Comparative Analysis of Robotic Gait Training and Sensory-Motor Rehabilitation in Multiple Sclerosis Patients

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Abstract

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 are women). Walking 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. Controversy exists about the association between fatigue and physical disability, between elevated fatigue, impaired balance and a higher risk of falls, between perceived fatigue and gait performance. We enrolled 16 patients with relapsing-remitting MS at early stage and low or mild disability, 11 females and 5 males, aged 27.1 (range 23-34 years), randomly divided into two groups: patients in group A underwent a robotic gait rehabilitation treatment which involved the use of SPAD® (Sistema Posturale Antigravitario Dinamico, Dynamic Antigravity Postural System), patients in group B underwent a cycle of sensory-motor physical activity in our laboratory of performance enhancement; patients in both groups were subjected to neuromuscular manual therapy. All treatment were 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 (FIM™), Expanded Disability Status Scale (EDSS), the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS), and gait analysis with MTX7® (Diagnostic Support, Rome, Italy). Results show statistically significant improvement of the FIM™ 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 temporal (but not spatial) gait parameters. So body weight supported gait training is feasible and could be safely used as additional therapeutic option in MS patients with mild walking disability.

Keywords: Multiple sclerosis, Fatigue, Walking disturbances, Gait analysis, Robotic gait training, Microgravity environment, Sensory-motor systems.

1. 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 are women). The disease is characterised 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. Walking disturbances are another key component of disability in patients with MS[1)]. Approximately 75% of patients with MS experience clinically significant walking limitations[2)-7)] , which may be present even in patients with mild disability since the early stages of the disease, and could be dued to tightness or spasticity, sensory deficit of lower limbs, weakness, fatigue[8)-10)]. Fatigue is defined by the MS Council as «a subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities» [11)] and is probably the most common (75-95% of patients, according to different studies[12)-16)]) but often unrecognised symptom of MS. Because of rapid physical fatigue, patients with MS often limit their physical activity, thus increasing deconditioning and altering fitness, with a substantial negative impact of this symptom on performance levels and outcome measures[17)-19)]. The association between fatigue and physical disability among patients with MS has been investigated by several studies, but

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results are controversial[20)-23)]. Like the association between fatigue and physical disability, an association between elevated fatigue, impaired balance and a higher risk of falls has been found in subjects with MS[24)25)], as well as an association between perceived fatigue and gait performance, although the link is unclear[26)-33)]. Both drugs and non-pharmacological interventions have been tested to improve MS-related fatigue and gait and balance impairment [34)-39)]. In literature there is a good evidence that multidisciplinary rehabilitation in an outpatient setting alleviates fatigue and improves quality of life[40)]. Aim of this study is to examine the implications of an intervention program of physical activity in relieving fatigue and improving gait and balance pattern in MS patients.

2. Materials and methods

Between June 2014 and June 2015, 30 patients with relapsing-remitting MS at early stage and low or mild disability 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 patients with Modified Ashworth Scale > 2 at lower limbs and patients which showed a relapse within 30 days prior to the beginning of treatment (9 subjects); so, 21 were enrolled and hence randomly divided into two groups: a group A composed of 10 subjects, and a group B composed of 11 subjects. 5 patients dropped out because of acute attack during the treatment, and so only 16 subjects reached the end point (*figure 1*). The two groups were so composed: the group A consisted of 8 individuals, including 6 females and 2 males, mean age 26.8 years (range 24-32 years); the group B consisted of 8 individuals, including 5 females and 3 males, mean age 27.3 years (range 23-34 years).

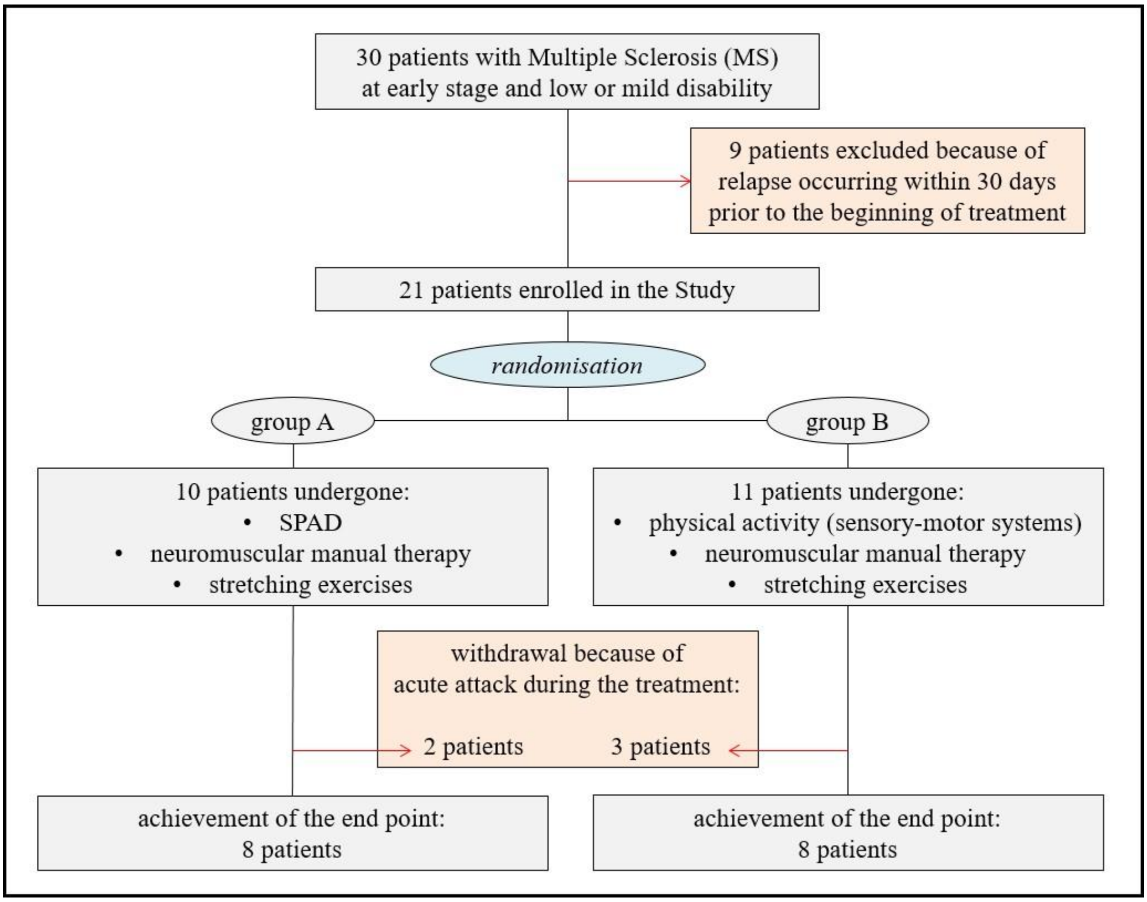


Figure 1. *Flow chart of the Study.*
SPAD, Sistema Posturale Antigravitario Dinamico (Dynamic Antigravity Postural System).

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 that a gait training can be made combining the motor task with sensory feedback, in line with the multisensory approach to postural balance. 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 proprioceptive informants, 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[41)]. Each session of SPAD provides a 20-30% mean body weight relief and a 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 the vertical excursion of the center of gravity of the subject, facilitating the execution of longer steps, according to the possibilities of the individual patient; the step performing is corrected continuously 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 change asymmetrical gait adaptations, working 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 minimises the energy consumption needed to maintain the 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 20 minutes of sensory rehabilitation exercises through sensory-motor systems (10 minutes with Imoove®, Allcare Innovations, France, and 10 minutes on Synergy Mat®, Human Tecar, Unibell International, Italy) and 10 minutes of sensory-motor and stability exercises on Bobath ball. Patients in both groups were subjected to neuromuscular manual therapy that makes 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 sensitised bench (Postural Bench, Tecnobody, Italy) and postural decompensated bench (FlexiMat, Deltadue, Italy), lying in supine position.

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

All patients enrolled underwent physiatrist examination, completed by:

- overall assessment of the degree of disability, by administration of the Functional Independence Measure (FIM™), a scale that detects the degree of autonomy with which activities of daily living (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;
- 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;
- gait analysis, performed with an electronic modular system, consisting of a platform of detection and a walkway (when seats are 25,600 to 36,864 active sensors on 160/200 cm^2), interfaced with the acquisition software MTX7® (Diagnostic Support, Rome, Italy). Firstly, the patient is analyzed on the platform barefoot, in relaxed standing position to evaluate the main characteristics of plantar support through static test (the software calculates the average swinging of the subject during the time of acquisition, equivalent to 5 seconds); then he is invited to walk on the platform for dynamic test (gait analysis): it is asked to repeat the walk three times in both directions, without leaving the platform, in order to detect instability in walking and changes in plantar support compared with what detected at the static test. The system can also perform the examination of balance (stabilometric test), conducted in conditioned orthostatism (standing at 30°, opened eyes for 50

seconds, and closed eyes for 50 seconds); swinging on antero-posterior and lateral-lateral plans data facilitate the identification of disorder of oculomotor, vestibular or proprioceptive system.

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-Wilk test was performed. Then baseline differences between groups of patients were assessed using Student's t-test for normally distributed parameters and Wilcoxon test for non-normally distributed parameters. Statistical significance was set to values of $p \leq 0.05$. Values are expressed as mean ± standard deviation (SD).

3. Results

At the end of the Study, the scores of the rating scales were modified as follows:

- statistically significant improvement of the FIM™ average score (from 77.7 to 90.3; p = 0.0011) in all patients, both in group A (from 76.5 to 88.3; p = 0.0306) and in group B (from 78.9 to 92.3; p = 0.0219) (*figure 2*);

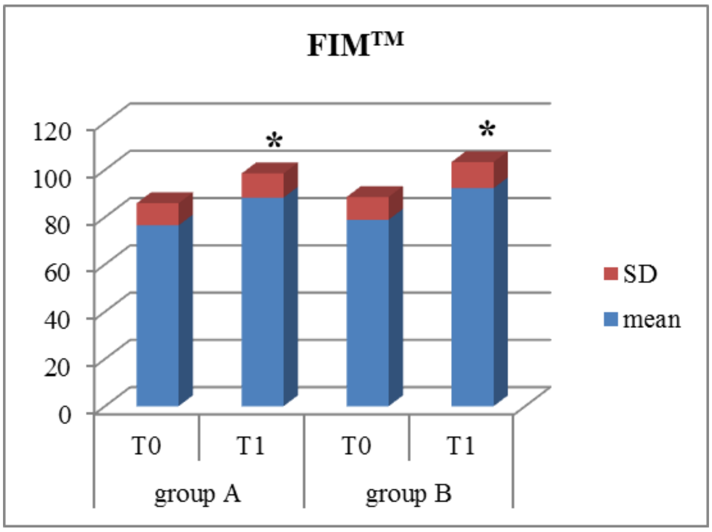


Figure 2. *Variation in the FIM™ average score.*
Asterisk indicates statistical significance.

- reduction of the EDSS average score (from 5.3 to 4.8; p = 0.0077) in all patients, in a statistically significant manner in group A (from 5.3 to 4.6; p = 0.0348), in a non-significant manner in group B (from 5.4 to 4.9; p = 0.1248), (*figure 3*);

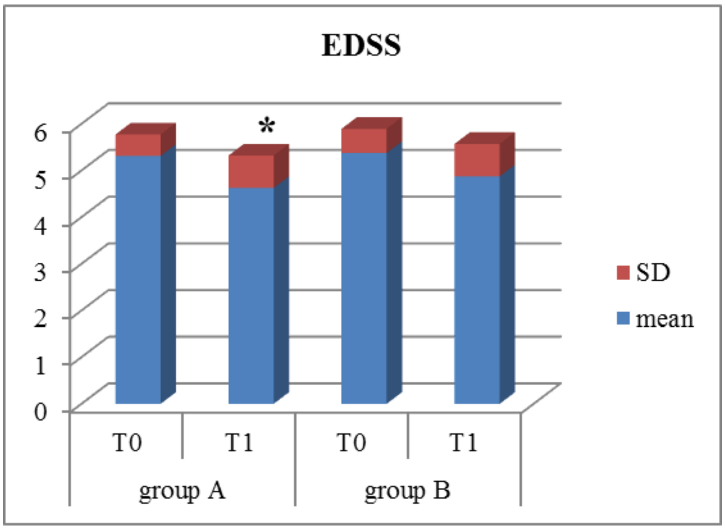
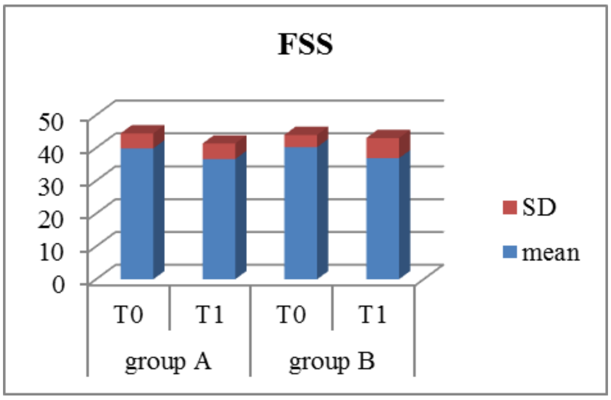


Figure 3. *Variation in the EDSS average score.*
Asterisk indicates statistical significance.

- 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 40.1 to 36.8; p = 0.0559) and in both groups (from 39.9 to 36.6, p = 0.1839 in group A, from 40.3 to 36.9, 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 43.8 to 39.1; p = 0.0018) and in both groups (from 43.9 to 39.4, p =
0.0337 in group A; from 43.6 to 38.9, p = 0.0353 in group B) (*figure 4*);



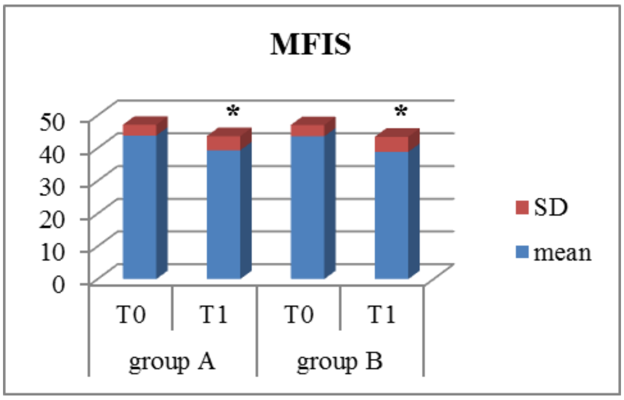


Figure 4. *Variation in the FSS (left) and MFIS (right) average scores.*
Asterisk indicates statistical significance.

- improvement in spatiotemporal gait parameters (*table 1*). In particular: in group A velocity significantly increased from 0.58 to 0.92 m/s (p = 0.0232), cadence significantly increased from 89.61 to 100.74 steps/min (p = 0.0365), step time significantly reduced from 0.75 to 0.62 s (p = 0.0333), step length increased from 61.12 to 62.72 cm (p = 0.0582), step width reduced from 14.2 to 12.4 cm (p = 0.0631), single support increased from 30.6 to 33.1% (p = 0.0498), double support reduced from 38.7 to 36.9% (p = 0.0529); in group B velocity significantly increased from 0.52 to 0.81 m/s (p = 0.0314), cadence significantly increased from 87.91 to 98.47 steps/min (p = 0.0394), step time significantly reduced from 0.77 to 0.63 s (p = 0.0435), step length increased from 60.56 to 61.71 cm (p = 0.0843), step width reduced from 13.2 to 11.4 cm (p = 0.0637), single support increased from 29.6 to 32.8% (p = 0.0479), double support reduced from 39.4 to 37.8% (p = 0.0563). The comparison of the results showed no statistically significant differences between the two groups.

Table 1. Spatiotemporal gait parameters. Asterisk indicates statistical significance.

Gait parameter	Group A			Group B		
	T0 (mean)	T1 (mean)	p value	T0 (mean)	T1 (mean)	p value
Velocity (m/s)	0.58	0.92	0.0232*	0.52	0.81	0.0314*
Cadence (steps/min)	89.61	100.74	0.0365*	87.91	98.47	0.0394*
Step time (s)	0.75	0.62	0.0333*	0.77	0.63	0.0435*
Step length (cm)	61.12	62.72	0.0582	60.56	61.71	0.0843
Step width (cm)	14.2	12.4	0.0631	13.2	11.4	0.0637
Single support (%)	30.6	33.1	0.0498*	29.6	32.8	0.0479*
Double support (%)	38.7	36.9	0.0529	39.4	37.8	0.0563

4. Discussion and conclusions

The obtained results demonstrate that 18 treatment sessions (provided with a scheme of 3 sessions per week for 6 weeks) of gait training in microgravity environment or simple proprioceptive rehabilitation, associated with manual therapy, are able to improve the performance of ADL in all individuals with MS at early stage and low or mild disability.

The sense of fatigue measured by MFIS but not through FSS is also improved; this could be due to the lower analytical sensitivity of the latter scale than the former, with which however shows a strong correlation **[42]**. In fact, the MFIS is structured in such a way to be divided into three functional macroareas ("cognitive", "physical", "psychosocial"); the statistical analysis on the so-isolated items shows that the average score of physical and psychosocial subscales improves in a greater extent (from 14.2 to 11.6, $p = 0.0147$ and from 6.1 to 5.2, $p = 0.0977$, respectively) than the average score the cognitive subscale, which nearly remains unchanged (and with no statistically significant differences) in all patients (from 21.3 to 19.9, $p = 0.4198$). As regards the gait performances, training in microgravity environment appears to be superior to simple proprioceptive rehabilitation when the outcome is measured by administration of the EDSS. In the last decade the use of robotic instruments spread among rehabilitation approaches for the recovery of sensorymotor functions; even if the use of this type of training has not yet been sufficiently investigated in the MS, the use of such devices is effective in patients with stroke, in which the results in favour of the use of robots are precisely measured through outcomes on disability (for example, the movement of the articular segments controlled directly by the devices). 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). The exercise offered to patients enrolled in group B are aerobic and very mild-intensity exercises; in particular, given the sensory deficits which characterise the course of MS, the work conducted in our laboratory of performance enhancement is specifically targeted to the training of the proprioceptive system, which can be adversely affected even in early stage and in intercritical periods of disease.

These results join the dispute in the literature on the mutual correlations between fatigue and gait abnormalities, and further studies are required to clarify the relationship between the two aspects of the disease. Nonetheless, body weight supported gait training is feasible and could be safely used as additional therapeutic option in MS patients with mild walking disability.

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