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Short communication

Does robotic gait training improve balance in Parkinson's disease? A randomized controlled trial

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A B S T R A C T

Background: Treadmill training (with or without robotic assistance) has been reported to improve balance skills in patients with Parkinson's disease (PD). However, its effectiveness on postural instability has been evaluated mainly in patients with mild to moderate PD (Hoehn & Yahr stage ≤ 3). Patients with more severe disease may benefit from robot-assisted gait training performed by the Gait-Trainer GT1, as a harness supports them with their feet placed on motor-driven footplates. The aim of this study was to determine whether robot-assisted gait training could have a positive influence on postural stability in patients with PD at Hoehn & Yahr stage 3–4.
Methods: Thirty-four patients with PD at Hoehn & Yahr stage 3–4 were randomly assigned into two groups. All patients received twelve, 40-min treatment sessions, three days/week, for four consecutive weeks. The Robotic Training group ($n = 17$) underwent robot-assisted gait training, while the Physical Therapy group ($n = 17$) underwent a training program not specifically aimed at improving postural stability. Patients were evaluated before, immediately after and 1-month post-treatment. Primary outcomes were: Berg Balance scale; Nutt's rating.
Results: A significant improvement was found after treatment on the Berg Balance Scale and the Nutt's rating in favor of the Robotic Training group (Berg: 43.44 ± 2.73; Nutt: 1.38 ± 0.50) compared to the Physical Therapy group (Berg: 37.27 ± 5.68; Nutt: 2.07 ± 0.59). All improvements were maintained at the 1-month follow-up evaluation.
Conclusions: Robot-assisted gait training may improve postural instability in patients with PD at Hoehn & Yahr stage 3–4.

1. Introduction

Postural instability is highly disabling in Parkinson's disease (PD) [1]. It has been partially determined that postural abnormalities may not be related to dopamine depletion. Indeed, medications aimed at increasing dopamine in the brain only slightly improve postural instability [1].

Physiotherapy complements pharmacological and neurosurgical treatments in PD [2]. Interestingly, there are indications that treadmill training (TT), with or without robot-assistance, may have beneficial effects on balance in PD [3–6]. However, its effectiveness on postural instability has mainly been evaluated in PD patients whose balance impairment is a minor problem, probably because TT may be difficult to carry out in patients with advanced PD. The Gait-Trainer GT1 (Reha-Stim, Berlin, Germany) allows for robot-assisted gait training (RAGT), with patients supported by a harness and their feet placed on motor-driven footplates. Its effectiveness for improving gait skills in patients with PD at Hoehn & Yahr (H&Y) stage <3 has recently been reported in the literature [7]. Considering the GT1 machine characteristics, it may be useful for treating patients with advanced phase PD.

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The main aim of this study was to evaluate whether RAGT could have a positive influence on postural stability in patients with advanced PD. The secondary aim was to examine whether RAGT could have a positive impact not only on the level of confidence perceived during those activities of dialing living requiring balance, functional mobility but also on severity of disease.

2. Methods

This study was performed in the Neurological Rehabilitation Unit of the University Hospital of Verona, Italy. Inclusion criteria [2]: a confirmed medical diagnosis of PD; H&Y stage of 3 or 4 (determined in the "on" phase); Mini Mental State Examination > 23. Exclusion criteria: severe dyskinesias or "on-off" fluctuations; the need to modify PD medication during the study; need for assistive devices to rise from chairs or beds; deficits of somatic sensation involving the legs; vestibular disorders or paroxysmal vertigo; other neurological, orthopedic or cardiovascular co-morbidity. All participants gave their informed consent for participation in the study, which was approved by the local Ethics Committee.

Prior to testing, participants were divided into two groups according to a restricted randomization scheme. We used a randomization list accessible only to the principal investigator. Participants were instructed to take their normal PD medications: they were tested and trained during the "on" phase, 1–2.5 h after taking their morning dose. Participants performed no rehabilitation treatment in the three months before the study and underwent no training other than that scheduled in the study protocol.

2.1. Treatment procedures

Each patient underwent twelve, 40-min training sessions (including rest periods), three days a week (Monday, Wednesday, Friday) for four consecutive weeks.

Patients allocated to the Robotic Training (RT) Group performed RAGT with the Gait-Trainer GT1 (Reha-Stim, Berlin, Germany) [7]. The GT1 machine is a static suspension system consisting of two motor-driven footplates that provide robot-assisted propulsion of gait, simulating stance and swing with a ratio of 60%–40% [7]. During RAGT, individuals were secured in a harness with their feet on footplates, while movements of the center of mass were controlled in a phase-dependent manner by ropes attached to the harness. The step-length was evaluated with the GAITRite system (CIR Systems, Havertown, PA) and individually defined [7]. Each training session consisted of two 15-min sessions separated by a 10-min rest. In the first session we trained patients at 20% of supported body-weight and 1.3 km/h of speed; in the second session at 10% of supported body-weight and 1.6 km/h of speed. Patients unable to maintain the pace were excluded.

Patients allocated to the Physical Therapy (PT) group performed exercises not specifically aimed at improving postural stability, such as lower limb active joint mobilization, muscle stretching and motor coordination exercises. Patients performed 10 exercises as follows: 6 supine (stretching, mobilization, coordination), 2 sitting (mobilization, coordination), and 2 standing (stretching, coordination) [2]. A physiotherapist assisted patients by demonstrating the exercises and providing verbal instructions.

2.2. Testing procedures

Patients were evaluated before (T0) and immediately after treatment (T1) (primary endpoint), as well as one month post-treatment (T2). The same examiner, who was blinded to the treatment allocation, evaluated all patients. Asking the assessor to make an educated guess tested the success of blinding.

2.2.1. Primary outcomes

The Berg Balance scale (BBS) is a 14-item scale that evaluates balance during sitting, standing and positional changes (best score = 56) [2]. The Nutt's rating (NUTT) evaluates the reaction to an unexpected shoulder pull-on a 4-point scale (0 = normal; 3 = worst performance) [8].

2.2.2. Secondary outcomes

The Activities-Specific Balance Confidence scale (ABC) examines the perceived level of confidence in balance while performing 16 daily living activities (each rated 0–100) [2]. The Timed Up & Go Test (TUG) is a balance test that requires a subject to stand up, walk 3 m, turn, walk back, and sit down [9]. Time taken to complete the test is correlated to the level of functional mobility. The Ten-Meter Walk Test (10 MWT) is a validated test requiring patients to walk on a flat hard floor for 10 m at the end of which walking speed is scored [7]. The Unified Parkinson's Disease Rating Scale (UPDRS) has 4 subsections and was used to follow the longitudinal course of PD. The score of UPDRS part III (motor examination) is reported [2].

2.3. Statistical analysis

Pre-study power calculation estimated that 22 subjects would provide 99% power to detect a difference of 4.67 in the BBS (SD 2.36) between groups [2]. We used the Mann–Whitney test to assess homogeneity before the study and compare the effect of treatment between groups. To determine this, we computed the differences between T1-T0 and T2-T0 performances for all outcomes. Descriptive analysis was used to evaluate the effect size between groups and the confidence intervals. The level for significance was $p < 0.05$. Statistical analysis was performed with SPSS 16.0 (SPSS Inc, Chicago, IL).

3. Results

Thirty-four subjects (20 males, 14 females; mean age: 68.3 years) with idiopathic PD (mean disease duration: 7.5 years; mean H&Y stage: 3.45) were selected from all outpatients with H&Y 3–4 consecutively admitted to our Neurorehabilitation Unit from October 2008 to July 2010. Seventeen patients were allocated in each group. Three patients withdrew from the study. No adverse events occurred in either group. The mean step-length on the GT1 machine for the RT Group was 40.17 ± 5.87 cm. The flow diagram of the study is shown in Fig. 1.

Multiple separate independent-sample Mann–Whitney tests showed that there was no significant difference between groups as to age, length and stage of illness, and all outcomes at T0.

3.1. Primary outcomes

As shown in Table 1, between groups comparisons showed that patients in the RT Group performed significantly better than those in the PT Group, on all primary outcomes at both T1 (BBS: $p < 0.001$; NUTT: $p = 0.001$) and T2 (BBS: $p < 0.001$; NUTT: $p = 0.002$) evaluations.

3.2. Secondary outcomes

As shown in Table 1, between groups comparison showed that patients in the RT Group performed significantly better than those in the PT Group, on all secondary outcomes at both T1 (ABC: $p < 0.001$; TUG: $p < 0.001$; 10 MWT: $p = 0.001$; UPDRS: $p < 0.001$) and T2 (ABC: $p = 0.001$; TUG: $p < 0.001$; 10 MWT: $p = 0.001$; UPDRS: $p < 0.001$) evaluations.

4. Discussion

We showed that RAGT could improve balance in patients with advanced PD suffering from postural instability (H&Y 3–4). Interestingly, our results regarding gait speed are in line with those reported in a previous study conducted by our research group on patients with PD and H&Y <3 [7].

Ability to maintain the upright position is a challenge for all humans, which becomes even more challenging when negotiating the environment and following complex trajectories (i.e. going from sitting to standing, walking, turning) [10]. Thus, balance control is a key element for the ability to walk, in order to stabilize the body and make postural adjustments during disturbances that occur during locomotion [10]. One pilot study examined the effectiveness of robot-assisted TT in 4 patients with PD (H&Y not specified): it reported a reduction of frequency and fear of falling after ten, 30-min, training sessions [6]. As to TT without robot-assistance, Toole et al. examined the effects of loading and unloading TT on balance, gait and risk of falls in 23 patients with PD (mean H&Y 2.5), observing significant improvements in posturography, falls, BBS, UPDRS and gait after treatment [3]. Protas et al. reported a significant reduction in falls and improvements in gait speed and balance after TT without body-weight support (3

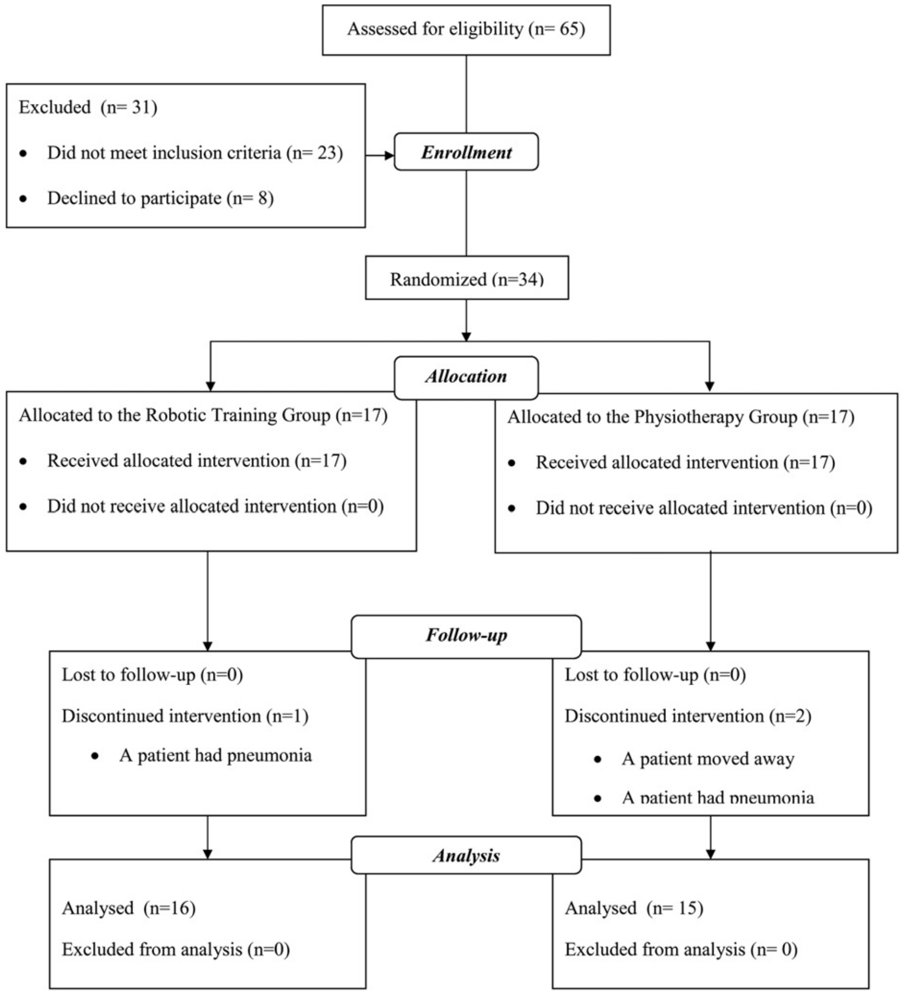

Fig. 1. Study flow.

sessions/week for 8 weeks) in 18 patients with PD (H&Y 2–3) [4]. Cakit et al. evaluated the effects of incremental speed-dependent TT in 21 patients with PD (H&Y < 3), revealing a significant reduction of postural instability and fear of falling after an eight-week treatment program [5]. Our randomized controlled trial showed that patients with advanced PD suffering from postural instability (H&Y 3–4) showed improved outcomes related to balance (such as the BBS, NUTT, ABC and TUG) after RAGT. In particular, the improvement of 5.56 points observed in the BBS after RAGT was not only statistically but also clinically relevant (≥5

Table 1
Treatment effects in all outcome measures.

	Group	Before mean (SD)	After mean (SD)	Follow-up mean (SD)	95% confidence interval		Between group comparisons		Effect size	
					After − before LB; UB	Follow-up − before LB; UB	After/before difference value (*Z*)	Follow-up/before difference *p* value (*Z*)	After	Follow-up
BBS (0–56)	RT	37.88 (3.38)	43.44 (2.73)	42.31 (2.75)	4.28; 6.83	3.02; 5.85	<0.001 (−4.485)*	<0.001 (−4.053)*	0.57	0.51
	PT	37.33 (4.25)	37.27 (5.68)	37.60 (4.84)	−1.72; 1.58	−0.41; 0.94				
Nutt's rating (0–3)	RT	2.13 (0.50)	1.38 (0.50)	1.31 (0.48)	−0.98; −0.51	−1.02; −0.59	0.001 (−3.421)*	0.002 (−3.036)*	−0.53	−0.46
	PT	2.13 (0.64)	2.07 (0.59)	1.93 (0.70)	−0.32; 0.18	−0.57; 0.17				
ABC scale (0–100)	RT	55.72 (8.57)	62.31 (9.16)	62.13 (10.96)	4.54; 8.62	2.01; 10.80	<0.001 (−3.882)*	0.001 (−3.362)*	0.24	0.25
	PT	56.67 (10.18)	57.33 (10.72)	56.46 (10.70)	−0.63; 1.96	−2.64; 2.24				
TUG test (s)	RT	13.04 (1.79)	11.60 (1.37)	11.48 (1.54)	−1.96; −0.91	−2.04; −1.06	<0.001 (−4.092)*	<0.001 (−4.132)*	−0.27	−0.27
	PT	13.67 (6.00)	14.16 (6.32)	13.89 (5.80)	−0.49; 1.02	−0.32; 0.76				
10 MWT (s)	RT	12.94 (1.99)	11.48 (1.62)	11.72 (1.81)	−1.77; −1.15	−1.53; −0.91	0.001 (−3.480)*	0.001 (−3.321)*	−0.07	−0.04
	PT	12.28 (4.77)	12.03 (4.94)	12.04 (4.39)	−1.15; 0.50	−1.08; 0.46				
UPDRS part III (0–108)	RT	46.31 (6.65)	40.00 (6.53)	39.69 (6.93)	−7.61; −5.01	−8.10; −5.14	<0.001 (−4.725)*	<0.001 (−4.732)*	−0.46	−0.46
	PT	47.20 (7.93)	47.33 (7.50)	47.27 (7.60)	−0.64; 0.91	−0.57; 0.71				

Abbreviations: SD, standard deviation; LB, lower bound; UB, upper bound; RT, robotic training; PT, Physical Therapy, BBS, Berg Balance scale; ABC, Activities-Specific Balance Confidence; s, seconds; TUG, Timed Up & Go; 10 MWT, Ten-Meter Walk Test; UPDRS, Unified Parkinson's Disease Rating scale.
* = statistically significant ($p < 0.05$).

points) [2]. This is important, considering the peculiar treatment conditions of the GT1 machine (harness support, feet placed on footplates, body-weight support, control of center of mass movements, the need for a single operator during training) [7]. Thus, it would be interesting to compare the effectiveness of RAGT and TT on PD patients with H&Y 3–4, taking into account the burden of RAGT in terms of financial, personnel and logistic resources.

A fundamental question now is to understand why RAGT effectively improved postural stability in PD. One possible explanation could be the facilitation of neuromuscular regulation produced by repetitive locomotor training. A disruption of the lower extremity proprioceptive reflexes, involved in the maintenance of equilibrium, has been proposed to explain gait disturbances in patients with PD [10]. Moreover, reduced activity of gastrocnemii has been observed in these patients, partially compensated by an increase in ankle dorsiflexors activation, leading to an alteration in stride height and length [10]. The GT1 machine provides repetitive, bilateral, distal-guided gait training and, it is most likely that several repetitions of gait-like movements could have had a positive influence on activation patterns within the leg muscles [7]. In addition, RAGT was performed at very slow walking speeds according to the GT1 machine characteristics (speed up to 2 km/h) and in order to increase patients' tolerance (no patient failed to maintain the chosen pace). At these speeds, it is possible that the weight shifting during RAGT may have played a role in training effectiveness by the constant balance from one leg to the other.

Another possible explanation could be the proprioceptive cueing effect of RAGT. Indeed, repetitions of gait-like movements provide an external rhythm that could compensate for the defective internal rhythm of the basal ganglia [11]. The effectiveness of rhythmic cueing for training balance has been confirmed by seminal studies such as the RESCUE trial, which examined the effect of three rhythmic cueing modalities, reporting significant improvements in gait and balance after treatment [11].

Finally, lower limb strengthening could have played a role [12]. Indeed, ankle weakness and an altered ratio of hamstring to quadriceps strength may impair the ability to mount postural responses of appropriate magnitude when balance is challenged in PD patients [12].

The main limitation of this study is the lack of a proper dose-matched control cohort treated with procedures aimed at improving balance. We compared RAGT with a sort of "placebo" training according to the recommendations of the local Ethics Committee. Moreover, we did not perform long-term follow-up assessments nor evaluate parameters such as the frequency or fear of falling. In addition, we did not test participants "off" medication. In order to be able to recommend RAGT for clinical use, future studies should establish its superiority over other properly dosed established training procedures (TT and physiotherapy) for postural instability in PD.

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