Case Reports

Involuntary Rhythmic Leg Movements Time-Locked With the Respiratory Cycle

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Introduction

Involuntary and rhythmical movements of the legs is a rare condition in childhood that can be found in the restless legs syndrome [1] and in periodic leg movements [2]. The localization of the generators of such an involuntary activity remains unknown, despite suggestions of a locus in the brainstem [3]. We report a patient with features providing important clues to the location of one of these generators.

Case Report

A male 3 years, 8 month of age was referred to the outpatient clinic of the Pediatric Neurology Unit of Hospital Dona Estefânia at Lisbon for neurologic evaluation. He was the second son of healthy and nonconsanguineous parents. There was no family history of movement disorders. During pregnancy, no problems were apparent, delivery was vaginal, and occurred at term. The birth weight was 3.2 kg, and no pathologic events were registered during the neonatal period.

By the age of 7 months, the parents detected rhythmic and continuous flexion/extension movements of the right foot; some weeks later these movements also involved the knee, producing a general flexion/extension of the right leg. Four months later, similar, but less apparent, movements were also present in the left leg, synchronous with the first movements. The involuntary activity was present throughout sleep and wakefulness (Fig 1A), both at rest and during voluntary movements.

The cognitive development was adequate (evaluated with the Mental Developmental Scale of Griffiths [4] at 18 months of age), but motor milestones were delayed, and he did not perform automatic stepping in the early months, he could only sit independently at 8 months, and started to walk at the age of 2 years, 4 months. The neurologic examination did not reveal abnormalities in muscle tone, strength, reflexes, sensation, or cranial nerves. The cognitive status was normal for age, and the coordination of the upper limbs was also normal.

In spite of the persistence of the rhythmic involuntary movements of the lower limbs, sleep was quiet. During wakefulness, the movements interfered significantly with gait and standing, but no sensory discomfort or motor restlessness was apparent in the child's behavior.

The gait remained laborious because of the interference of the involuntary leg movements, and in the subsequent months he developed an internal rotation of the knees and feet, which became more pronounced as he improved his gait capabilities. This abnormal posture was not present during resting, and was interpreted as compensatory and leading to a decreased interference of the involuntary movements in gait.

An hematologic and biochemical evaluation (including liver and renal functions) for metabolic abnormalities was negative.

Involuntary rhythmic leg movements in childhood is an uncommon condition, the generators of which remain unknown. We report on a male 3 years of age with distinct features providing important clues concerning the location of one of these generators. At the age of 7 months, the previously healthy young male started with low frequency, rhythmic, and continuous (both during wakefulness and sleep) flexion/extension movements of the lower limbs. Movements interfered significantly with gait acquisition, and, despite normal cognitive development, he was able to walk only at age 2 years, 4 months. The neurologic examination revealed the absence of automatic stepping in the neonatal period, but was otherwise normal. A polygraphic electroencephalogram/electromyogram (EEG/EMG) recording, at the age of 2 years, 9 months, revealed rhythmic and synchronous legs with EMG activity at 0.5 Hz. A more complete polygraphic recording at the age of 3 years, 10 months, showed a lower frequency (0.35 Hz) for the movements, which were time-locked with the respiratory cycle. Magnetic resonance imaging (MRI) of the brain revealed an increased T_2 signal in the upper medulla-lower pons regions. The generator of the rhythmic legs movements is postulated to be the respiratory center, connecting with the reticulospinal projecting neurons through an aberrant pathway. © 2001 by Elsevier Science Inc. All rights reserved.

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a)

Wakefulness · Non-REM sleep

EEG

EMG

b)
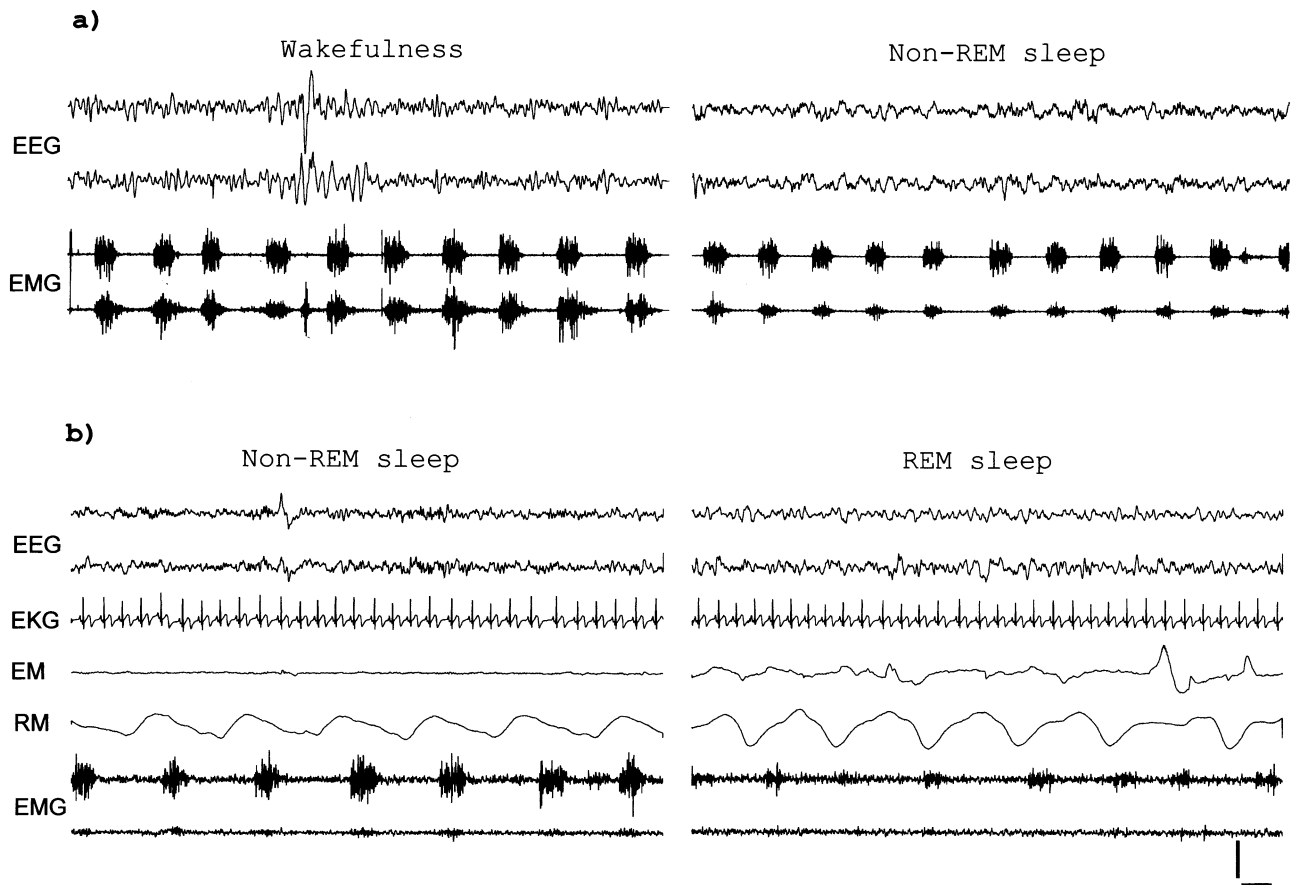
Non-REM sleep · REM sleep

EEG

EKG

EM

RM

EMG

Figure 1. (A) Polygraphic recordings of EEG (right hemisphere above, left hemisphere below) and legs EMG (right leg above, left leg below), during wakefulness and non-rapid eye movement sleep at 2 years, 9 months of age. (B) Polygraphic recording of EEG/EMG, as previously, with thoracic respiratory movements (RM), eye movements (EM), and electrocardiogram (EKG), during non-rapid eye movement sleep and rapid eye movement sleep, at 3 years, 10 months of age. (A) and (B): EEG, EMG, and eye movement were recorded with surface AgCl-coated disk electrodes. For the EEG electrodes at the positions C3, C4, Cz, O2, and O1 of the 10-20 system were used with the reference on the mastoid. Bipolar montages (C_4-O_2 and C_3-O_1) for the right and left hemisphere were used; the EMG was recorded with electrodes in a belly tendon distribution on the tibialis anterior muscles of both legs (right above, left below); for eye movements, a bipolar montage between electrodes on the right and left outer canthus was used; respiratory movements were recorded using a thoracic band. Scale bars: horizontal = 1 second; vertical = EEG (100 μV), EKG (800 μV), EM (30 μV), RM (25 μV), and EMG (4 μV).

The patient was referred for neurophysiological study at the age of 2 years, 9 months. The electroencephalogram (EEG) and somatosensory evoked potentials (right tibialis and median nerves stimulation) were normal. A polygraphic recording of EEG and surface electromyogram (EMG) revealed rhythmic activity at 0.5 Hz in the tibialis anterior muscles of both legs, persisting throughout wakefulness and quiet sleep (Fig 1A). The muscular activity occurred in synchronous bursts of 0.5-1-second duration, and no myoclonic-type activity was present.

A few months after the initial investigation, we became aware of a coincidence between the frequency of the rhythmic leg movements recorded in the polygraphic study (approximately 0.5 Hz) and the respiratory cycle at the age of test. The hypothesis postulated was that the central pattern generator for the legs movements was the respiratory center.

A polysomnographic afternoon recording (3 hours long) was done at the age of 3 years, 10 months, to test the previous hypothesis (Fig 1B). The sleep latency and architecture were preserved, and no pathologic activity was detected on the EEG. The rhythmic leg EMG activity was then found to be time-locked with the respiratory cycle at a frequency of approximately 0.35 Hz, in line with our expectation for the normal maturational decrease in frequency of the respiratory cycle. A backaveraging triggered by the EMG burst onset failed to show an EEG correlate for the leg movements, but preserved the respiratory movement amplitude (Fig 2). Furthermore, we could observe the persistence of the movements during rapid eye movement sleep as well as during wakefulness and non-rapid eye movement sleep (Fig 1B), therefore establishing their presence throughout all stages of the sleep

cycle. There was some variability in the phase relation between the EMG bursts and the thoracic movements throughout the record, mainly with changes in sleep stages and with body movements, but the one-to-one relation was preserved between the two events. In rapid eye movement sleep, the movements were less rhythmic and regular, in line with the more variable respiratory cycle typical of this stage. No recordings could be done during wakefulness at this time because of lack of cooperation.
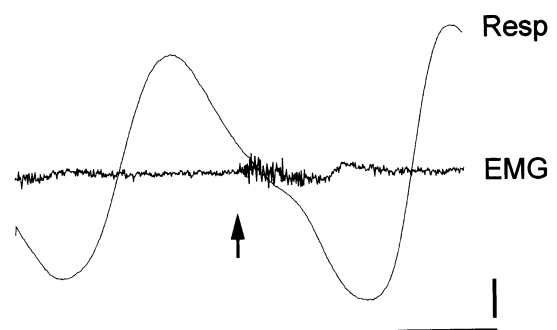

Figure 2. Backaveraging of 100 consecutive artifact-free respiratory movements triggered by the onset of legs EMG. The vertical arrow represents the EMG trigger point. Scale bars: horizontal = 1 second; vertical = RM (5 μV) and EMG (2 μV).
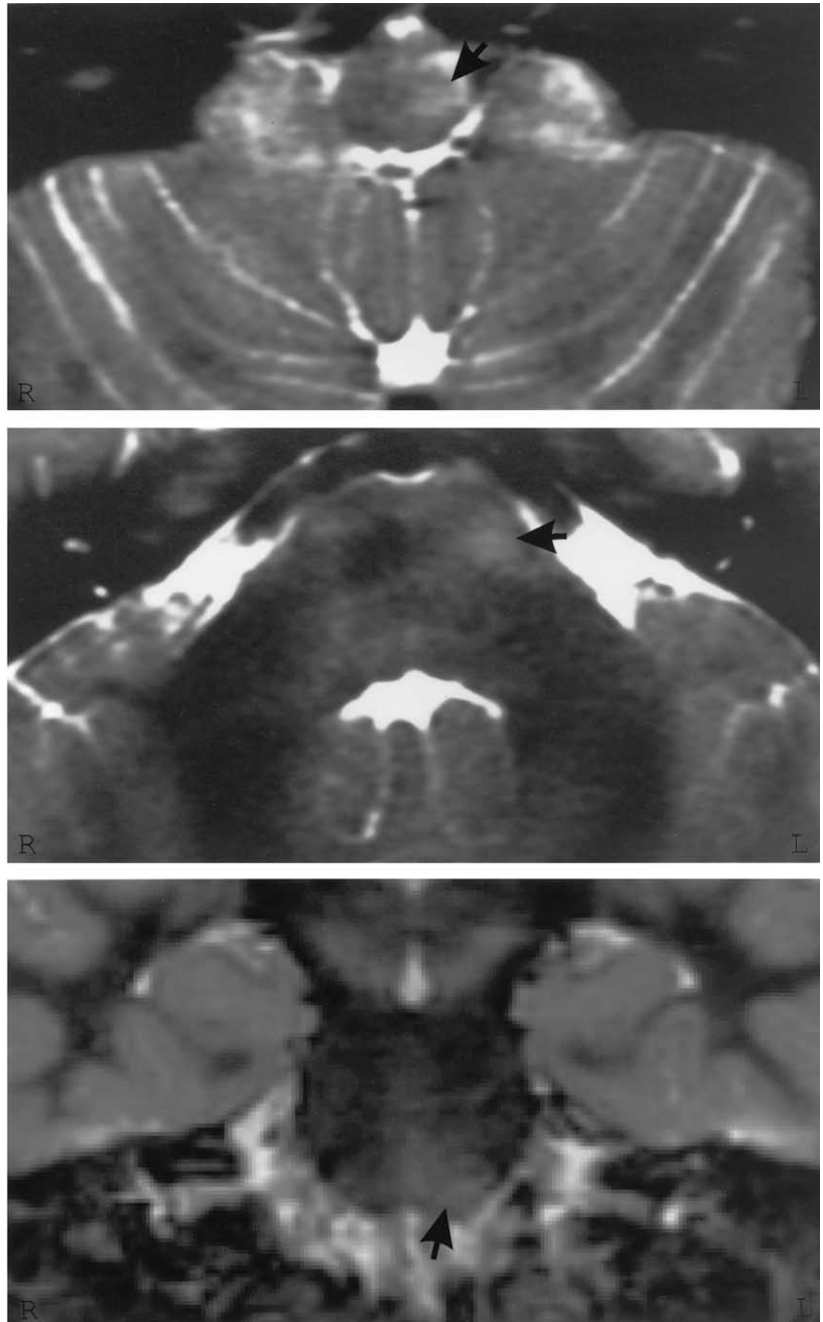
Figure 3. (A) Axial plane through the medulla, demonstrating an increased and heterogeneous signal in the T_2 sequence, lateralized to the left (arrow). (B) Axial plane through the lower pons, demonstrating extension of the signal abnormality to the pons, persistently lateralized to the left (arrow). (C) Coronal T_2 sequence through the brainstem demonstrating the lower pons increased signal (arrow). (A-C): The axial and coronal T_2 sequences were obtained in a 1.5 T scanner (SIGNA GE), using a fast spin echo (FSE 6500/84), high resolution, and T_2 sequence with slices 0.9-mm thick.

An early brain study targeting the brainstem and using a T_2-weighted sequence (fast spin echo 6500/84) revealed a blurred, hyperintense, area extending from the medulla to the pons localized in the left region, that could be found both in axial and coronal sequences (Fig 3).

A therapeutic trial with carbamazepine (up to 15 mg/kg) did not produce any relevant clinical improvement.

Discussion

This case exhibits features that, to the best of our knowledge, have not been described previously in the literature, namely, persistence of the movements throughout the wakefulness-sleep cycle without significant changes in rhythm, no change with resting or action, strong synchronization with the respiratory cycle, and evolution of the frequency of movements in line with the maturational decrease of the respiratory cycle frequency. The MRI finding of a lesion in the upper medulla-lower pons area gives additional support to the hypothesis that the generator for the rhythmic movements lies in the brainstem in the neighborhood of the respiratory center [5,6].

The possibility that we are in the presence of an atypical early-onset restless legs syndrome was considered [1]. The present case, however, does not fulfill the minimal criteria for this syndrome, according to the International Restless Legs Syndrome Study Group [7], in which the patient shows no apparent urge to move the legs, no motor restlessness, no significant change with rest or action, and no apparent worsening with sleep. The few cases involv-

ing infants that have been described in the literature [1,8] all had a clear family history, increased sleep latency, disturbed sleep, and the complains were irregular in the first years. The absence of sleep disturbances, no family history of the condition, and persistent character from onset, further rule out the diagnosis of restless legs syndrome for our patient.

The periodicity of the movements during sleep can remotely evoke the periodic leg movements of sleep, which are known to persist throughout wakefulness [8]. However, periodic leg movements of sleep have a larger intermovement interval (4-90 seconds [8] as compared with the 2-3 seconds in our case), and decrease in the deeper phases of non-rapid eye movement and rapid eye movement sleep [2], in contrast with our case, which shows no variability throughout the sleep cycle.

The frequency variation of the abnormal leg movements with increasing age and in parallel with the respiratory frequency maturation is a feature not described in other periodic movements of sleep. The existence of a significant connection between the two phenomena is also suggested by the results of the backaverage analysis (Fig 2), demonstrating synchronization of respiratory movements to the EMG onset, as well as by the similar changes in rhythm in non-rapid eye movement and rapid eye movement sleep from a regular to an irregular pattern.

The persistent synchronization with the respiratory movements throughout wakefulness and sleep strongly suggests a subcortical generator, most likely located in the neighborhood of the reticular formation of the brainstem responsible for the generation of the respiratory rhythm [5,6]. The demonstration of an abnormal hypersignal in the MRI T_2 sequence of the upper medulla-lower pons supports the existence of a structural lesion in the predicted area.

The existence of a lesion in the brainstem, in the proximity of the reticular formation, suggests the diagnostic possibility of reticular myoclonus. An argument against this explanation is the fact that the leg movements in our patient are slower than the shocklike movements usually seen in myoclonus. This likelihood is supported by the surface EMG recordings, which demonstrate bursts lasting more than 500 ms, much longer than the 300 ms seen in the slower types of myoclonus [9]. The lack of EEG correlation with the movements in the backaveraging, lack of involvement of other segments besides the lower limbs, and lack of stimulus sensitivity are additional features that, in our view, rule out the hypothesis of reticular myoclonus.

The existence of bulbospinal neurons projecting from the reticular formation to the lumbar level of the spinal cord is well established [10], and low-intensity electrical stimulation in the medullary reticular formation can produce flexion-extension sequential responses limited to isolated limbs or synchronous bilateral movements [11]. The clearest responses seem to arise from the area of origin of the reticulospinal tracts [11], and the bilateral responses can be explained by the fact that these neurons project to the ipsi- and contralateral side of the spinal motoneurons [10]. The overall experience with low-intensity stimulation of the reticulospinal projections suggests that activation of a small number of reticular neurons can produce fractionated and coordinated limb movements [12]. The data reviewed previously further suggest that a "leaky" respiratory center could drive a group of spinal projecting neurons, and produce the rhythmic and coordinated leg movements present in our patient.

Our final interpretation of the reported patient is that early in life he suffered a brainstem lesion that led to reactive sprouting and the establishment of an abnormal connection between the respiratory center and the reticulospinal motor pathways for the lower limbs, leading to an aberrant expression of the normal respiratory rhythm. The lower frequency of the rhythmic movements and the development of corrective postures seem to explain the overall improvement in motor abilities, because no evidence of a decrease in the amplitude or persistence is present at this age.

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