predictors of improvement in total displacement of the COG and maximum anterior and posterior speed of the C7 marker. No other significant relationships were observed between clinical characteristics and improved PI (**Table 5**).

Discussion

PD and the immediate effects of Physical therapy

Through improvements in gait, postural stability, and muscle power, physical capacity has been shown to be improved in PD with the use of cueing strategies in long-term physical therapy and home training [**5**-**7**,**15**]. Moreover, treadmill training sessions have been shown to immediately improve gait in PD [**16**,**17**]. It is important, however, to clarify not only the long-term effects but also the immediate effects of physical therapy because it may immediately improve physical capabilities and thus help to prevent falls [**18**]. Therefore, to investigate whether physical therapy intervention could immediately improve PI in PD patients, our physical therapy session consisted of intervention activities that are reported to be effective for PI improvement, namely, stretching exercises, balance training, and gait training with external auditory cueing [**19**].

FLD and motor symptoms

FLD, including executive dysfunction, is the main feature of non-motor symptoms in PD [**3**]. Non-motor symptoms are closely connected with the effects of physical therapy on motor symptoms. A physical exercise program was reported to improve executive function in PD patients [**20**], and accordingly in this study we focused especially on the immediate effects of physical therapy on PI and FLD.

FAB score and FLD

We decided to use FAB as a convenient evaluation tool for FLD in this study. FAB is a short, simple instrument consisting of six subtests that explore different abilities related to frontal lobe functions. Its results correlate with those of other commonly performed evaluation tools for PD, namely, the Wisconsin card sorting test and symbol search, the standardized tests for the assessing executive function [**14**].

FAB score and the immediate effects of physical therapy on PI

In this study, we wanted to address the question of whether a physical therapy session could immediately improve PI (confirmed kinematically) and whether FAB score could reflect the improvement in PI. Using detailed kinematics data recorded using both 3D-MAS and 3D-IHSS, we could accurately detect post-intervention alterations in not only displacement of the COG, but also C7 displacement and speed. We were then able to determine, for the first time, an association between these post-intervention changes in postural parameters and FAB

Table 5. Stepwise logistic model for predicting the immediate effects of physical therapy on postural instability.

	FAB score		MMSE score		UPDRS part 3 score		LED	
	p value	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)
Total displacement of COG	n.s.		n.s.		0.026	1.046 (0.903-1.212)	n.s.	
Total AP displacement of C7 marker	0.045	1.268 (0.708-2.270)	n.s.		n.s.		n.s.	
Maximum AP displacement of C7 marker	0.0002	5.713 (0.801-40.758)	n.s.		n.s.		n.s.	
Maximum anterior speed of C7 marker	0.044	1.445 (0.525-3.978)	0.010	2.077 (0.806-5.353)	n.s.		0.043	1.005 (0.996-1.015)
Maximum posterior speed of C7 marker	n.s.		0.017	1.385 (0.699-2.742)	n.s.		n.s.	

FAB: Frontal Assessment Battery, MMSE: Mini-Mental State Examination, UPDRS: Unified PD Rating Scale, LED: levodopa equivalent dose, COG: Center of gravity, AP: anterior–posterior, C7: spinous process of the 7th cervical vertebra, OR: odds ratio, CI: 95% confidence interval, n.s.: not significant

score. Specifically, the FAB high-score group showed several immediate improvements in trunk movement: decreased changes in total displacement of the COG and in total AP displacement, maximum AP displacement, maximum anterior speed, and maximum posterior speed of the C7 marker. The low-score group showed no significant changes. Moreover, FAB score correlated positively with the changes in maximum AP displacement and maximum anterior speed of the C7 marker. Thus, the present study shows an association between the immediate effects of physical therapy on PI and FAB score. Multivariate logistic regression analysis then revealed that FAB score was a predictor of improvement in PI. Thus, FAB score could be useful for predicting the immediate effects of physical therapy on PI in PD.

FAB domain scores and the immediate effects of physical therapy on PI

The FAB low-score group showed significantly lower scores in the domains of inhibitory control and environmental autonomy. Inhibitory control assesses control of impulsiveness and withholding of a response to external stimuli through practice, while environmental autonomy assesses the spontaneous tendency to adhere to the environment through prehension behavior [4]. Both skills are essential for postural stability and avoiding falls caused by external stimuli. Kataoka et al found a significantly lower score for inhibitory control among fallers with PD than in non-fallers with PD [21]. Deficits in environmental autonomy mean that PD patients are more susceptible to external stimuli, which makes avoiding falls difficult.

In the present study, the FAB low-score group also showed a lower score for motor programming compared with the high-score group, albeit not significantly lower. This finding reflects a process of improved motor performance through practice during physical therapy, and has previously been associated with the positive effects of rehabilitation [22].

Our FAB results therefore show an association between the immediate effects of physical therapy on PI and FLD with FAB domain scores. Meanwhile, we should note that the correlation coefficients were not high (Table 4, Figure 2). It means most of the variance between variables cannot be explained. We intend to solve the problem by increasing the number of subjects in future research.

It is also important to note that our findings do not suggest physical therapy is ineffective for PD patients with a low FAB score because only PI was investigated and the aims and content of physical therapy interventions are numerous and diverse.

Frontal lobe connections and immediate effects of physical therapy on PI

King et al hypothesized that frontal lobe connections with the basal ganglia and brainstem posture and locomotor centers are responsible for postural deficits in PD patients and play a role in rehabilitation efficacy [23]. The immediate effects of physical therapy on PI can be seen when damage to these connections is mild, and progressive damage to these connections may decrease the immediate effects. So, a decline in frontal lobe function with the progression PD may affect the immediate effects. Because it is difficult to predict the immediate effects of physical therapy by neurological examination and use of evaluation scales (e.g., UPDRS), FAB score could be a useful predictor of which patients could benefit most from the immediate effects of PT.

Other predictors and the immediate effects of physical therapy

Of note, multivariate logistic regression also indicated that MMSE score, UPDRS part 3 score, and LED were predictors of the immediate effects of physical therapy. MMSE is the basic examination for cognitive impairment. Although no significant difference was noted between the FAB high- and low-score groups in the present study, cognitive impairment develops as PD progresses. UPDRS part 3 involves motor examination and includes evaluations of posture and postural stability [11]. It is not surprising that MMSE and UPDRS part 3 were identified as predictors. Moreover, it has been reported that antiparkinsonian medication, particularly L-dopa, dopamine agonists, and anticholinergic drugs can affect frontal function [24]. Although differences in LED doses were not found to be significant between the groups in the present study, they were higher in the high-score group than in the low-score group (Table 1).

Limitations

Some limitations of this study should be noted. First, the number of subjects was small, which limits the generalization of the results. Second, we used FAB alone to evaluate FLD, and further studies should use additional evaluation tools to verify our results. In addition, the test-retest reliability of FAB has not been investigated for PD patients. We should examine the reliability in the future. Going forward, the long-term effects after several physical therapy sessions should be compared with the immediate effects of a single session investigated here, and other disturbances aside from postural instability should be investigated. We intend to address these limitations in future research.

Conclusion

We demonstrated an association between the immediate effects of physical therapy on PI and FLD in PD. Our findings suggest that FAB scores could be useful for predicting which PD patients would be more likely to show the immediate effects of PT on PI.

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