EUR J PHYS REHABIL MED 2009;45:53-9

Treadmill exercise in early mutiple sclerosis: a case series study

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Aim. **The effect of specific exercise therapy programs on the management of balance and walking disorders in multiple sclerosis (MS) patients have not been fully explained yet. Reproducible measurement systems are especially required to show their efficacy. The aim of the present case series study was to explore the feasibility of an aerobic treadmill rehabilitation protocol (endurance training protocol) and its effects on walking parameters, muscular activity and postural balance. An adequate instrumental measure set was adopted to provide evidence of minimal motor dysfunction, not quantifiable by means of standard clinical examination.**

Methods. **Three minimally impaired MS patients were enrolled. The patients underwent endurance training on a treadmill for four weeks. Posturographic assessment, energy cost measurement and gait analysis by basography and surface electromyography recordings were used as outcome measures.**

Results. **Energy cost during treadmill walking was generally reduced in the three patients after exercise. Indexes of both sway path and sway area used for postural stability measurement were reduced after exercise in two patients, particularly with eyes closed. Minor changes were observed in gait pattern in terms of foot placement. Muscular activity pattern tended to normalize after training.**

Conclusion. **The aerobic treadmill exercise is feasible, safe and it may improve early anomalies of posture and gait in early MS patients. In the context of an impairment oriented rehabilitation approach, the set of instrumental measurements proposed seems to be able to identify subclinical anomalies in a very low degree of functional involvement on an individual basis.**

Key words: Multiple sclerosis - Rehabilitation - Energy metabolism - Musculoskeletal equilibrium - Gait.

Acknowledgments.—The authors wish to thank Ivo Bisi and the Cosmed Company@ for the instrumentation employed and for the elaboration of the energy consumption data and Marco Knafitz and the DEM Company@ for EMG Data Management.

Received on December 10, 2007.
Accepted for publication on October 23, 2008.
Epub ahead of print on January 21, 2009.

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Locomotor disability in multiple sclerosis (MS) patients can be considered as an emergent characteristic deriving from several mechanisms of functional impairments (coordination of posture and gait, energy cost, cognitive involvement and impaired execution of automatic tasks) whose role is not easy to establish.[1] Furthermore, walking performance can be seriously compromised by fatigue, which is an etiologic multifactor symptom in itself. The abnormal pattern of walking characterized by co-contractions or high contractions of agonistic-antagonistic muscles due to the composite spasticity-ataxia picture increases energy cost.[2] Reduced physical activity, consequent to this multifactor scenario, is responsible for physical deconditioning in MS patients, which further increases disability.[3]

TABLE I.—*Clinical and functional features of patients.*

Case	Sex	Age (yrs)	Disease duration (yrs)	EDSS	Kurtzke's functional system							
					Pyramidal function	Cerebellar function	Brainstem function	Sensitive function	Sphincterial function	Visual function	Mental status	Other (spasticity)
1	F	41	13	2,5	1	0	0	2	0	0	0	0
2	F	53	1	1,5	0	1	0	1	0	0	0	0
3	M	38	13	1,5	1	0	0	0	1	0	1	0

EDSS: expanded disability status scale.

TABLE II.—*Summary of the sequence of the tasks during the energy consumption test.*

Duration min	Description of task
03:00	Resting period
03:00	1 km/h gait
05:00	Recovery period
03:00	3 km/h gait
05:00	Recovery period
03:00	4 km/h gait
05:00	Recovery period
03:00	6 km/h gait
05:00	Recovery period

Several papers have been recently published showing a strong positive effect of exercise therapy on muscle power function, exercise tolerance functions, and mobility-related activities.[3-6] While aerobic training seems to be effective in correcting the decline in physical conditioning,[7-15] we have little evidence, based on clinical [16] or instrumental outcome measurements,[17, 18] on its effect also on walking and balance alterations. Studies on treadmill training in MS patients are also very rare,[11, 18] although there is a lot of evidence that it is associated with improved walking in stroke patients.[19]

The aim of the present case-series study, designed as prospective non-consecutive pre-post exercise control, was to explore the feasibility of an aerobic treadmill rehabilitation protocol (endurance training protocol) in three minimally impaired MS patients and its effects on energy expenditure, walking parameters, muscular activity and postural balance. The hypothesis was that an aerobic treadmill exercise in MS patients with subclinical motor dysfunction, might improve fitness and also walking and postural anomalies.[20] An adequate instrumental measure set was adopted to provide evidence of minimal motor dysfunction, not quantifiable by means of standard clinical examination.

Materials and methods

Case studies

Three patients diagnosed for MS [21, 22] with slight walking disability were enrolled by the referring physiatrist among the wide sample of patients of the MS Rehab Center of Bologna (Italy). The patients were selected according to the presence of a minimal motor impairment, *i.e.* the presence of neurological signs but no evidence of abnormal walking, similar age, style of life (Table I), different follow-up from the onset of the disease, and different clinical expression of the disease, no previous specific rehabilitation training. The first patient (case 1) (age 41, expanded disability status scale [EDSS] [21] 2.5, 13 years from onset) presented signs of abnormal sensitive and pyramidal function (lower limb apallestesia, left patellar hyperreflexia, left ankle clonus), in the second patient (case 2) (age 53, EDSS 1.5, 1 year from onset) there was a prevalent sensitive function deterioration (hypopallestesia left patella and bilateral ankle) and in the third patient (case 3) (age 38, EDSS 1.5, 12 years from onset) there was a prevalent pyramidal involvement (bilateral patellar hyperreflexia, ankle clonus). All of the three patients gave their informed consent to participate to the study. None of the patients had previously performed treadmill training. No other rehabilitation programs during the study period was allowed.

Therapeutic notes

INTERVENTION

Subjects were submitted to endurance training on the treadmill for four weeks (ten sessions). A preliminary session was performed to familiarize the subject with the equipment and the procedure. Each session was preceded and followed by lower limb and trunk stretching exercises. The schedule used for the training is reported in Table II.

Outcome measures

Before and after the four weeks of aerobic exercise training on the treadmill, the following measurements were evaluated as follows.

a) Measure of energy cost: the measure was made by telemetric spirometry (Cosmed K4 b2@, Cosmed, Pavona di Albano, Rome, Italy). At the first registration patients were allowed to familiarize with the instrumentation before the test, in order to eliminate any level of anxiety which would artificially scale up consumption preintervention values. The test protocol was the following: three minutes rest, to get used to the breathing mask, and 4 steps of treadmill walking respectively at zero-load (1 km/h, 3 km/h, 4 km/h and 5 km/h). Each 3 min step was followed by a 5 min rest period. Oxygen consumption was calculated as an average during every walking phase and during the last 3 min of each resting period. The energy cost of walking was calculated according to the formula (O_2 cost=[$\dot{V}O_2$/kg walking-$\dot{V}O_2$/kg rest]/speed).

The first resting period was shorter than expected, because the whole session was exceedingly time consuming and the patients were showing increasing discomfort wearing the mask. Since a resting period of 3 min before the test was not enough to compute a reliable basal O_2 cost (a few minutes may overestimate the basal value), we chose to consider the basal value of $\dot{V}O_2$ calculated by the software (3.5 mL/min/kg) and widely accepted as representative of basal O_2 consumption (Table III).

Due to the lack of a standard indication in the literature on the treadmill protocol in MS patients, the proposed test protocol was an empirical compromise to minimize the effects of abnormal fatigue, so often affecting performance in MS patients, as well as the possible transitory worsening of neurological function due to even minimal metabolic changes. It could be argued whether an average of 3 min assessment offers the most reliable measure but, at least, it seems not to be affected by confounding factors that certainly increase with longer durations.

b) Postural analysis: a Bertec dynamometric computer-assisted force-plate (4060A, Bertec Inc., Cherry Valley, IL, USA) was used according to the current standardization:[23] three trials of 60 s (excluding initial and terminal 10 s) both for eyes open (EO) and eyes closed (EC) modes; the best trial in each mode was chosen for further analysis. Two main parameters were considered: the sway path and the sway area both with eyes open and eyes closed.

c) Gait pattern analysis was performed by the StepPc integrated system (DEM Italia, Leinì, Turin, Italy) including basography and surface electromyography (EMG) recordings. Gait analysis was performed at the most comfortable speed for patients on the treadmill before and after training, wearing their own sports shoes. Surface EMG from rectus femoris, lateral hamstrings, gastrocnemius medialis and tibialis anterior was recorded on a mean of 50 strides during treadmill walking. The software of the system automatically performs the statistical analysis on the registered steps in terms of phases of contact of the foot with the ground on a three level scale (heel, sole, forefoot) and muscular activity (mean interval of activation percentage of stride and standard deviation [24]). Active clip-type adhesive pregelled disposable Ag/AgCl bipolar 3M EKG electrodes for pediatric application, with an interelectrode distance of 20 mm were used for EMG signal detection. The sampling rate of acquisition was 1 000 Hz, low and high cutoff frequencies of the amplifier were 40 Hz and 200 Hz, respectively. Three adhesive footswitches (heel, first and fifth metatarsal heads) were used to detect foot contact.

Table III.—*O_2 cost at different speeds of treadmill gait before training and after training. The variation before- after training is reported as percentage for each gait speed trial.*

Speed (km/h)	O_2 cost (mL/kg*m) Before training	O_2 cost (mL/kg*m) After training	O_2 cost variation % Difference pre-post
Case 1			
1	0.267	0.268	0.37%
3	0.136	0.135	-0.73%
4	0.157	0.137	-12.73%
6	0.174	0.139	-20.11%
Case 2			
1	0.299	0.231	-22.74%
3	0.161	0.145	-9.90%
4	0.169	0.46	-13.60%
6	0.198	0.17	-14.14%
Case 3			
1	0.364	0.371	1.92%
3	0.171	0.154	-9.90%
4	0.149	0.128	-14.09%
6	0.146	0.142	-2.73%

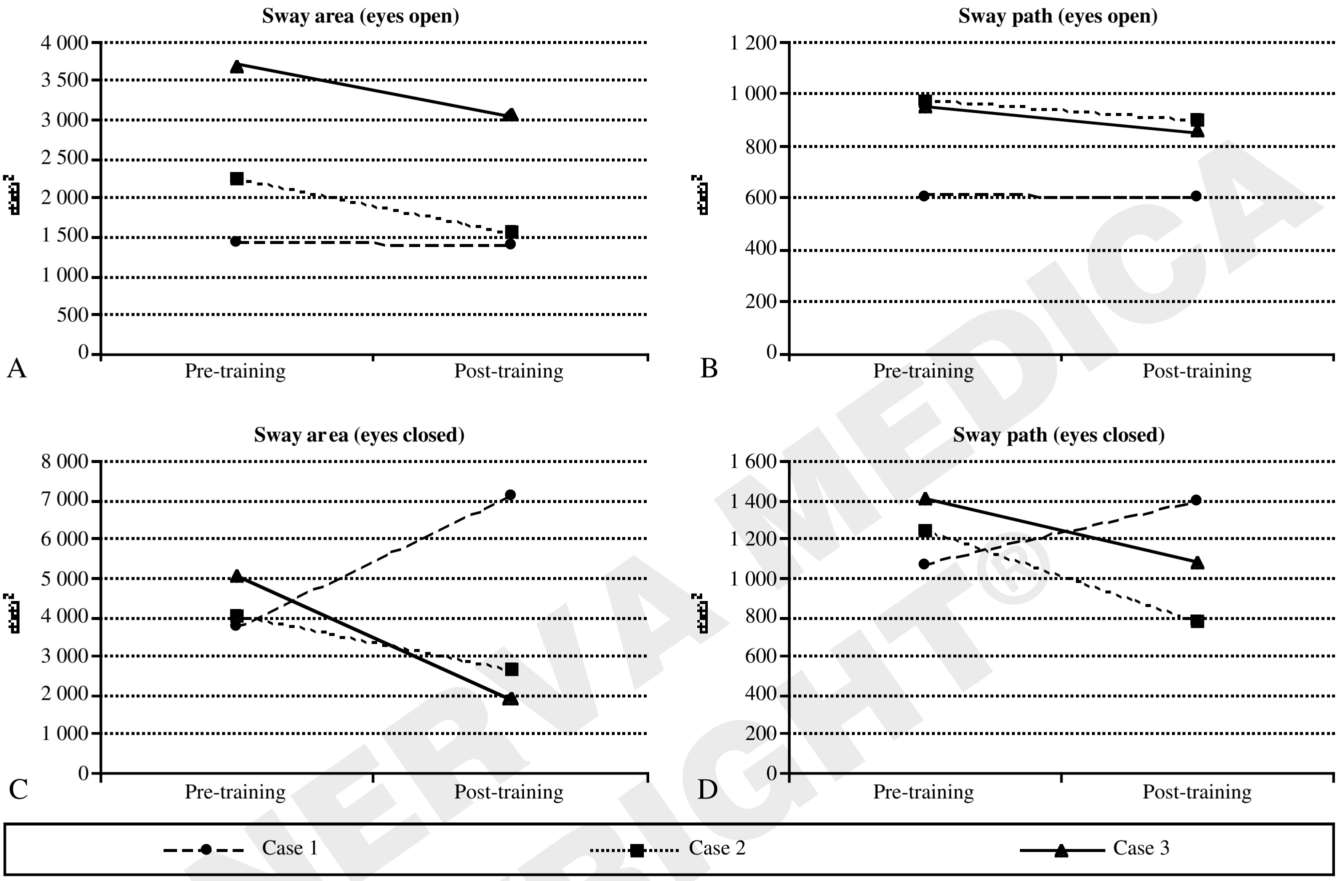

Figure 1.—Postural analysis: sway path and sway area's data before and after training.

Results

Measure of energy cost

At a speed of 4 km/h a reduction in the O_2 cost was evident in all three patients (respectively -12.7, -13.6 and -14%) (Table II). At 6 km/h Case 1 showed the highest reduction of O_2 cost (-20.1%), Case 2 a value of -14.1%, and Case 3 showed a small difference (-2.7%).

Postural analysis

The indexes of both sway path and sway area were reduced after exercise in two of the three patients of this case series study (Figure 1). A more evident decrease was evidenced in the EC mode (Figures 1C, D) compared to EO one (Figures 1A, B). Case 1 (EDSS 2.5 and more composite clinical picture) did not show any improvement after exercise. In this patient, while the EO test index was more or less unchanged, the EC showed a worse performance after treadmill training.

Gait pattern analysis: basography and dynamic EMG

A comfortable speed of progression was 3.6 km/h for Case 1 and 2, and 4.2 km/h for Case 3 before training. After training the same speed condition was maintained for comparison. In two patients there was a normal rate of different parts of foot contact, unchanged before and after training. Case 2 showed a prolonged duration of heel contact and reduced forefoot support, unchanged after exercise. The pattern of muscle activation during treadmill gait showed some difference in the timing of activation before and after training (Figure 2). In Case 1 a premature activation of the gastrocnemius at heel strike (activity

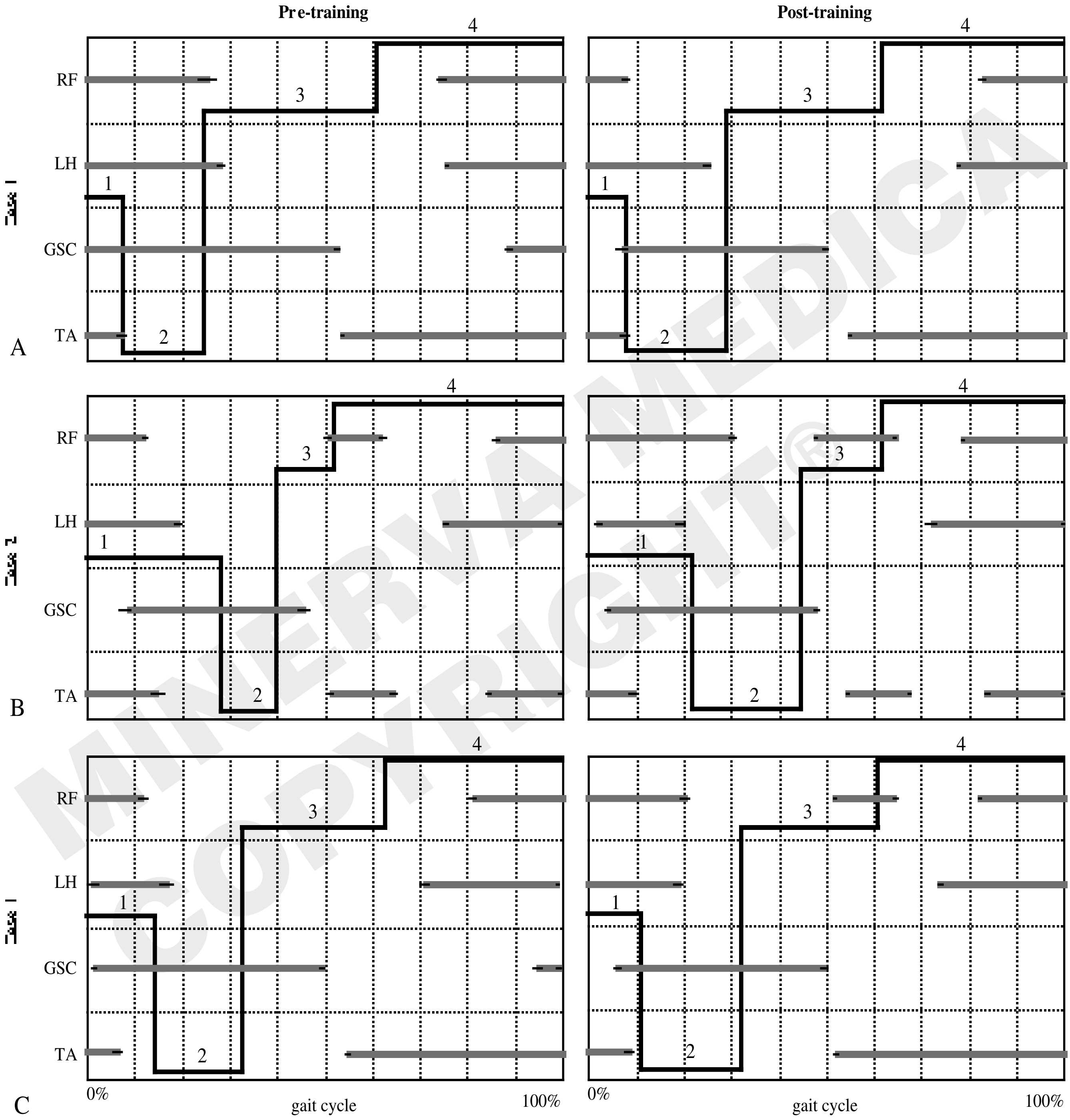

Figure 2.—Gait pattern analysis: basography and dynamic EMG during treadmill training. Light bars represent intervals of muscle activation as automatically statistically detected by the computer. Dark small bars at the beginning and at the end of large bars represent one standard deviation on a mean of 50 strides on the treadmill. RF: rectus femoris; LH: lateral hamstrings; GSC: gastrocnemius medialis; TA: tibialis anterior. The horizontal thin line represents the duration of swing and stance foot contact phases: heel contact (1), foot contact (2), forefoot contact (3) and swing phase (4). For Case 1 and Case 2 EMG data is from the left side, and for Case 3 data is from the right side.

was already present at terminal swing) was present in both legs, which normalized on the left (Figure 2A). Case 2 showed a normal activation phasing of the gastrocnemius on the left side and a slight premature activation on the right side which normalized after training (Figure 2B). In this patient an "out-of-phase" activation of the lateral hamstrings was present before training at terminal stance and disappeared after exercise. Case 3 presented bilateral premature activation of the gastrocnemius which tended to reduce after training (Figure 2C). No differences were found for the other muscles explored.

Discussion

The present study investigated the feasibility of an aerobic treadmill exercise protocol and its effects in a context of impairment on walking parameters, muscular activity and postural control in a small case series of patients with early MS.

The results of this study showed that the four-week aerobic exercise program on the treadmill was safe for the three patients. They concluded the rehabilitation program without difficulties. The training exercise made walking on a treadmill less energy expensive, particularly at higher speeds, albeit with individual differences. This finding was in agreement with other recent studies and confirmed the relevance of this kind of training in rehabilitation protocols even at the stage of mild or minimal neurological impairment. Certainly a more robust statistical study (*e.g.* randomized controlled trial) is required to confirm this result on a larger, controlled scale, to avoid over-interpretation of the results which might be affected by a learning effect for the metabolic measurements during walking or simply by the different patient performance over time.

According to the hypothesis formulated in the present study, instrumental measures provided information about the individual effect of the aerobic training even in postural and gait performance in early stage MS patients. The parameters of postural stability improved in two patients, thus showing a positive effect of training on balance, standing with both open and closed eyes. One patient had a worse sway path and sway area with closed eyes. It could be supposed that this patient had a paraclinical exacerbation of the disease [16, 25] with no evidence of clinical symptoms while the trial was ongoing.

Changes were noted in the gait pattern before and after treadmill exercise training in terms of muscles activation, particularly for the gastrocnemius. This finding is of interest, since the premature activation of the gastrocnemius during the first double support phase was already found in previous studies.[20, 26] The premature gastrocnemius activation pattern was present in differing degrees in the two legs of the three patients and was probably closely related to the distribution of neurological signs. Case 1, presenting a selective pyramidal involvement of the left lower limb showed improvement only on this side after training. Case 2, with a prevalent sensitive involvement, shows minimal changes after training for gastrocnemius, while a complete correction of the abnormal use hamstrings at terminal stance (usually this is a compensation for scarce plantarflexors). Case 3, with a prevalent pyramidal involvement seems to take the most advantage by the training, improving the premature gastrocnemius pattern bilaterally. These findings suggest that MS patients, due to the heterogeneity of their symptoms even in the early stage of disease, should be assessed individually for better rehabilitation planning. However, general fitness recovery through treadmill exercise seems to be effective also at modifying muscle pattern during gait, probably by reducing those protective mechanisms we previously hypothesized [20] that are responsible for stiffening the ankle when perceived reliability of balance control is lowered.

Treadmill training represents a "task-oriented" exercise for gait training, effective both at enhancing walking ability and fighting cardio-vascular de-conditioning in chronic diseases as previously demonstrated for chronic stroke patients.[19] Increasing interest has recently been paid to the use of aerobic training on the treadmill in patients with MS. Newmann and colleagues [18] reported that a four-week aerobic treadmill training program resulted in a reduction in resting metabolism, increased walking endurance, more normal time-spatial gait pattern, increased self-selected walking speed and a decrease in walking effort. Van der Berg *et al.*[11] showed in their study that aerobic treadmill training increased walking speed and endurance, with no effect on fatigue. These results are only partially confirmed by our study, as it was devoted to gait and balance impairment in terms of muscular activation, phases of foot contact and postural stability. Although there is actually some evidence that aerobic treadmill training is safe and effective in people with MS, locomotor training as a rehabilitative approach is not widespread in a clinical context. More studies are needed to establish what benefit MS patients can get from aerobic treadmill training, both for general fitness and for walking and balance impairment, and what regimen should be adopted in terms of exercise protocol and its duration over time.

Conclusions

In conclusion, although this study has the limitation of a restricted number of minimally impaired MS patients, the measurement set proposed was able to detect the effect of an aerobic treadmill rehabilitation protocol on an individual basis, not quantifiable by means of clinical assessment. In the context of an impairment-oriented rehabilitation approach, instrumental measures are a valuable tool for functional assessment,[27] even in a very low degree of functional involvement, to identify subclinical anomalies of posture and gait in MS patients. The hypothesis that an aerobic treadmill exercise is feasible and safe and, besides the general physical conditioning effect in mildly involved patients, has very good effects also in improving early anomalies in postural and gait stability as previously suggested also by White [7] can be supported by the preliminary findings of the present study.

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