Long-term effects of automated mechanical peripheral stimulation on gait patterns of patients with Parkinson's disease

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New treatments based on peripheral stimulation of the sensory–motor system have been inspiring new rehabilitation approaches in Parkinson's disease (PD), especially to reduce gait impairment, levodopa washout effects, and the incidence of falls. The aim of this study was to evaluate the change in gait and the clinical status of PD patients after six sessions of a treatment based on automated mechanical peripheral stimulation (AMPS). Eighteen patients with PD and 15 age-matched healthy individuals (control group) participated in this study. A dedicated medical device delivered the AMPS. PD patients were treated with AMPS six times once every 4 days. All PD patients were treated in the off-levodopa phase and were evaluated with gait analysis before and after the first intervention (acute phase), after the sixth intervention, 48 h after the sixth intervention, and 10 days after the end of the treatment. To compare the differences among the AMPS interventions (pre, 6 AMPS, and 10 days) in terms of clinical scales, a *t*-test was used ($\alpha \leq 0.05$). In addition, to compare the differences among the AMPS interventions (pre, post, 6 AMPS, 48 h and 10 days), the gait spatiotemporal parameters were analyzed using the Friedman test and the Bonferroni post-hoc test ($\alpha \leq 0.05$). Also, for comparisons between the PD group and the control group, the gait spatiotemporal parameters were analyzed using the Mann–Whitney test and the Bonferroni post-hoc test ($\alpha \leq 0.05$). The results of the study indicate that the AMPS treatment has a positive effect on bradykinesia because it improves walking velocity, has a positive effect on the step and stride length, and has a positive effect on walking stability, measured by the increase in stride length. These results are consistent with the improvements measured with clinical scales. These findings indicate that AMPS treatment seems to generate a more stable walking pattern in PD patients, reducing the well-known gait impairment that is typical of PD; regular repetition every 4 days of AMPS treatment appears to be able to improve gait parameters, to restore rhythmicity, and to reduce the risk of falls, with benefits maintained up to 10 days after the last treatment. The trial was registered online at ClinicalTrials.gov (number identifier: NCT0181528). *International Journal of Rehabilitation Research* 38:238–245 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

Introduction

Impairment of the motor system (basal ganglia and motor cortex) is traditionally considered the major cause of Parkinsonian symptoms. Individuals with Parkinson's disease (PD) have been reported to have deficits in both sensorimotor integration (Fuhrer *et al.*, 2014) and peripheral sensory function (Pratorius *et al.*, 2003). Although these sensory system impairments are believed to result in poor feedback to the motor system, thereby producing observable motor deficits, whether these deficits are because of reduced peripheral sensory receptor function or impaired central sensorimotor integration is unknown (Lewis and Byblow, 2002). Treatments based on automated mechanical peripheral stimulation (AMPS) of the sensory–motor system (bottom-up stimulation) have been inspiring new rehabilitation approaches in PD (Jenkins *et al.*, 2009).

Different methods of plantar sensory stimulation have been studied, including insoles with a raised ridge located at the foot's perimeter (Maki *et al.*, 2007; Perry *et al.*, 2008), mechanical pressure on the sole of the foot (Maurer *et al.*, 2001), and vibratory insoles (Priplata *et al.*, 2003; Novak and Novak, 2006). Duysens *et al.* (2008) found that vibration to the soles of the feet elicited stretch reflexes. Mechanical facilitation, by way of vibration, could induce a response from the proprioceptors, which can in turn affect the gait of an individual. This is reasonable as various types of sensory receptors work together to provide accurate feedback to the central nervous system during locomotion.

Jenkins et al. (2009) evaluated the effects of a facilitatory insole that provided increased plantar sensory stimulation to PD patients during gait. The results indicated that the use of the facilitatory insole induced a significant increase in single-limb support time. In addition, the muscle activation sequence of the tibialis anterior was normalized by the facilitatory insole at the point of initial ground contact. Thus, mechanical facilitation of the plantar surface may be able to increase the sensory stimulation received to overcome the proprioceptive deficits that impair gait in individuals with PD.

In a recent study by Barbic et al. (2014), the effects of a manual mechanical peripheral stimulation (manual MPS) in PD patients have been studied. The treatment investigated in that study consisted of the application of a punctual pressure in a range of 0.3–0.9 N/mm^2 in a sequence of four specific foot points. The authors evaluated a group of 16 patients with PD preacute phase and postacute phase ('post' meaning immediately after one manual AMPS treatment only). The authors measured significant improvements in step length and gait velocity, showing that manual MPS could be an encouraging treatment to reduce motor impairment in PD patients.

The manual MPS treatment used in that study, however, may be operator dependent, resulting a nonhomogenous application of the treatment to all participants. In addition, the manual treatment can be provided only in a clinical environment, not in a domestic scenario.

To make the application of the MPS treatment available in an automated way, a new non-operator-dependent medical device (Gondola; Ecker Technologies, Lugano, Switzerland) has been developed. The aim of the present study is to verify the effect of the AMPS treatment for the rehabilitation of gait and for the functionality of patients with PD. More specifically, the current study aims to evaluate the effect of the AMPS treatment by analyzing both clinical scales and gait analysis tests to measure gait spatiotemporal parameters at the following time points: basal condition (pretreatment), after a cycle of six treatments, and 48 h and 10 days after the end of a 3-week treatment cycle.

The hypothesis of this study is that the AMPS stimulation improves the gait of patients with PD as well their clinical status, that these improvements exert positive effects on motor capabilities, and that these improvements are maintained up to 10 days after a treatment cycle.

Methods
The study was approved by the Ethics Research Committee of the IRCCS San Raffaele Institute and written informed consent was obtained by the patients. The investigation was registered online at ClinicalTrials. gov (number identifier: NCT0181528). All procedures were explained and performed with an adequate understanding and written informed consent of the participants.

Participants
We studied 18 patients with idiopathic PD (age: 67.58 ± 8.74 years; height: 1.60 ± 0.10 m; weight: 73.77 ± 14.13 kg). The group was characterized by a moderate motor impairment (Hoehn and Yahr, 1967, scale 2–3) and had been referred to the outpatient clinic of the Parkinson's Disease Center. Each case of PD was diagnosed on the basis of clinical criteria (Nutt and Wooten, 2005), a dopamine transporter scan, and/or MRI. Patients were homogeneous in terms of disease duration and were free of peripheral sensory neuropathy and/or other disorders on the basis of their reported history, symptoms, physical examination, and routine tests. Patients with liver, kidney, lung, heart disease, diabetes, or other causes of autonomic dysfunction were not included in the study. Treatments for PD remained unchanged for the 30 days preceding the study. A clinical team comprising a neurologist and a physical therapist examined all participants. They were assessed by clinical evaluation and gait analysis before and after AMPS treatment.

A control group of 15 healthy individuals (age: 68.11 ± 8.70 years; height: 1.56 ± 0.09 m; weight: 72.66 ± 15.50 kg) was used as a normality group for gait analysis. This group was included in the study to define a reference set of data of age-matched healthy participants and to compare data of the patient group with the data of the control group. Exclusion criteria for the healthy participants included a previous history of cardiovascular, neurological, or musculoskeletal disorders. They showed normal flexibility and muscle strength and no obvious gait abnormalities.

Definitions and AMPS procedures
A dedicated medical device (Gondola; Ecker Technologies, Lugano, Switzerland) was used to deliver the AMPS (Fig. 1a). The system consists of feet supports (left and right) with electrical motors that activate two actuated steel bars with a diameter of 2 mm (Fig. 1b); the motor-activated stimulators apply a mechanical pressure in two specific areas for each foot (Fig. 1c): on the head of the hallux, left and right, and on the first metatarsal joint, left and right.

Before treatment, the device needs to be adjusted to the patient's feet: a plantar of the correct size is mounted on each unit (left and right) to accommodate the feet; the feet are inserted in the two units and tied using three straps per foot; and then steel bars of the correct length are mounted on the axis of the electrical motors. The next step consists of positioning the motors – which are mounted on adjustable platforms – in order to make the steel bars interact with the areas to be stimulated (head of the hallux and first metatarsal joint of both feet). When the device has been adjusted, the excursion of the four motors (independently for each one) is programmed with a remote control to apply the correct pressure stimulation in each area. The pressure of stimulation – always applied in a range of 0.3–0.9 N/mm^2 – is set for each participant

Fig. 1
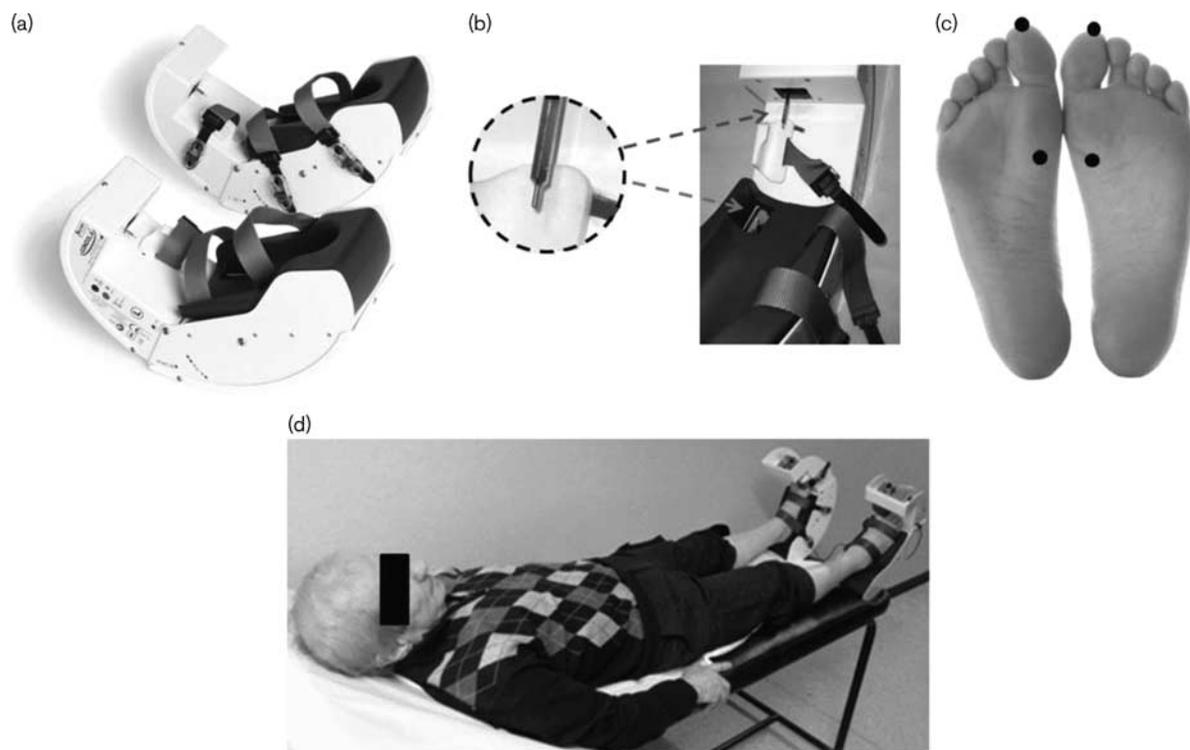
(a) The Gondola device; (b) two moving steels; (c) points of stimulation on the feet; (d) patient positioning.

upon appearance of the monosynaptic reflex in the tibialis anterior muscle by the detection of a liminaris contraction while applying pressure in the contact areas. Once the pressure value has been set using this procedure, the value is recorded to administer the AMPS. This preparatory procedure requires ~10 min.

The treatment consists of four cycles; one cycle included a stimulation of the four target areas requiring 24 s, whereas the overall treatment included four cycles lasting a total of 96 s. During the AMPS treatment, patients lay down (Fig. 1d).

At the end of the AMPS stimulation, both units of the device are removed from the feet of the patient; this final action is very easy and fast (less than 1 min).

During the current study, every patient underwent two AMPS sessions per week for 3 weeks (total: 6 AMPS sessions/patient).

Intervention
PD patients were treated with the AMPS six times at four intervals. All patients with PD were in a defined off-phase.

All patients with PD were evaluated by gait analysis before and after the first intervention ('acute' phase),

after six interventions, 48 h after the sixth intervention, and 10 days after the end of the treatment cycle. The clinical tests were applied before the treatment (pre), at the end of the treatment (after the cycle of 6 AMPS sessions), and 10 days after the end of the treatment cycle.

Clinical evaluations
The patients in the PD group were assessed using the following clinical scales:

(1) Unified Parkinson's Disease Rating Scale III (UPDRS III): UPDRS is a rating scale used to follow the longitudinal course of PD; section III refers to clinically scored motor evaluation. It has ratings ranging from 0 to 4, in which the severity of the symptoms is rated 0 (normal) to 4 (severe) (Goetz *et al.*, 2008).
(2) Functional ambulation classification: categorization patients according to the basic motor skills necessary for functional ambulation, from 1 (nonfunctional) to 6 (independent) (Holden *et al.*, 1984);
(3) Parkinson's Disease Questionnaire (PDQ39): a self-completion questionnaire designed to address aspects of functioning and well-being for patients affected by PD. Patients are asked to think about their health

and general well-being and to consider how often in the last month they have experienced certain events (e.g. difficulty walking 100 yards) and to indicate the frequency of each event by selecting one of 5 options, ranging from 0 (never) to 4 (always) (Peto *et al.*, 1998).

(4) Tinetti Assessment Tool: a simple, easily administered test that measures a patient's gait and balance. The test is scored on the patient's ability to perform specific tasks. Scoring of the Tinetti Assessment Tool is calculated on a three-point ordinal scale with a range of 0 (the most impairment) to 2 (independence). The individual scores are then combined to form three measures: an overall gait assessment score, an overall balance assessment score, and a gait and balance score. The maximum score for the gait component is 12 points. The maximum score for the balance component is 16 points. The maximum total score is 28 points. In general, patients who score below 19 are at a high risk for falls. Patients who score in the range of 19 to 24 indicate that the patient has a risk for falls (Tinetti, 1986).

(5) 10 Meters Walk Test (10MWT): assesses walking speed in meters per second over a short duration. Older adults should walk between 0.9 and 1.3 m/s (Bohannon, 1997).

(6) Timed Up and Go (TUG): assesses the time that an individual takes to rise from a chair, walk 3 m, turn around, walk back to the chair, and sit down. One source suggests that scores of 10 s or less indicate normal mobility, 11–20 s are within normal limits for frail elderly and disabled patients, and greater than 20 s means that the individual needs assistance outside and indicates further examination and intervention. A score of 14 s or more suggests that the individual may be prone to falls (Bischoff *et al.*, 2003; Podsiadlo and Richardson, 1991).

Experimental procedures for gait analysis

All participants were assessed for gait analysis using an optoelectronic system (BTS, Milan, Italy) with passive markers positioned according to the Davis marker-set (Davis *et al.*, 1991) and a synchronic video system (BTS). After the collection of some anthropometric measures (height, weight, tibial length, distance between the femoral condyles or diameter of the knee, distance between the malleoli or diameter of the ankle, distance between the anterior iliac spines, and thickness of the pelvis), passive markers were placed at special points of reference, directly on the patient's skin, as described by Davis *et al.* (1991) to evaluate the kinematics of each body segment. In particular, they were placed at C7, sacrum and bilaterally at the anterior superior iliac spine, greater trochanter, femoral epicondyle, femoral wand, tibial head, tibial wand, lateral malleolus, lateral aspect of the foot at the fifth metatarsal head, and at the heel (only

for static offset measurements). To assure the reproducibility of the aquisition technique and to avoid the errors due to different operators the same health professional made all aquisitions. The participant was asked to walk barefoot at a self-selected speed along a 10 m flat walkway. A minimum of seven trials were acquired for each session to ensure repeatability of the measure. At least four steps for each trial were acquired and among these, two subsequent strides (one for the right side and one for the left side) were considered for each trial; the selected strides are those in the center of the lab so that the participant is assessed at the steady-state walking condition.

All data obtained from gait analysis were normalized as % of the gait cycle. Although kinematics (angles of the main lower limbs) were also acquired during this study, these are not included in the present analysis and are not discussed in this paper. In the present study, only spatio-temporal gait variables were analyzed.

Dependent variables

The following parameters were considered.

(1) Mean velocity (m/s): mean velocity of progression, computed as the average instantaneous speed of the marker placed on sacrum.

(2) Swing velocity (m/s): velocity of each leg during the swing phase according to the ratio between the distance covered during the limb swing phase and the time of the swing phase.

(3) Cadence (steps/min): number of steps in a time unit.

(4) Stride length (m): longitudinal distance between successive points of heel contact of the same foot.

(5) Step length (m): longitudinal distance from one foot strike to the next one.

(6) Step width (m): mediolateral distance between the two feet during double support.

(7) Stance phase (as % of the gait cycle): percentage of the gait cycle when both feet are on the ground.

(8) Swing phase (as % of the gait cycle): percentage of the gait cycle when foot swings forward between one episode of ground contact and the next.

(9) Double support (as % of the gait cycle): the duration of the phase of support on both feet as percentage of gait cycle.

Statistical analysis

For the statistical analysis, an analysis of variance one-way ($\alpha \leq 0.05$) was first used for the comparison for anthropometric data (age, body mass, and height) between the PD and the control groups.

For the statistical analysis, the data normality was tested using the Kolmogorov–Smirnov test. Then, *t*-tests were used to compare the differences among AMPS interventions (pre, 6 AMPS, and 10 days after the last treatment) and clinical scales. To compare the differences among the

AMPS interventions (pre, post, 6 AMPS, 48 h, and 10 days) for the gait spatiotemporal parameters, the nonparametric data were analyzed using the Friedman test and Bonferroni post-hoc test ($\alpha \leq 0.05$). Finally, the Mann–Whitney test and the Bonferroni post-hoc test ($\alpha \leq 0.05$) were used to compare the gait spatiotemporal parameters of the PD group versus the control group. The SPSS software (version 19 IBM Corp, Armonk, New York, USA) was used to carry out all statistical analyses.

Results

A one-way analysis of variance showed no significant differences between the patients with Parkinson's and the control group in terms of age ($P = 0.883$), body mass ($P = 0.291$), or height ($P = 0.853$).

Clinical scales results

Below, the results of the evaluation of clinical scales are reported as described in the material and methods section, applied before the treatment, after the last (sixth) stimulation, and 10 days after the last stimulation (Table 1). As shown, all scales showed a statistically significant improvement at the end of the treatment (after six stimulations), and this improvement was maintained after 10 days after the completion of treatment; the only value that was not significant at the 10-day follow-up is that of the Tinetti scale.

Spatiotemporal variables results

Figure 2 presents the results of the percentage of improvement for each presented variable. Differences were found between pre-AMPS intervention and all other postintervention trials for stride (Fig. 2a), step length (Fig. 2b), mean velocity (Fig. 2c), swing velocity (Fig. 2d), and cadence (Fig. 2e).

Differences were found between the control group and all intervention trials for step length, step width, stride length, swing phase, stance phase, double support, mean velocity, stride velocity, and swing velocity. The only difference between pre-AMPS and the control group was found in cadence; for the other postintervention trials and the control group, no differences were found. Table 2 shows these data.

Discussion

In this study, we evaluated from a longitudinal perspective the effects of an innovative treatment for the AMPS of the afferent pathways of the foot in patients with PD.

When the clinical scales were compared, the results showed that PD patients had a decrease in the severity of symptoms, an increase in functionality and independence to perform their day-to-day activities, and a reduced risk of falling. Moreover, participants with PD showed improvement in gait parameters after intervention with AMPS. PD patients showed significant improvements in the spatiotemporal parameters of gait. Interestingly, after the first AMPS, the cadence of PD group patients reached normative values. Because no differences were recorded in values after six AMPS treatments and 10 days after the last treatment, it appears that AMPS treatment reduces gait impairment (according to all parameters and spatiotemporal gait parameters) in PD patients, with positive effects lasting for at least 10 days after the treatment cycle.

Seiss et al. (2003) found evidence that muscle spindle sensitivity is normal in individuals with PD and concluded that proprioceptive impairment is in the central processing of the sensory information. Pratorius et al. (2003) carried out a study investigating the sensitivity of the sole of the foot in individuals with PD. They found that PD patients have significantly higher thresholds of sensitivity, and thus, PD patients require an amplified stimulus to overcome the increased threshold. They also found a relationship between severity and threshold, in which more severely affected patients show higher sensitivity thresholds (Pratorius et al., 2003). In accordance with this, Dietz and Colombo (1998) found that individuals with PD show reduced load sensitivity and, therefore, an increased threshold in the lower leg receptors, which may also contribute toward the movement deficits found in PD. If the deficit lies solely in the sensory receptors themselves, then an increase in stimulus intensity should be able to overcome the defective sensory receptors that may be responsible for the proprioceptive deficit, as suggested in previous research (Tsuchida et al., 2013; Raggi et al., 2014).

On the basis of these findings, we hypothesize that AMPS elicited stretch reflexes in the muscle throughout the leg. The AMPS can induce a response from the

Table 1 Clinical scales' comparisons

Intervention	UPDRS III	PDQ39	TUG	FAC	10MWT	Tinetti
Pre	27.44 ± 6.42	51.87 ± 31.320	16.12 ± 5.51	3.75 ± 1.035	0.4925 ± 0.04	11.42 ± 1.90
Post 6 AMPS	19.22 ± 3.66*	39.5 ± 23.25*	12.75 ± 1.75*	4.5 ± 0.75*	0.53 ± 0.06*	14.71 ± 1.60*
Post 10 days	23.66 ± 4.03**	42.12 ± 22.29**	14.37 ± 2.13**	4.25 ± 0.88**	0.51 ± 0.05	13 ± 1.82**

AMPS, automated mechanical peripheral stimulation; FAC, Functional Ambulation Classification; 10MWT, 10 Meters Walk Test; PDQ39, Parkinson's Disease Questionnaire; Tinetti, Tinetti Assessment Tool; TUG, Timed Up and Go; UPDRS III, Unified Parkinson's Disease Rating Scale III.
*$P \leq 0.05$, pre versus post 6 AMPS.
**$P \leq 0.05$, pre versus post 10 days.

Fig. 2
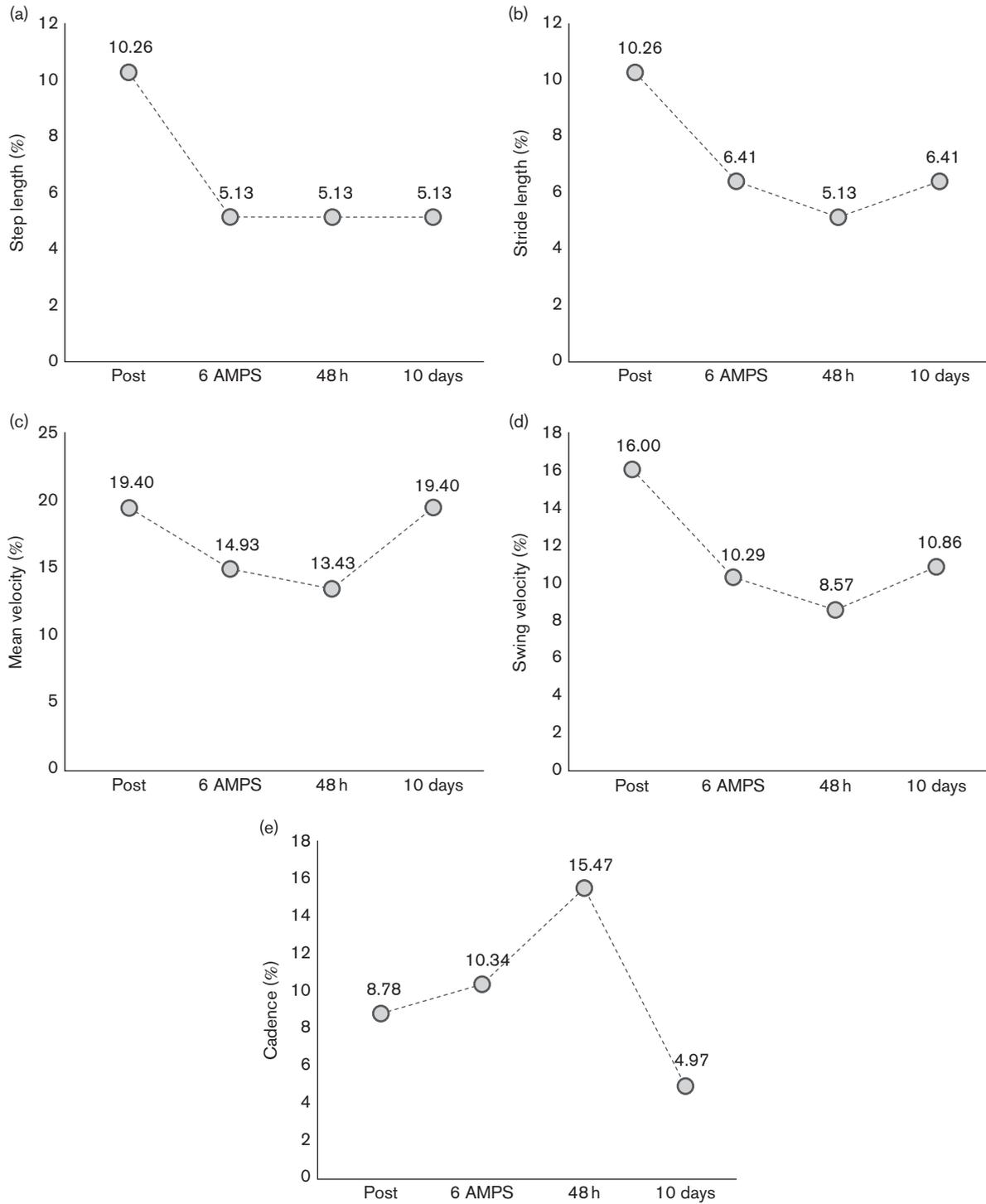
The percentage of improvement postacute phase, post 6 AMPS, post 48 h, and post 10 days for (a) stride length; (b) step length; (c) mean velocity; (d) swing velocity; (e) cadence for the PD group. AMPS, automated mechanical peripheral stimulation; PD, Parkinson's disease.

proprioceptors, which in turn can affect the gait of an individual. This is reasonable to expect because various types of sensory receptors work together to provide accurate feedback to the central nervous system during locomotion. Thus, mechanical facilitation of the plantar surface may be able to increase the sensory stimulation

Table 2 Gait variables' comparison between the PD and the CG

Variables	Pre	Post	6 AMPS	48 h	10 days	CG
Step length (m)	0.39 ± 0.14[a]	0.43 ± 0.13[b]	0.41 ± 0.13[c]	0.41 ± 0.13[d]	0.41 ± 0.12[e]	0.54 ± 0.08[a,b,c,d,e]
Step width (m)	0.18 ± 0.01[a]	0.18 ± 0.01[b]	0.18 ± 0.01[c]	0.19 ± 0.01[d]	0.19 ± 0.01[e]	0.20 ± 0.02[a,b,c,d,e]
Stride length (m)	0.78 ± 0.28[a]	0.86 ± 0.26[b]	0.83 ± 0.27[c]	0.82 ± 0.27[d]	0.83 ± 0.24[e]	1.09 ± 0.17[a,b,c,d,e]
Swing phase (%)	36.08 ± 4.79[a]	37.11 ± 3.98[b]	37.46 ± 4.51[c]	37.76 ± 3.81[d]	37.13 ± 5.35[e]	39.45 ± 1.76[a,b,c,d,e]
Stance phase (%)	63.91 ± 4.79[a]	62.88 ± 3.98[b]	62.53 ± 4.51[c]	62.23 ± 3.81[d]	62.86 ± 5.35[e]	60.55 ± 1.76[a,b,c,d,e]
Double support (%)	13.5 ± 4.54[a]	12.88 ± 3.46[b]	12.49 ± 4.39[c]	12.92 ± 5.05[d]	13.11 ± 5.13[e]	10.83 ± 1.76[a,b,c,d,e]
Mean velocity (m/s)	0.67 ± 0.3[a]	0.8 ± 0.3[b]	0.77 ± 0.29[c]	0.76 ± 0.31[d]	0.8 ± 0.29[e]	1.04 ± 0.15[a,b,c,d,e]
Stride velocity (m/s)	0.73 ± 0.31[a]	0.86 ± 0.31[b]	0.83 ± 0.3[c]	0.81 ± 0.32[d]	0.84 ± 0.30[e]	1.09 ± 0.15[a,b,c,d,e]
Swing velocity (m/s)	1.75 ± 0.63[a]	2.03 ± 0.60[b]	1.93 ± 0.64[c]	1.90 ± 0.67[d]	1.94 ± 0.62[e]	2.46 ± 0.32[a,b,c,d,e]
Cadence (steps/min)	100.66 ± 12.47[a]	109.05 ± 14.24	111.07 ± 14.7	116.23 ± 33.84	105.66 ± 17.36	110.73 ± 5.34[a]

AMPS, automated mechanical peripheral stimulation; CG, control group; PD, Parkinson's disease.
[a]Differences between Pre and CG.
[b]Differences between Post and CG.
[c]Differences between 6 AMPS and CG.
[d]Differences between 48 h and CG.
[e]Differences between 10 days and CG.

received to overcome the proprioceptive deficits that impair gait in individuals with PD.

Current therapeutic options for treating these gait disturbances and reducing patients' risk of fall in PD are quite limited. Despite advances in pharmacologic therapy and surgical procedures, impairments in gait and balance remain common in PD patients (Grimbergen et al., 2004). The development of an add-on therapy and rehabilitation-like approaches is important for the management and the well-being of patients living with PD. The results of this study provide new insights into using the AMPS as an effective therapy for the well-being of PD patients through improvement in gait.

In any case, the current study has some limitations, primarily because of the limited strength of the statistical findings because of the reduced number of participants studied. Despite this limitation, the outcomes show that this innovative treatment can provide patients living with PD with a noninvasive add-on therapy to reduce gait and balance impairments. Additional studies are advised to further document and confirm the positive, encouraging effects of AMPS treatment in PD. Parameters of gait kinetics should also be included in a future study because they have not been analyzed in this study.

Conclusion
The study outcomes indicate that AMPS treatment applied to PD patients improves gait, mobility, and quality of life. These findings indicate that AMPS may promote a more stable walking pattern in patients with PD and that long-term repetition of AMPS treatment is apparently able to restore the rhythmicity of gait and reduce the risk of falls. In most cases of patients living with PD, the goal of treatments is 'maintenance' care; this study shows that rehabilitation approaches can indeed reduce gait and balance impairments because of this neurodegenerative condition, improving the patient's quality of life. This study contributes toward a

growing body of evidence that AMPS may be a useful approach to treat neurodegenerative diseases such as PD.

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