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Effect of Two Different Rehabilitation Training with a Robotic Gait System in Body Weight Support and a Proprioceptive Sensory-motor Exercises on Unstable Platforms in Rehabilitation of Gait and Balance Impairment and Fatigue in Multiple Sclerosis

Saggini R[1*], Ancona E[2], Supplizi M[3], Barassi[4], Carmignano SM[2] and Bellomo RG[5]

[1]Department of Medical Oral and Biotechnological Sciences, Physical and Rehabilitation Medicine, School of Specialty in Physical and Rehabilitation Medicine, "Gabriele d'Annunzio" University of Chieti-Pescara, Italy

[2]School of Specialty in Physical and Rehabilitation Medicine, "Gabriele d'Annunzio" University of Chieti-Pescara, Italy

[3]Section of Physical and Rehabilitation Medicine, "Gabriele d'Annunzio" University of Chieti-Pescara, Italy

[4]Faculty of Physiotherapy "Gabriele d'Annunzio" University of Chieti-Pescara, Italy

[5]Department of Medicine and Sciences of Aging, Physical and Rehabilitation Medicine, "Gabriele d'Annunzio" University of Chieti-Pescara, Italy

[*]**Corresponding author:** Raoul Saggini, Department of Medical Oral and Biotechnological Sciences, Director of the School of Specialty in Physical and Rehabilitation Medicine, "Gabriele d'Annunzio" University of Chieti-Pescara, Italy, Tel: +39-0871-3553005/3553007; E-mail: raoul.saggini@unich.it

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Abstract

Walking and balance disturbances and fatigue are key symptoms in patients with MS, and major causes of discomfort, even in patients with mild disability since the early stages of the disease.

The aim of this study was to compare the effectiveness of end-effector robot-assisted gait training (RAGT) and proprioceptive sensory-motor exercises on unstable platforms in improving walking and balance performance. We enrolled 41 patients with relapsing-remitting MS at early stage and low or mild disability: patients in group A underwent a robotic gait rehabilitation treatment which involved the use of SPAD (Sistema Posturale Antigravitario Dinamico), patients in group B underwent a cycle of sensory-motor training in our laboratory of performance enhancement; patients in both groups were subjected to neuromuscular manual therapy. All treatment was provided with 3 sessions per week for 6 weeks (for a total of 18 sessions). Patients were evaluated by administration of the Functional Independence Measure (FIMTM), the Expanded Disability Status Scale (EDSS), the Berg Balance Scale (BBS), the Fatigue Severity Scale (FSS), and the Modified Fatigue Impact Scale (MFIS), and by performing stabilometric and gait analysis.

Results show statistically significant improvement of the FIMTM and the BBS average score in all patients, reduction of the EDSS average score in all patients (but in a statistically significant manner only in group A), reduction in average scores obtained in both evaluation questionnaires of fatigue (non-significant improvement of the FSS average score in the overall sample and in both groups, statistically significant reduction of the MFIS average scores), improvement in stabilometric parameters in all patients (but in a statistically significant manner only in group B) and statistically significant improvement in temporal parameters of gait in all patients.

So body weight supported gait training and sensory-motor exercises on unstable platforms are feasible and could be safely used as additional therapeutic.

Keywords: Multiple sclerosis; Fatigue; Balance; Walking disturbances; Stabilometry; Gait analysis; Robotic gait training; Microgravity environment; Sensory-motor systems

Introduction

Multiple Sclerosis (MS) is a chronic immune-mediated disease of the central nervous system, most often diagnosed in young and middle-aged subjects (two-third of which is women). The disease is characterized by the triad inflammation, demyelination, gliosis, and the most common signs and symptoms are fatigue and weakness, gait and balance impairment (up to ataxia), numbness or tingling, dizziness and vertigo, vision problems, spasticity, pain, cognitive and emotional changes, with a strong impact on activity of daily living [1].

Posture, balance and dynamic movement as during gait need continuous integration of signals coming from visual, vestibular, and proprioceptive apparatus, which are part of the sensory-motor system. All these informations travels along myelinated long nervous fibers belonging to the central nervous system (CNS) [2,3]. So the mechanism underlines impairments balance strategy during functional movements and gait in people with multiple sclerosis (MS) may be correlate to abnormal integration of sensorimotor stimuli [4].

Gait and balance impairment and the underlying physical functions are common findings in people with MS [5]. Approximately 75% of subjects with MS experience clinically significant walking limitations [6-11], which may be present even in patients with mild disability since the early stages of the disease (a cerebellar and brainstem involvement has been shown in 25% of patients already at the onset of disease [12]), and could be due to tightness or spasticity, sensory deficit of lower limbs, weakness, fatigue [13-15].

Patients with MS have a range of gait abnormalities, including decreased step length, decreased cadence, reduced joint movement, and increased variability of most gait parameters. These changes lead to decreased velocity, reduced [16]. It has been suggested that alterations in gait performance, particularly temporal spatial characteristics, may be associated with impaired balance [17], however no studies have investigated the relationship between gait and balance parameters in MS patients. Abnormal gait has been related to deficits in muscle strength and fatigue, manifested as decreased joint torques [18-20] and joint torque asymmetries even in early stages of MS [21]. Herbert et al. hypothesized that because alteration of sensation of dizziness due to loss of balance reflect central processing, impairments of central sensory processing may contribute to fatigue in patients with MS [22]. The difficulty in maintaining the balance involves a reduced ability to perform a specific function [23] as well as increased postural sway, related to the processing of sensorimotor information. The central integration deficits of sensory impulses related to loss of balance and fatigue are often underestimated in MS patients especially at an early or mild phase [24].

Both drugs and non-pharmacological interventions have been tested to improve MS-related fatigue and gait and balance impairment [25-36]. Numerous studies have investigated the effect of rehabilitation on patient mobility with MS, an analysis of reviews [37-38] and meta-analysis [39] show that physical exercise can be associated with a minimal improvement in gait and posture for MS patients.

Some studies report traditional over-ground walking training hat gravitational rehabilitation is associated with risk of falling for patients with a balance deficit and is often not included in the treatment of patients with MS in initial and mild stages [40].

Other studies have shown that new strategies for balance and gait rehabilitation in microgravity environment and/or body weight support are effective in patients with stoke or Parkinson's disease, not only showing an improvement of gait but also balance parameters [41-43].

Few studies have demonstrated the effectiveness of robot-assisted gait training (RAGT) for SM or sensorimotor therapy focusing on sensory facilitation and integration provides controlled sensory input from the vestibular, tactile, and proprioceptive systems [44,45].

The aim of this study was to compare the effectiveness of end-effector robot-assisted gait training (RAGT) and proprioceptive sensory-motor exercises on unstable platforms in improving walking and balance performance in patients with MS. The rationale was that both two training modalities might promote central neural integration linked to feedback and feed forward processes related to gait and balance. Furthermore, we would explore the potential application of new technological devices for treatment of MS, still efficacy in other neurological disease.

Materials and Methods

Subjects

Between June 2014 and June 2016, 50 patients with relapsing-remitting MS at early stage and low or mild disability (ability to stand independently in upright position for at least 30 seconds, ability to walk independently or with an intermittent or unilateral constant aid such as a cane or a crutch, with an Expanded Disability Status Scale ≤ 6) came to the University Centre of Physical and Rehabilitation Medicine (CUMFeR) of "Gabriele d'Annunzio" University of Chieti-Pescara, Italy. We excluded from the Study 9 patients which who showed a clinically defined relapse within 30 days prior to the beginning of treatment; so, 41 were enrolled and hence randomly divided into two groups: a group a composed of 20 subjects, and a group B composed of 21 subjects. 7 patients dropped out because of acute attack during the treatment, and so only 34 subjects reached the end point (Figure 1). The two groups were so composed: the group A consisted of 16 individuals, including 12 females and 4 males, mean age 26.8 years (range 24-32 years); the group B consisted of 18 individuals, including 11 females and 7 males, mean age 27.3 years (range 23-34 years).

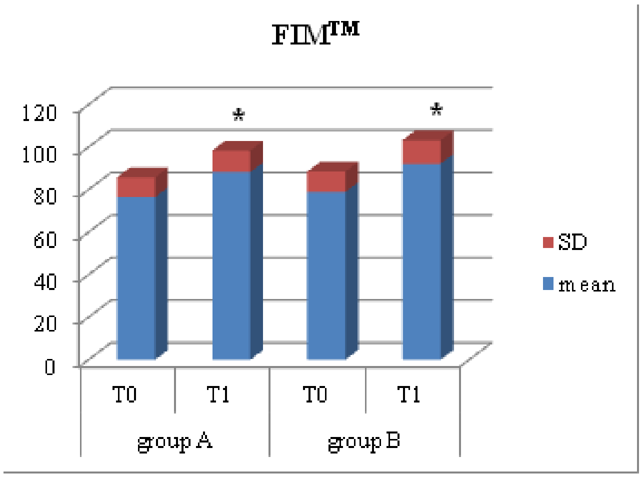

Figure 1: Flow chart of the Study (SPAD, Sistema Posturale Antigravitario Dinamico (Dynamic Antigravity Postural System)).

Interventions

Patients in group A underwent a gait rehabilitation treatment which involved the use of SPAD (Sistema Posturale Antigravitario Dinamico, Dynamic Antigravity Postural System), a device for body weight relief consisting of a machinery designed to reduce, modify, and condition the force of gravity acting on the body structures of movement during the act of rectilinear motion. The system is based on the rational rationale that gait training can be made combining the motor task with sensory feedback, in line with the multisensory approach to postural control. The machinery consists of a treadmill on which the patient carries out training in body weight support and of a structure to which the patient is harnessed by means of a pneumatic belt placed between the iliac crests and the costal arches, connected to lifting system with four tie-rods attached to the body and to the pelvic girdle; equipment is completed by four front pads (two on the humeral heads for the shoulder girdle and two on the anterior superior iliac spine for the pelvis), which act as stabilisers (as they prevent possible twisting of the pelvis or shoulder during movement on the treadmill), and at the same time as informants proprioceptive, and two rear pads (placed on the infrascapular region and on the sacral apex); according to the characteristics of the patient, an inflatable collar to get even the alignment of the subsystem skull-mandibular can be also used [45].

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Each session of SPAD provides a 20-30% mean body weight relief and training on the treadmill with adjustable speed (down to 0.01 km/h during the first session, allowing to become familiar with the machine and thus obtaining a higher compliance). The harnessing in body weight support allows to: follow the excursion of the subject's center of mass in its vertical range (due to the opening of the lower limb compass), reduce the load on the spine (through the degravitation of the body weight on the pelvis), produce homogeneous ground-foot reactions, with restoration of physiological proprioceptive inputs and consequent recovery of a correct gait motor schema; the step performing is continuously corrected by the operator, inviting the patient to get an ordered cadence with sequential placement of heel-plant-toe. In this way, session after session, SPAD allows to manage asymmetrical gait adaptations, separately working on the two body hemisoma with a dual action: a mechanical one, which allows a neuromotor retraining with cortical-subcortical learning aimed to the reacquisition of a balanced body schema which minimizes the energy consumption needed to maintain a correct posture, and a proprioceptive one, which acts on the maintenance of automatic and induced-over-time walking adaptations. The last part of the session provides for the reduction of body weight relief gradually to 0% and the reduction of the speed of the treadmill until the stop; in this way, in the last part of the session the patient, continuing to maintain the proprioceptive stimulus, reaccustom himself to the gait without body weight support.

Patients in group B underwent a cycle of physical activity in our laboratory of performance enhancement, consisting of 10 min of traditional stability exercises with Bobath ball, Bosu platform, Freeman tablets, Synergy Mat® (Human Tecar, Unibell International, Italy), and 20 minutes of sensory-motor exercises on Imoove® (Allcare Innovations, France), an unstable platforms platform with a particular elispheric movement that allows to influence and condition the proprioception, balance and motor coordination, as well as joint mobility and muscle tone.

Patients in both groups were subjected to neuromuscular manual therapy and stretching exercises that makes make it possible to treat trigger points in chronically contracted muscles by correcting wrong compensatory postures in patients suffering from disorders of gait pattern due to hypertonia of specific muscle groups; in particular, the treatment was focused on muscles of the side chain of the trunk and of the anterior and posterior-lateral of the leg, as well as on the respiratory muscles (pectoralis minor), and was completed by stretching exercises with postural sensitized bench (Postural Bench®, Tecnobody, Italy) and postural decompensated bench (FlexiMat®, Deltadue, Italy), lying in supine position.

All treatment was provided with 3 sessions per week for 6 weeks (for a total of 18 sessions).

Clinical and instrumental assessment

All patients enrolled underwent physiatrist examination, completed by: assessment of the overall degree of disability, by administration of the Functional Independence Measure (FIMTM), a scale that detects the degree of autonomy with which activities of daily living (ADL) ADL and communication and interpersonal relation-related cognitive activities are carried out;

- quantification of disability in MS by administration of the Expanded Disability Status Scale (EDSS), which assigns a functional system score in each of eight functional systems involved in the disease (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, other), and also allows to evaluate the effect of treatment on disease progression [46];

- evaluation of balance by administration of the Berg Balance Scale (BBS), a 14-item scale exploring the ability to sit, stand, lean, turn, and maintain the upright position on one leg, initially developed for the elderly [47-49], later validated also for MS [50-52];

- evaluation of the impact of fatigue by administration of two self-report questionnaires, the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS); the latter one provides an assessment of the effects of fatigue in terms of cognitive, physical, and psychosocial functioning [53];

- stabilometric and gait analysis, performed with an electronic modular system, consisting of a platform of detection and a walkway (with 7 active sensors per cm^2), interfaced with the acquisition software MTX7® (Diagnostic Support, Rome, Italy). Firstly, it was conducted the examination of static balance (stabilometric test), performed in conditioned orthostatism (barefoot standardized position obtained placing a 30° V-shaped frame between the feet), both with open eyes and closed eyes, for 30 seconds with a 30-second rest period between each trial; for each condition, once detected the instantaneous position of the Centre of Pressure (CoP), the software calculates the length of trajectory of the CoP, the sway area (area of the ellipse that encloses 95% of instantaneous positions of the CoP), and the velocity of oscillations of the CoP. Secondly, the patient was invited to walk on the platform for dynamic test (gait analysis): it he/she was asked to repeat the walk three times in both directions, without leaving the platform, in order to detect instability in walking and deviation in trajectory compared with oscillations detected at the static test.

Data analysis

Data obtained were analyzed with NCSS 9 software for Windows. In order to to check the normality of distribution and the homogeneity of variances Shapiro-Wilks and Levene tests were performed. Then baseline differences between groups of patients were assessed using χ^2-test for qualitative parameters and Student's t-test for quantitative parameters. Statistical significance was set to values of $p \leq 0.05$. Values are expressed as mean ± standard deviation (SD).

Results

At the end of the Study, the scores of the rating scales were modified as follows: statistically significant improvement of the FIMTM average score (from 77.69 ± 9.25 to 90.25 ± 10.48; p=0.0011) in all patients, both in group A (from 76.50 ± 9.34 to 88.25 ± 10.20; p=0.0306) and in group B (from 78.88 ± 9.64 to 92.25 ± 11.06; p=0.0219), with no statistical difference between the two groups (Figure 2);

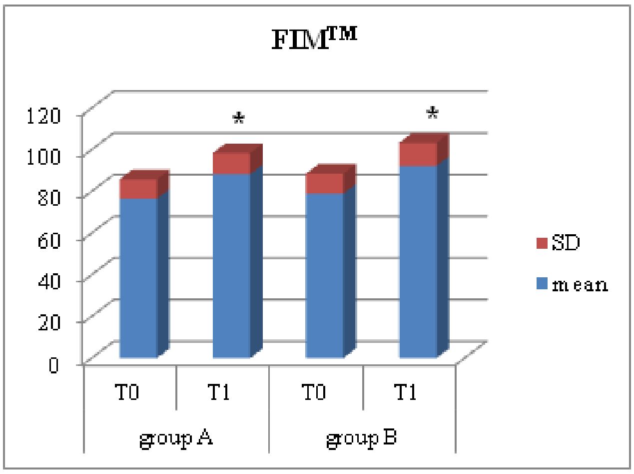

Figure 2: Variation in the FIMTM average score (Asterisk indicates statistical significance).

reduction of the EDSS average score (from 5.34 ± 0.47 to 4.75 ± 0.68; p=0.0077) in all patients, in a statistically significant manner in group A (from 5.31 ± 0.46 to 4.63 ± 0.69; p=0.0348), in a non-significant manner in group B (from 5.38 ± 0.52 to 4.88 ± 0.69; p=0.1248) (Figure 3);

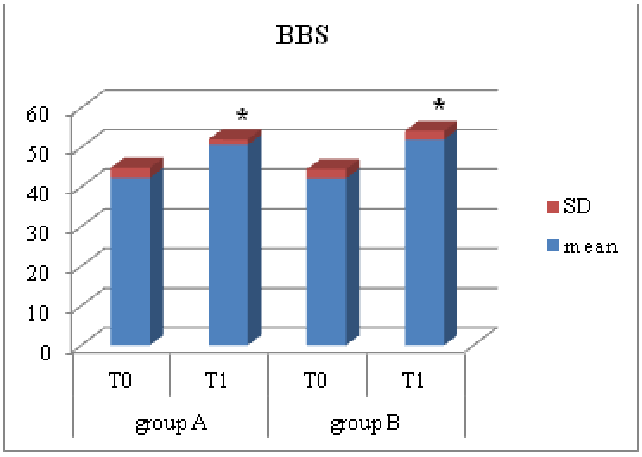

Figure 3: Variation in the EDSS average score (Asterisk indicates statistical significance).

Statistically significant improvement of the BBS average score (from 42.19 ± 2.37 to 51.31 ± 1.89; p<0.0001) in all patients, both in group A (from 42.25 ± 2.55 to 50.63 ± 1.41; p<0.0001) and in group B (from 42.13 ± 2.36 to 52.00 ± 2.14; p<0.0001), with no statistical difference between the two groups (Figure 4);

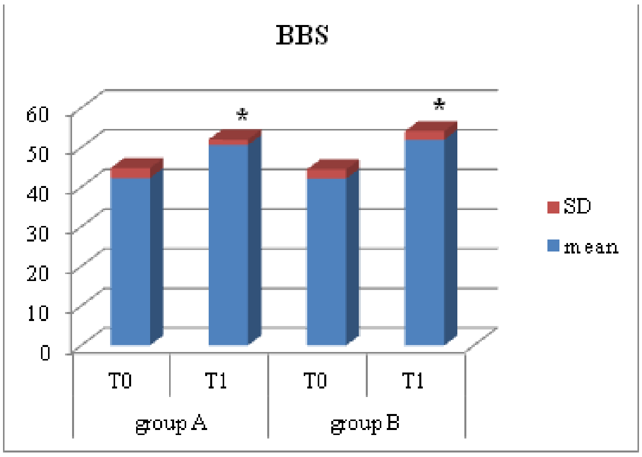

Figure 4: Variation in the BBS average score (Asterisk indicates statistical significance).

reduction in average scores obtained in both evaluation questionnaires of fatigue, in particular: as regards the FSS, it has been obtained an improvement of the average score in the overall sample (from 40.06 ± 4.04 to 36.75 ± 5.30; p=0.0559) and in both groups (from 39.88 ± 4.58 to 36.63 ± 4.72, p=0.1839 in group A, from 40.25 ± 3.73 to 36.88 ± 6.15, p=0.2058 in group B), although without statistical significance; as regards the MFIS, the reported variation is statistically significant in the overall sample (from 43.75 ± 3.26 to 39.13 ± 4.32; p=0.0018) and in both groups (from 43.86 ± 3.27 to 39.38 ± 4.31, p=0.0337 in group A; from 43.63 ± 3.46 to 38.88 ± 4.61, p=0.0353 in group B), with no statistical difference between the two groups (Figure 5);

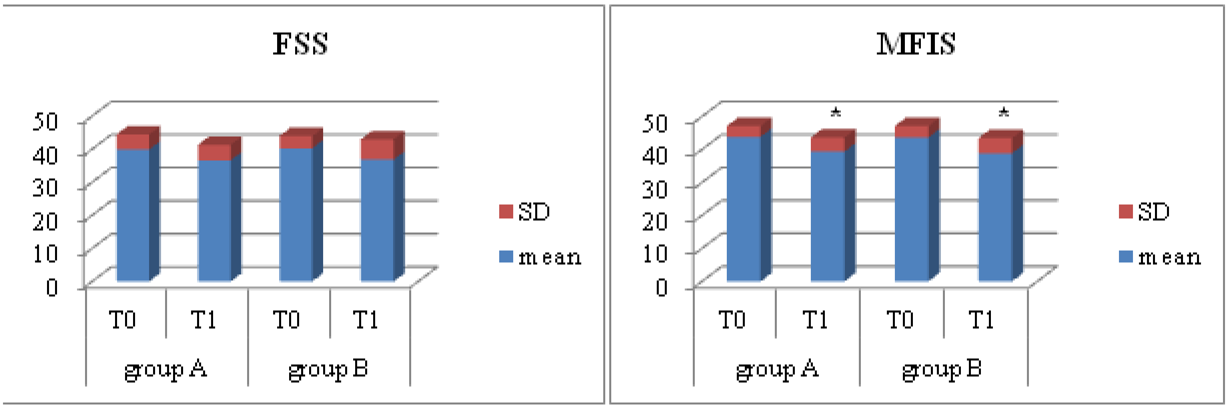

Figure 5: Variation in the FSS (left) and MFIS (right) average scores (Asterisk indicates statistical significance).

Improvement in stabilometric analysis (Table 1). In particular, at open-eye stabilometry: in group A the length of CoP trajectory reduced from 90.58 ± 84.92 to 37.46 ± 27.19 mm (p=0.1141), the sway area reduced from 179.67 ± 105.88 to 151.77 ± 56.39 mm2 (p=0.5213), the velocity of CoP oscillations significantly increased from 1.57 ± 0.85 to 2.45 ± 0.72 mm/s (p=0.0432); in group B the length of CoP trajectory significantly reduced from 109.21 ± 71.89 to 39.96 ± 24.31 mm (p=0.0218), the sway area significantly reduced from 218.27 ± 93.87 to 134.29 ± 54.25 mm^2 (p=0.0459), the velocity of CoP oscillations significantly increased from 1.74 ± 0.83 to 2.92 ± 1.31 mm/s (p=0.0497). At closed-eye stabilometry: in group A the length of CoP trajectory reduced from 153.07 ± 194.00 to 76.59 ± 61.34 mm (p=0.3057), the sway area reduced from 321.61 ± 173.02 to 246.75 ± 76.61 mm^2 (p=0.2972), the velocity of CoP oscillations increased from 3.07 ± 1.59 to 5.05 ± 2.37 mm/s (p=0.0694); in group B the length of CoP trajectory reduced from 180.52 ± 136.79 to 89.09 ± 66.33 mm (p=0.1111), the sway area significantly reduced from 319.44 ± 103.99 to 225.48 ± 65.86 mm^2 (p=0.0487), the velocity of CoP oscillations significantly increased from 2.46 ± 1.32 to 5.30 ± 2.39 mm/s (p=0.0106);

Stabilometric parameter		**Group A**			**Group B**		
		T0	T1	p value	T0	T1	p value
Open eyes	Length of trajectory (mm)	90.58 ± 84.92	37.46 ± 27.19	0.1141	109.21 ± 71.89	39.96 ± 24.31	0.0218*
	Sway area (mm^2)	179,67 ± 105.88	151.77 ± 56.39	0.5213	218.27 ± 93.87	134.29 ± 54.25	0.0459*
	Velocity of oscillations (mm/s)	1.57 ± 0.85	2.45 ± 0.72	0.0432*	1.74 ± 0.83	2.92 ± 1.31	0.0497*
Closed eyes	Length of trajectory (mm)	153.07 ± 194.00	76.59 ± 61.34	0.3057	180.52 ± 136.79	89.09 ± 66.33	0.1111
	Sway area (mm^2)	321.61 ± 173.02	246.75 ± 76.61	0.2972	319.44 ± 103.99	225.48 ± 65.86	0.0487*
	Velocity of oscillations (mm/s)	3.07 ± 1.59	5.05 ± 2.37	0.0694	2.46 ± 1.32	5.30 ± 2.39	0.0106*

Table 1: Stabilometric assessment parameters (Asterisk indicates statistical significance).

Improvement in spatiotemporal gait parameters (Table 2). In particular: in group A velocity significantly increased from 0.58 ± 0.14 to 0.92 ± 0.34 m/s (p=0.0232), cadence significantly increased from 89.61 ± 12.73 to 100.74 ± 32.96 steps/min (p=0.0365), step time significantly reduced from 0.75 ± 0.51 to 0.62 ± 0.11 s (p=0.0333), step length increased from 61.12 ± 32.85 to 62.72 ± 33.47 cm (p=0.0582), step width reduced from 14.20 ± 33.47 to 12.41 ± 3.89 cm (p=0.0631), single support increased from 30.63 ± 19.58 to 33.13 ± 17.82% (p=0.0498), double support reduced from 38.77 ± 27.95 to 36.90 ± 15.39% (p=0.0529); in group B velocity significantly increased from 0.52 ± 0.49 to 0.81 ± 0.38 m/s (p=0.0314), cadence significantly increased from 87.91 ± 21.64 to 98.47 ± 26.94 steps/min (p=0.0394), step time significantly reduced from 0.77 ± 0.39 to 0.63 ± 0.38 m/s (p=0.0435), step length increased from 60.56 ± 26.93 to 61.71 ± 22.84 cm (p=0.0843), step width reduced from 13.27 ± 2.71 to 11.45 ± 2.39 cm (p=0.0637), single support increased from 29.60 ± 15.27 to 32.84 ± 18.57% (p=0.0479), double support reduced from 39.49 ± 13.42 to 37.81 ± 13.42% (p=0.0563). The comparison of the results showed no statistically significant differences between the two groups.

Gait parameter	Group A			Group B		
	T0	T1	p value	T0	T1	p value
Velocity (m/s)	0.58 ± 0.14	0.92 ± 0.34	0.0232*	0.52 ± 0.49	0.81 ± 0.38	0.0314*
Cadence (steps/min)	89.61 ± 12.73	100.74 ± 32.96	0.0365*	87.91 ± 21.64	98.47 ± 26.94	0.0394*
Step time (s)	0.75 ± 0.51	0.62 ± 0.11	0.0333*	0.77 ± 0.39	0.63 ± 0.38	0.0435*
Step length (cm)	61.12 ± 32.85	62.72 ± 33.47	0.0582	60.56 ± 26.93	61.71 ± 22.84	0.0843
Step width (cm)	14.20 ± 3.54	12.41 ± 3.89	0.0631	13.27 ± 2.71	11.45 ± 2.39	0.0637
Single support (%)	30.63 ± 19.58	33.13 ± 17.82	0.0498*	29.60 ± 15.27	32.84 ± 18.57	0.0479*
Double support (%)	38.77 ± 27.95	36.90 ± 15.39	0.0529	39.49 ± 13.42	37.81 ± 13.42	0.0563

Table 2: Spatiotemporal gait parameters (Asterisk indicates statistical significance).

Discussion

Many therapies have been proposed to improve gait and balance or to decrease fatigue in people with MS [54-57] often with often with controversial effects. Few studies [58-62] evaluated whether RAGT may be superior to conventional walking training in terms of gait performance and balance or unstable platforms for balance. The correct perception and integration of physical stimuli by visual, vestibular and somatosensory systems is related to a control of balance and gait pattern, and that a dysfunction in processing inputs from so much as one of the systems could lead to balance and gait impairment, as occurs in persons with MS [63].

The literature points out that imbalance in SM are correlated not only with a deficit, but with a defect in programming and execution of motion due to a different integration of input and output information. [64] It has been demonstrated that human action execution (i.e., to make a cup of coffee) required three main phases: motor planning, motor execution, and movement control. [62] It is necessary in patients with SM to stimulate feedback and feed forward mechanisms and sensorimotor integration especially during the motion control phase [65]. In in this way rehabilitation can determine what we consider as "corticalization of the movement", that for other authors is defined as the constitution of an "internal model", which is an internal representation of motor and sensorial signals related to a specific execution of the movement [66,67]. This is the rational of this study which verifies the effectiveness of two approaches based on the ability to generate a new dynamic environment that can generate an internal model that needs to be learned to be able to walk effectively. Furthermore, the use of robotized systems has been widely used in recent years, with the rationale of sensorimotor integration and recovery of gait in patients with stroke or Parkinson's disease, with a demonstrated efficacy on disability, gait cycle and balance deficiency [68-69].

Most of the studies used for recovery of balance and gait Lokomat system and control groups consisted of ground-based training. [59,70,71].

Thus, the novelty of the study is twofold. The system used in this study is a system that acts on the characteristics of the gait and overall postural in a microgravity environment and where the patient is not assisted but actively proceeds to the therapeutic session and the control group carries out a specific protocol for sensorimotor recovery with technologically advanced systems.

SPAD allows to correct the gait and to correct the asymmetry of the two emisoma, leading to a more physiological gait, which is critical in Parkinson's disease. It acts as an external cue able to normalize the parameters of gait and to improve the action of neuronal circuits which contribute to the gait pacing. It was also suggested that treadmill training determines a "cortical reorganization," and that this reorganization will be the basis of the improvements presented by patients. Unlike the gait carried on the ground, where there are evident the oscillations and the variability, on treadmill the patient should follow the speed of movement of the platform, generating a more rhythmic gait. We could therefore define the treadmill as a "pitch external pacemaker. In the study the advantages obtained with the BWST are amplified by the use of the metronome during the training session which combines the effects of proprioceptive blocks and the visual cue given by the mirror.

In the present study we chose a double proprioceptive rehabilitation training that could have a clearly positive spill over on patient's impairment and sense of fatigue and gait and balance impairment. Results obtained demonstrate that 18 treatment sessions (provided with a scheme of 3 sessions per week for 6 weeks) of gait training in microgravity environment or stability and sensory-motor exercises on unstable platforms plus neuromuscular manual therapy and stretching exercises are able to improve first of all the overall performance of ADL in all individuals with MS at early stage and low or mild disability.

Considering the several presentation patterns of MS, our protocol included-to our knowledge, the first of this type-a training on treadmill in microgravity environment. Such training appears to be superior to other forms of sensory-motor exercises when the outcome is measured by administration of the EDSS. This is probably due to the fact that the EDSS is more sensitive to evaluate the ability and autonomy in walking rather than postural and balance changes, as observed at the stabilometric analysis of subjects undergone sensory-motor exercises (group B) and detected through the administration of the BBS (the most commonly adopted scale for balance among those validated for MS). However, taking into account the spatiotemporal parameters of gait cycle, this superiority disappears: in both groups, there is overall a greater improvement in the temporal parameters (velocity, cadence, step time) than the spatial parameters (step length, step width). Also at the stabilometry subjects undergone training with

SPAD got good performance, at least with open eyes, relating to the velocity of CoP oscillations, in the same way of subjects specifically trained for that. In all subjects, improvements could be suggestive of increased reactivity in performing adjustment of CoP dislocation. These findings are consistent with those relating to the reduction of the length of CoP trajectory and the sway area, greater in group B, revealing a more correct postural control.

Nevertheless, when considered together the EDSS and MFIS outcomes in group A could be read and justify the action of the body weight supported gait training as a form of patient's re-education to the adoption of a more physiological and less energy-consuming gait schema, an aspect that has not yet been adequately investigated in literature.

Furthermore, as noted by Gandolfi et al. [62] with a more numerous sample could possibility stratified of patients by EDSS and would allow us to better understand which approach (robot assisted balance training or motor exercises on unstable platforms) and for which patients would be more useful to improve balance task related domains and/or gait related domains.

However, taking into account the spatiotemporal parameters of gait cycle, this superiority disappears: in both groups, there is overall a greater improvement in the temporal parameters (velocity, cadence, step time) than the spatial parameters (step length, step width). Walking can be seen as a repeated sequence of balance challenges and changes in gait observed in people with MS are largely the result of changes in postural control [72].

Despite the purely proprioceptive rehabilitation protocol employed in the present study had a positive feedback on the sense of fatigue, the seemingly conflicting results obtained from stabilometric and gait analysis between the two treatment groups join the wider long-time controversy of task-dependent recovery of balance and walking impairment and not-transferability non-transferability of a sensory-motor skill learned in a specific rehabilitation setting to another not trained context [73-77].

Coherently with the theory that improved gait and balance performances reflect an optimization of energetic cost of compensation motor strategies, the sense of fatigue appears to be reduced when measured by MFIS, but not by FSS; this might be due to the lower analytical sensitivity of the latter scale than the former, with which however shows a strong correlation [78].

Although the present Study has some limitations-firstly, the small size of subject recruited, and secondly, the heterogeneity of patients' drug therapy (indeed, whereas a number of drugs could have "fatiguing" effects, other such as amantadine, modafinil and 4-aminopyridine are commonly prescribed to relieve it) even more it support the need to adopt a rehabilitation approach to MS that is complex and multidisciplinary, yet modulated at the beginning of treatment according to the major deficit (for example, static versus dynamic equilibrium) so that the treatment is patient-tailored.

Conclusions

Results from this Study match the dispute on the mutual correlations between gait and balance impairment and fatigue in MS, and further studies are required to clarify the relationship between the different aspects of the disease. Nonetheless, body weight supported gait training and sensory-motor exercises on unstable platforms appears to be feasible and could be safely used as additional therapeutic option in patients with MS in early stage and in intercritical periods of disease.

Further studies are needed to evaluate new technologies that may include, for example, exercises with sensory augmentations for impaired self-visualization, mechanical vibration, functional electrical stimulation, and electrical stimulation with continuous transcranial currents.

Conflicts of Interest

The authors declare no conflicts of interest in relation to this article.

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