Spinal Cord (2002) 40, 646–649

www.nature.com/sc

Original Article

Reduction of periodic leg movement in individuals with paraplegia following aerobic physical exercise

MT De Mello*[,1], AC Silva[2], AM Esteves[1] and S Tufik[1]

[1]*Department of Psychobiology, UNIFESP, São Paulo, Brazil;* [2]*Department of Physiology, UNIFESP, São Paulo, Brazil*

Purpose: According to the American Association of Sleep Disorders, periodic leg movements (PLM) are classified into the group of intrinsic sleep disorders. Studies on PLM in individuals with spinal cord injury are very recent. The objective of the present study was to assess the efficacy of aerobic training in reducing the index/score of PLM in individuals with complete spinal cord injury.
Methods: Twelve male volunteers with complete spinal cord injury between T7 and T12 were submitted to six polysonographies (PSG Oxford Medilog SAC system; EEG, EMG and EOG: (1) basal night, (2) 12 h after a maximum effort test, (3) 36 h after a maximum effort test, (4) after 44 days of aerobic physical training, (5) 12 h after the last training session, and (6) 36 h after the last training session. All volunteers participated in a physical training program for 44 days using an arm crank ergometer. Data were analyzed statistically by the Wilcoxon test, with the level of significance set at α5%.
Results: The results demonstrated a statistically significant reduction ($P \leqslant 0.05$) in the comparison of first evaluation (35.1 PLM/h) with fifth (12.70 PLM/h) and sixth evaluation (18.5 PLM/h).
Conclusion: This study suggests that a program of regular and systematized physical activity promotes an effective reduction of PLM in individuals with spinal cord injury.
Spinal Cord (2002) **40,** 646–649. doi:10.1038/sj.sc.3101381

Keywords: periodic leg movement (PLM); physical exercise; aerobic training; spinal cord injured; sleep disorders

Introduction

The restless legs syndrome (RLS) and periodic leg movement (PLM) were first described by Ekbom in 1945 and 1960, respectively.[1,2]

Periodic Leg Movement can be characterized as rapid leg movements during sleep, most commonly consisting of dorsiflexion at the ankle and extension of the big toe and sometimes accompanied by flexion of the knee and/or hip. These movements, when they occur, are repeated in a regular manner at 20 to 40 s intervals, with each movement lasting 0.5 to 5.0 s. An individual may continue to experience this disorder for periods of time ranging from a few minutes to several hours. Insomnia followed by marked somnolence during the day are aspects associated with this syndrome. This disorder usually occurs during the period of NREM (Non Rapid Eye Movement) sleep.

Periodic Leg Movements occur in three grades: mild – when 5 to 24 movements/hour occur, resulting in daytime somnolence; moderate – when 25 to 49 movements/hour occur, resulting in moderate insomnia and somnolence, and severe – when more than 50 movements/hour occur with 25 awakenings per hour, causing severe insomnia and daytime somnolence.[3]

According to Bixler *et al*,[4] the prevalence of PLM is higher among older people: 5% in individuals aged 30 to 50 years, 29% in individuals aged 51 to 64 years, and 44% in individuals older than 65. Furthermore, 11% of the individuals suffering PLM present problems of insomnia, 17% present hypersomnolence and 11% are individuals with mental problems (fatigue, stress, etc.). It is associated with pathological states such as myelopathies, peripheral neuropathies, diabetic states, leukemia, rheumatoid arthritis, fibromyositis, and serum iron deficiency, among others.[5] Brown *et al*[6] detected a dopamine

*Correspondence: MT De Mello, Department of Psychobiology UNIFESP, Rua Marselhesa, 535-Vila Clementino, São Paulo-SP-Brazil-04.020-060

deficit in the CNS and recommended the use of dopaminergic agonists in the treatment of PLM and RLS.

Several types of drugs have been used for the treatment of PLM. Ekbom[1,2] reported the treatment of these syndromes with opioids, which effectiveness was recently confirmed in other studies.[7–9] However, although the literature reports that opioids are potent suppressors of these pathologies, the abuse of their administration causes severe organic problems. Thus, these drugs should be restricted to individuals with high PLM or RLS rates and should be administered in a controlled manner. In addition to these substances, benzodiazepines and dopaminergic drugs have been demonstrated to be effective in the reduction of PLM and RLS symptoms.[10]

Studies of sleep disorders in individuals with total spinal cord section are recent. Yokota *et al*[11] studied ten volunteers with physical deficiencies, two of them with total spinal cord injury. In these two individuals, leg movements during sleep were observed and were related to PLM, with both volunteers already presenting these limb movements before the injury. Lee *et al*[12] reported abnormal lower limb movements during sleep in three individuals with spinal cord injury at the thoracic level and related them to PLM.

De Mello *et al*[13] demonstrated that the incidence of PLM was reduced in individuals with spinal cord injury after acute physical exercise and concluded that this type of manipulation can modulate or change the incidence of this disorder by releasing endorphins. Another study conducted by our group in order to correlate brain waves characteristic of stage 2 of NREM sleep, or K complexes, with PLM[14] demonstrated a positive correlation between PLM and K complexes.

The objective of the present study was to observe the effect of physical training (aerobic physical exercise) on the incidence and modulation of PLM in individuals with complete section of the spinal cord.

Methodology

Thirteen male volunteers (mean age: 31.6 ± 8.3), after the study design was approved by the institutional ethics committee, were contacted through associations of persons with physical conditions and were selected by clinical evaluation. The selected individuals were clinically stable, with no complications and had a spinal cord injury between T7 and T12 and total injury to the upper motoneurons as confirmed by radiologic and tomographic examination.

Polysonography (PSG Oxford/Medilog 8 channels) was performed at the Sleep Institute of the Federal University of São Paulo (UNIFESP/EPM) and the variables observed were three electroencephalogram (EEG) channels, two electrooculogram (EOG) channels, and three electromyogram (EMG) channels, one of them submandibular and two on the legs. Electromyographic recordings of the lower limbs were obtained from the tibial muscle and femoris of the thigh.

Each volunteer was submitted to six PSG along the period of training:

- Phase I; basal;
- Phase II: 12 hours after the maximum effort test;
- Phase III: 36 hours after the maximum effort test;
- Phase IV: Return after 44 days of training, with no physical exercise on the day of evaluation;
- Phase V: 12 hours after the last training (45th day of physical training);
- Phase VI: 36 hours after the last day of physical training.

The functional effort test is used to determine exercise capacity and cardiopulmonary responses in 'healthy' patients who require orientation for exercise prescription. The effort test, together with ergospirometry, is used to determine VO_{2max} (maximal oxygen consumption, which is equivalent to the highest oxygen uptake that can be achieved during exhaustive exercise of large muscle or ml per Kg per minute) and VO_{2peak} (maximum O_2 consumption achieved during exhaustive exercise without reaching a plateau or during exercises with small muscle mass (arms), and the anaerobic threshold (weight work load that can be sustained without progressive increase in blood lactic acid concentration).[15] The anaerobic ventilatory threshold is a convenient mark used to delimit the upper intensity of aerobic exercise in training programs, corresponding to the work intensity at which the respiratory response to gradual exercise first deviates from linearity – LV1.[15]

Data obtained by Silva *et al*,[16] as well as data for walking, have shown that LV1 can be used as a parameter for the prescription of aerobic exercise for individuals with spinal cord injury.

Training was prescribed on the basis of the data obtained in the maximum effort test on an arm cycle ergometer (MET 300/Cybex, USA) in which peak O_2 consumption (VO_{2peak}, ml kg^{-1} min^{-1}), heart rate (HR, bpm) and maximum power (PO_{max}, Watts) were determined. The protocol of the maximum effort test consisted of a 2 min warm-up with a load of 25 Watts in 5 Watts/min load increments until exhaustion, with 3 min of active recovery at a load of 25 Watts. Mean rotation speed was 70–80 rpm. The test/protocol was performed with an ergospirometry system with a Vista Cx mixture chamber (Vacumed, USA) and a two-way respiratory valve (R2600/Hans Rudolph, USA). Respiratory and metabolic variables were measured and calculated at 20 s intervals throughout the test and calibrated before and after the test was performed using a gas mixture of 16% O_2, 5% CO_2 and N_2 (White Martins – Brazil).

The training sessions were held on 45 consecutive days three times a week, with a mean duration of 30 min, according to the results obtained during the maximum effort test. Total training time depended on the parameters evaluated. During the sessions, heart rate was monitored and kept at the values established for LV1. Blood pressure measurements were made before and after each training session.

Data on leg movements (PLM) were analyzed by the Wilcoxon matched paired test. The level of significance was set at $P<0.05$.

Results and discussion

The mean values obtained for the ergospirometric test referring to the maximum effort on an arm cycle ergometer (VO_{2peak}, ml kg^{-1} min^{-1} – peak O_2 consumption, HR bpm – heart rate, PO_{MAX} Watts – Maximum power) are shown in Table 1.

The present results suggest an effective reduction of PLM in subjects with spinal cord injury after an appropriate program of aerobic physical exercise, with a statistically significant relative decline in PLM rate when basal values (Phase 1) were compared to final values (Phase VI) Table 2.

Sherrill *et al*[17] compared regular and sporadic practice of physical activity in people with sleep disorders and demonstrated that both men and women had a significant reduction of these disorders when practicing a regular program of physical activity. Youngstedt *et al*[18] also demonstrated a positive correlation between physical exercise and a good night's sleep.

Which may be explained by increased activity of the opioid system, with increased β-endorphin release during exercise. Goldfarb[19] demonstrated increased β-endorphin levels in the blood stream in response to aerobic and anaerobic exercise, suggesting that, according to the type of exercise, different mechanisms may be involved in the regulation of β-endorphin release.

Table 1 Values referring to the maximum effort test

n	*VO_{2peak} ml kg^{-1} min^{-1}*	*HR bpm*	*PO_{MAX} watts*
12	25.77 ± 4.12	188 ± 10	88 ± 24

VO_{2peak} ml kg^{-1} min^{-1} - which peak O_2 consumption, HR bpm - heart rate, PO_{MAX} watts - maximum power

β-Endorphins are endogenous morphine-like opioid that interact with opioid receptors in the brain areas involved in the transmission of information about pain. β-Endorphin forms in the anterior pituitary from β-lipotrophin, which in turn is generated during the formation of adrenocorticotropic hormone (ACTH).[20] Since different studies have demonstrated the effectiveness of the opioid system in the reduction of PLM and data obtained in our studies (protocol) may suggest the hypothesis that these mechanisms may interact with the consequent release of β-endorphin during aerobic physical exercise, we propose that these peptides may influence the reduction of PLM during sleep.

However, a limiting factor in our study was that β-endorphin levels were not measured before, during or after physical exercise or during sleep. The same protocol with determination of β-endorphin is being currently evaluated in another study on volunteers with pathological PLM scores who have no spinal cord injury.

Conclusion

The leg movements observed in our volunteers with total spinal cord section cannot be correlated with RLS, since they do not have the same clinical description, but they may be correlated with PLM.[6,13,17,19] The present study demonstrates a significant reduction of PLM after systematized aerobic physical exercise.

The decrease in PLM after physical activity may be due to the release of β-endorphin, showing the participation of the opioid system.

On the basis of the results obtained, aerobic physical exercise with training intensity and volume at LV1, can be seen as a first approach to the treatment of PLM, since its benefits in terms of quality of life and sleep have been reported, while pharmacological treatment should be applied only to paraplegic individuals who do not respond to treatment with aerobic physical exercise.

Acknowledgements

The authors would like to acknowledge to Secretaria Nacional de Esportes/Governo Federal do Brasil, CENESP/UNIFESP, Associação Fundo de Incentivo à Psicofarmacologia (AFIP) and FAPESP (CEPID/SONO - FAPESP - UNIFESP, proc. 98/143033).

Table 2 Results obtained in the PSG evaluation during the phases analyzed

	Phase I	*Phase II*	*Phase III*	*Phase IV*	*Phase V*	*Phase VI*	*NS*
PLM/H	35.1 ± 39.2	21.0 ± 40.3	$19.7^* \pm 4.7$	26.0 ± 40.3	$12.7^* \pm 23.3$	$18.5^* \pm 29.5$	$^*P \leqslant 0.05$

Phase I: basal; *Phase II*: 12 h after the maximum effort test; *Phase III*: 36 h after the maximum effort test; *Phase IV*: Return after 44 days of training, with no physical exercise on the day of evaluation; *Phase V*: 12 h after the last training - 45th day of physical training; *Phase VI*: 36 h after the last day of physical training

References

1 Ekbom KA. Restless legs syndrome. *Neurologym* 1960; **10:** 868 – 873.
2 Ekbom KA. Restless legs. *Acta Med Scand* (Suppl) 1945; **158:** 123 (Abstract).
3 The International Restless Legs Syndrome Study Group (Arthur S. Walters MD – Group Organizer and Correspondent). Towards a better definition of the Restless Legs Syndrome. *Mov Disord* 1995; **10:** 634 – 642.
4 Bixler EO *et al*. Nocturnal myoclonus and nocturnal myoclonic activity in the normal population. *Res Commun Chem Pathol Pharmacol* 1982; **36:** 129 – 140.
5 Montplaisir J, Lorrain D, Godbout R. Restless legs syndrome and periodic leg movements in sleep: the primary role of dopaminergic mechanism. *Eur Neurol* 1991; **31:** 41 – 43.
6 Brown KW, Glen SE, White T. Low serum iron status and akathisia. *Lancet* 1987; **1:** 1234 – 1236.
7 Hening WA *et al*. Dyskinesias while awake and periodic movements in sleep in restless legs syndrome: treatment with opioids. *Neurology* 1986; **36:** 1363 – 1366.
8 Sandyk R, Gillman MA. The opioid system in the restless legs and nocturnal myoclonus syndromes. *Sleep* 1986; **9:** 370 – 371.
9 Walters AS *et al*. Successful treatment of the idiopathic restless legs syndrome in a randomized double-blind trial of oxycodone versus placebo. *Sleep* 1993; **16:** 327 – 332.
10 Montplaisir J, Godbout R, Pellether G, Warnes H. Restless legs syndrome and periodic limb movements during sleep. In: Kryger MH, Rath T, Dement WC (eds). *Principles and practice of sleep medicine*. 2nd edn. Philadelphia: W.B. Saunders Company, 1994, p 589.
11 Yokota T, Hirose K, Tanabe H, Tsukagoshi H. Sleep-related periodic leg movements (nocturnal myoclonus) due to spinal cord lesion. *J Neurol Sci* 1991; **104:** 13 – 18.
12 Lee MS, Choi YC, Lee SH, Lee SB. Sleep-related periodic leg movement associated with spinal cord lesions. *Movement Disorders* 1996; **11:** 719 – 722.
13 De Mello MT, Lauro FA, Silva AC, Tufik S. Incidence of periodic leg movements and of the restless legs syndrome during sleep following acute physical activity in spinal cord injury subjects. *Spinal Cord* 1996; **34:** 294 – 296.
14 De Mello MT *et al*. Correlation between K complex, periodic leg movements (PLM), and myoclonus during sleep in paraplegic adults before and after an acute physical activity. *Spinal Cord* 1997; **35:** 248 – 252.
15 American College of Sports Medicine. *Guidelines for Exercise Testing and Prescription*. 6th edn. Philadelphia, PA: 2000; 91 – 114.
16 Silva AC *et al*. Effect of aerobic training on ventilatory muscle endurance of spinal cord injured men. *Spinal Cord* 1998; **36:** 240 – 245.
17 Sherrill DL, Kotchou K, Quan SF. Association of physical activity and human sleep disorders. *Arch Intern Med* 1998; **158:** 1894 – 1898.
18 Youngstedt SD, O'Connor PJ, Dishman RK. The effects of acute exercise on sleep: a quantitative synthesis. *Sleep* 1997; **20:** 203 – 214.
19 Goldfarb AH, Jamurtas AZ. β-Endorphin response to exercise. *Sports Med* 1997; **24:** 8 – 16.
20 Powers SK, Howley ET. *Fisiologia do Exercício: teoria e aplicação ao condicionamento e ao desempenho*. São Paulo: Manole, 2000, 525 p il.