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Original article

The neurophysiology of the alternating leg muscle activation (ALMA) during sleep: Study of one patient before and after treatment with pramipexole

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Abstract

Background and purposes: To report the neurophysiological features of a patient with alternating leg muscle activation (ALMA) during sleep, a quickly alternating pattern of anterior tibialis activation which might represent transient facilitation of a spinal central pattern generator for locomotion, perhaps due to the serotonergic effects of antidepressant medication.

Patient and methods: A 33-year-old male patient with ALMA. The patient underwent a complete and detailed study of his neurophysiological parameters during sleep, before and after treatment with pramipexole.

Results: The treatment with pramipexole was followed by a significant reduction in the rate of occurrence of ALMA, in reported insomnia, and in daytime sleepiness. The ALMA generally were preceded by cyclic alternating pattern A phases and increased heart rate in most instances. Visual scoring and spectral analyses suggested that after pramipexole more intense arousal was required to trigger ALMA.

Conclusion: The evident beneficial effect induced by the treatment with pramipexole indicates that the spinal networks involved in the generation of ALMA might also be under the inhibitory control of dopaminergic networks. We suggest that ALMA can be seen even in the absence of other factors such as antidepressant therapy, sleep apnea or periodic leg movements during sleep, and might be considered as an additional phenomenon influenced by sleep instability. Our patient seems to indicate also that treatment with dopamine agonists can be useful in such patients because the treatment can be followed by a good clinical response.

Keywords: Alternating leg muscle activation; Restless legs syndrome; Periodic leg movements during sleep; Cyclic alternating pattern; Sleep instability; Dopamine agonist therapy

1. Introduction

The term ‘alternating leg muscle activation’ (ALMA) during sleep has been recently introduced by Chervin et al. [1] to describe a quickly alternating pattern of anterior tibialis activation, found in nocturnal polysomnography of 12 men and 4 women (aged 12–70 years) evaluated for sleep-disordered breathing. These authors reported leg muscle activations occurring at a frequency of approximately 1–2 Hz, which lasted between 0.1 and 0.5 s, organized in sequences of alternating activations lasting up to 20 s. The phenomenon was reported to occur in all sleep stages but particularly during arousals. Ten of the 16 patients also presented periodic leg movements during sleep at a rate >5.0 per hour, and 12 of them were on antidepressant medication. Chervin et al. [1] concluded that ALMA might represent transient facilitation of a spinal central pattern generator for locomotion, perhaps due to the serotonergic effects of antidepressant medication.

To our knowledge, there are no other similar ALMA patients reported in the literature; for this reason, it is important to confirm with new cases the report by Chervin et al. [1]. We describe here a new patient with ALMA who underwent a complete and detailed study of his neurophysiological parameters during sleep, before and after treatment with pramipexole.

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2. Clinical study

The patient, a 33-year-old male, was born at term from non-consanguineous parents; psychomotor development was normal and the patient attained a university degree. His clinical history was completely uneventful until the age of 30 years when he started to present nonrestorative sleep because of frequent and easy to provoke awakenings. This condition caused, from the start, excessive daytime sleepiness and tendency to fall asleep with serious consequences on the patient's social and family interactions. The subject has no bed partner and had never taken drugs either acting at the level of the central nervous system or known to have effects on sleep. There was no complaint of restless legs, but mild snoring was reported.

The patient was referred to us by his mother who is affected by restless legs syndrome (RLS) and currently under drug therapy for this disturbance. During the brief hospitalization, the subject underwent a battery of tests and exams which are briefly summarized here. Neurological examination was normal and psychological testing (Instrumental Activities of Daily Living Scale, Index of Independence in Activities of Daily Living, Geriatric Depression Scale, Mini Mental State Examination, Hamilton Rating Scale for Depression, Milan Overall Dementia Assessment, verbal span, attention matrices, bisyllabic word repetition) indicated normal cognitive functioning. Heart examination and electrocardiogram (ECG) were also normal, as well as clinical chemistry (glucose, potassium, sodium, total and HDL cholesterol, triglycerides, creatinine, protein electrophoresis, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) Bence-Jones bodies, alkaline and prostate acid posphatase, γ-glutamyl-transferase, lactic dehydrogenase, cholinesterase, creatine posphokinase), clinical haematology and urine analyses; in particular, serum iron was 86 mcg% (normal range 53–167) and ferritine 125 ng/ml (normal range 12.8–454). Only a mild deviation of the nasal septum was found at the otorhinolaryngologic examination. Body mass index (BMI) was 29.8, basal pulse rate was 68, systolic blood pressure was 110 mmHg and diastolic 70 mmHg.

A score of 16 was obtained at the Epworth Sleepiness Scale (EES)[2,3], indicating the presence of moderate-to-severe sleepiness. The patient did not meet the minimal criteria accepted for the diagnosis of RLS, in accordance with the International RLS Study Group criteria [4].

The patient underwent an overnight polysomnographic recording which comprised electro-oculogram (EOG) (2 channels), EEG (F3, C3, and O1 referred to A2), electromyogram (EMG) of the submentalis muscle, ECG, oro-nasal airflow with thermistors, chest and abdominal movements, and EMG of the right and left tibialis anterior muscles. The recording was carried out using a Brain Quick Micromed System 98 recording machine and signals were sampled at 128 Hz and stored on hard disk in European data format (EDF) [5] for further analysis. EEG signals, in particular, were digitally band-pass filtered at 0.1–70 Hz, 12-bit A/D precision.

Sleep stages were scored following standard criteria [6] on 30-second epochs; subsequently, cyclic alternating pattern (CAP) and non-CAP periods were visually detected in each recording, during non-rapid eye movement (NREM) sleep, according to the rules defined by Terzano et al. [7], and manually marked on screen by means of the sleep analysis software Hypnolab 1.2 (SWS Soft, Italy) which also allowed us to obtain, at the end, a series of parameters related to sleep stage structure and CAP. Table 1 shows the results obtained from this analysis, together with our normative data for the age group of these patients. Sleep structure in pre-treatment condition is abnormal because of low sleep efficiency, high number of awakenings and increased percentage of wakefulness after sleep onset and sleep stage 1. Baseline CAP is also abnormal because CAP

Table 1
Sleep structure and CAP parameters found in our patient with ALMA, before and after treatment with pramipexole; also, the normative data of our lab for the patient's age group are reported in the two columns on the right (37 healthy volunteers, 23 women and 14 men, mean age 28.9 years, SD 7.9 years)

	Patient		Normal controls ($n=37$)	
	Before pramipexole	After pramipexole	Mean	SD
Sleep staging				
Time in bed, min	577.0	579.0	443.0	52.65
Sleep period time, min	525.0	489.0	426.5	54.55
Total sleep time, min	472.0	471.5	409.9	54.52
Sleep latency, min	39.0	88.0	12.9	11.74
Rapid eye movement sleep latency, min	104.5	77.5	81.6	50.39
Stage shifts/hour	12.5	7.1	11.1	2.75
Awakenings/hour	2.7	1.5	1.6	1.18
Sleep efficiency, %	81.8	81.4	92.5	5.06
Wakefulness after sleep onset, %	13.1	3.6	3.9	3.60
Sleep stage 1, %	9.5	6.9	1.6	1.75
Sleep stage 2, %	43.3	63.2	46.1	7.15
Slow-wave sleep, %	17.9	10.0	25.5	7.33
Rapid eye movement sleep, %	19.1	16.4	22.9	5.14
CAP parameters				
CAP Rate, %	67.9	64.6	34.8	9.14
Total A1, %	68.6	66.6	81.5	7.32
Total A2, %	12.2	18.9	9.2	4.08
Total A3, %	19.2	14.5	9.3	4.83
A1 duration, s	5.8	5.4	8.1	1.94
A2 duration, s	10.3	9.5	11.2	2.11
A3 duration, s	14.1	13.2	15.4	2.92
B duration, s	16.9	19.9	23.2	2.36

CAP A1 subtypes are characterized by sequences of K-complexes or delta bursts in NREM sleep stages, associated with mild or trivial polygraphic variations and activation of somatic and autonomic systems; the other two subtypes (A2 and A3) contain variable amounts of the above slow components and increasing quantities of more rapid EEG activities; these two CAP elements correspond to the classic ASDA arousals.