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Neurophysiological correlates of sleep leg movements in acute spinal cord injury

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HIGHLIGHTS

- Leg movements during sleep are recorded in spinal cord injury patients with completely absent volitional activity in their lower limbs but they show clear periodicity only in a small subgroup of them.
- The disconnection from higher nervous structures, in these patients might allow the appearance of leg movements due to the activity of spinal generators not inhibited by higher influences.
- Leg movements during sleep in spinal cord injury patients might assume the periodic character when a genetic predisposition is present.

ABSTRACT

Objective: The objective of this study was to analyze the periodicity of leg movement activity emerging during sleep in a group of patients with spinal cord injury and to evaluate their pathophysiological features.
Methods: Twenty patients (16 males, mean age 34.0 years) with traumatic spinal cord lesions were recruited (5 cervical, 15 thoracic; 16 level A and 4 level B at the American Spinal Injury Association impairment scale). Periodicity of sleep leg movements was analyzed; electroencephalographic spectral analysis and heart rate were evaluated for 20 s preceding and 30 s following the onset of leg movements.
Results: Periodic leg movements during sleep (PLMS) index >5/h was found in only 4 patients and only 2 of these had PLMS index >15/h. Eleven patients (group I) did not show any increase in heart rate related to the occurrence of leg movements while the remaining 9 did (group II). Two patients in each group had American Spinal Injury Association impairment level B; 5 patients of group I and none of group II had cervical lesions while 6 patients of group I and all 9 of group II had thoracic lesions. Only 2 patients in group I presented clearly periodic leg movements during sleep and PLMS index >15/h. Electroencephalographic delta, alpha and beta bands around leg movements increased clearly in group II while the changes in group I were very limited or absent.
Conclusion: Leg movements during sleep are recorded in spinal cord injury patients with completely absent volitional activity in their lower limb but they show clear periodicity only in a small subgroup of them.
Significance: The disconnection from higher nervous structures, in patients with spinal cord injury might favor the appearance of leg movements due to the activity of spinal generators not inhibited by higher influences; correlated autonomic and electroencephalographic changes can be absent. This motor activity might assume the periodic character when a genetic predisposition is present.

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1. Introduction

Periodic leg movements during sleep (PLMS) and restless legs syndrome (RLS) have been reported to occur in myelopathy (Brown et al., 2000; de Mello et al., 1999; Lee et al., 1996; Nogues et al., 2000; Telles et al., 2011; Yokota et al., 1991) and a recent case report with spinal cord injury has shown that they might bear a striking resemblance with PLMS occurring in patients with RLS and respond to dopaminergic agents (Salminen et al., 2013). The same authors have reported that these PLMS are disconnected from cortical arousals and are not accompanied by changes in autonomic function, as indicated by the absent heart rate (HR) changes.

However, the pathophysiological basis of leg movements (LMs) occurring in spinal cord injury is incompletely known. The aims of this study were to analyze in detail the leg movement activity emerging during sleep in a group of patients with spinal cord injury in order to detect PLMS and to evaluate their pathophysiological features by analyzing their association with the autonomic function (HR) and brain rhythms. In particular, we also aimed at evaluating if the disconnection between LMs and autonomic changes is a phenomenon detectable in all patients with spinal cord injury or if it occurs only in a subgroup of them; in such a case, our aim was to detect eventual differences between these two subgroups.

2. Subjects and methods

2.1. Subjects

Twenty patients with traumatic spinal cord lesions (16 males and 4 females, mean age 34.0 years, 12.76 S.D.), referred to the spinal unit of the Niguarda Hospital (Milan, Italy) from September 2010 to December 2011, were recruited for this prospective observational study. Exclusion criteria were: (a) inability to give informed consent, (b) any significant head injury, (c) presence of tracheostomy at enrolment, (d) ventilator-dependent at enrolment, (e) other respiratory problems (chest infection, pneumothorax, haemothorax, effusion, intercostal catheter, sleep apnea). The location of the lesion and its extent was assessed in each patient by MRI, evoked potentials and electromyography. Five patients had lesions localized in the cervical region of the cord while the remaining 15 had lesions localized in the thoracic segment. The sensory and motor impairments presented by the patients were evaluated following the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) (Burns et al., 2012) of the American Spinal Injury Association (ASIA) and the ASIA impairment scale was assessed; at this scale, 16 patients presented the level A and the remaining four the level B. Prior to administering the ISNCSCI, it was established that all subjects had the cognitive ability to accurately respond to the test instructions. The polysomnographic data used for this study were collected after an average of 0.25 years (0.21 S.D.) from the traumatic event.

This study was approved by the local ethics committee and all subjects provided informed consent, according to the Declaration of Helsinki, before entering the study.

2.2. Polygraphic sleep recording

Each subject underwent a polysomnographic full night recording. Standard overnight polysomnography was performed in the ward in an attended setting using a portable sleep monitoring (AURA® PSG Ambulatory System; GRASS Technologies), including electro-encephalography, bilateral electro-oculography, chin and tibial electromyography, electro-cardiography, oronasal airflow, chest and abdominal effort (recorded using respiratory inductance plethysmography), pulse oximetry, and body position; patients with an apnea/hypopnea index $\geqslant$5 were not included.

Sleep signals were sampled at 256 Hz and stored on hard disk for further analysis. EMG signals, in particular, were digitally band-pass filtered at 10–100 Hz, with a notch filter at 50 Hz.

At the beginning of each session and before the start of recording, the sleep technician checked that the amplitude of the EMG signal from the two tibialis anterior muscles was below 2 μV at rest.

2.3. Sleep scoring and detection of leg movements

Sleep stages were visually scored following standard criteria on 30-s epochs (Rechtschaffen and Kales, 1968); arousals were also detected following standard criteria (Iber et al., 2007). LMs during sleep were first detected by the sleep analysis software Hypnolab 1.2 (SWS Soft, Italy), which allows their computer-assisted detection. With this software, the detection is performed by means of a human-supervised automatic approach controlled by the scorer, but for this study one scorer (R.F.) visually edited the detections proposed by the automatic analysis, before the computation of the various parameters which were automatically generated by the same software adopting the criteria set by the International RLS Study Group and endorsed by the World Association of Sleep Medicine (Zucconi et al., 2006). In particular, the PLMS index was calculated as the number of LMs included in a series of four of more, separated by more than five and less than 90 s, per hour of sleep.

We also obtained a distribution histogram of all inter-LM intervals and, subsequently, the number of intervals included in sequences of at least three, all 10–90 s long, was divided by the total number of intervals and we will refer to this ratio as the periodicity index (PI); this index can vary between 0 (absence of periodicity, with none of the intervals having a length between 10 and 90 s) to 1 (complete periodicity, with all intervals having a length between 10 and 90 s) (Ferri et al., 2006). PI is independent on the absolute number of LMs recorded and was calculated for all the subjects included in this study.

2.4. Heart rate and spectral EEG analysis

In this study, we analyzed HR and EEG spectral content accompanying LMs without arousals (Iber et al., 2007) and arousals without LMs. These LMs and arousals were included if they were not preceded or followed by another LM or arousal by at least 30 s. This time was chosen in order to avoid possible summation of the effects of separate movements on the variables under consideration; moreover, 30 s is well in the main peak of the intermovement interval histogram expected for PLMS (Ferri et al., 2006). Up to five (but not less than 3) LMs and arousals were chosen from NREM sleep, for each patient.

In order to reduce or eliminate baseline variability of the parameters considered in this study and induced by intersubject and sleep stage differences, a fixed-time window of 50 s (20 preceding and 30 following the onset of each LM or arousal) was used, with its first 10 s which served for the calculation of the baseline; subsequently, each value was expressed as a percentage of this baseline value, for all parameters calculated around each LM or arousal. After this, individual averages were obtained for each individual included in the study, which served for the subsequent computation of the group average.

HR was measured and its value calculated for each round second by means of a linear interpolation between the measured values; EEG power spectra were calculated, after Welch windowing, by means of the Fast Fourier Transform. The power spectrum