The Importance to Assess the True “Periodicity” of Leg Movements during Sleep in Narcolepsy

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We have read with interest the paper “Periodic Limb Movements during Sleep in Children with Narcolepsy” by Jambhekar and colleagues recently published in the *Journal of Clinical Sleep Medicine*.¹ These authors have made a very simple analysis of periodic leg movements during sleep (PLMS), based on the current AASM criteria² for their scoring and have found that only 4 patients had a PLMS index $\geq 5/h$ (9%). The authors have then considered the 16 patients (36%) that had “any PLMS” (PLMS index $> 0/h$) in whom they claim that sleep was significantly more disrupted than those without PLMS (PLMS index = 0), based on the finding of a higher arousal index while none of the only two additional sleep parameters provided (total sleep time and sleep efficiency) was significantly different. In this comparison, the authors also found that the mean sleep latency at the multiple sleep latency test was shorter. The authors then conclude that children with PLMS and narcolepsy have more sleep disruption and shorter mean sleep latencies than those with narcolepsy but without PLMS.

Beside the general interest of the topic, this article was disappointing from several points of view. First of all, the analysis of PLMS has undergone in recent years a profound improvement, and it appears now clear that the classical PLMS index is inadequate to detect real periodicity in the LM activity during sleep.^{3,4} Based on newer and detailed methods of analysis, we have already published two papers on the topic of PLMS in narcolepsy, one in adults⁵ and another in children,⁶ completely omitted by Jambhekar and colleagues. We have shown that periodicity is almost absent in narcoleptic children, associated with a decrease of arousal indexes; in adults the periodicity of LM is also decreased and clearly lower than that expected for restless leg syndrome patients (RLS). In fact, in another paper in adult narcoleptic patients, we have also shown that the occurrence of real PLMS appear to be connected with the presence of RLS,⁷ which can be found in about 15% of individuals with narcolepsy/cataplexy.⁸ Moreover, the distribution of

LM activity during the night in adults is clearly different from that expected for PLMS in RLS.

In the paper by Jambhekar and colleagues,¹ an unusually average low value of PLMS is reported (PLMS index 1.3/h, SD 2.5) that was not compared to that of normal controls because no such a group was included in the analysis. These values are clearly lower than the values reported by other studies even in normal controls^{6,9} and might indicate that if a control group was included the authors would have found no differences with their patients; this makes the conclusions of this study weak and doubtful.

A tentative explanation of the results of Jambhekar and colleagues¹ can be attempted by considering also our recent report on LM activity during quiet wakefulness preceding sleep in normal controls and RLS patients.¹⁰ In this study we have found that the distribution of leg intermovement intervals during wakefulness is very similar, if not identical, to that of the first peak at about 2–4 s in the same type of analysis performed during sleep, when also the true periodic peak appears, starting at approximately 10 s and reaching its maximum at approximately 20 s.³ The striking similarity between these two peaks prompted us to hypothesize that, when occurring during sleep, such a peak might be the expression of LM activity, spaced by short intervals, occurring during arousals. In children,¹¹ and in narcoleptic children in particular,⁶ only this peak can be found during sleep which might be correlated with the amount of arousal activity, which was also found to be increased in narcoleptic children.⁶

Thus, in our view, the main result reported by Jambhekar and colleagues,¹ i.e., a higher number of arousals in children with “PLMS,” might be considered the cause of the occurrence of LM activity rather than the effect.

We believe that the conclusions of this type of methodologically limited studies should be considered with great caution as they can only introduce doubtful and not sound data to the current literature on PLMS. Their recent possible re-evaluation as a pos-

sible risk factor for cardiovascular consequences¹²⁻¹⁴ is plagued by the presence in the literature of noncontrolled studies that have included in their “PLMS” analysis a wide variety of different LM activities, ranging from the true periodic LM to isolated leg jerks or arousal-related irregular activity, because several of these movements meet the criteria for PLMS, as coded by the AASM² or WASM/IRLSSG¹⁵ rules. It should be noted that the classical PLMS index can be considered as a reliable indicator only when LM activity is really periodic; however, finding a high PLMS index by no way can represent a proof that the LM activity is actually periodic.⁴ This can be done only by applying more detailed and accurate methods of analysis, including the “periodicity index.”^{3,5-7,11}

CITATION

Ferri R; Bruni O; Zucconi M; Plazzi G. The importance to assess the true “periodicity” of leg movements during sleep in narcolepsy. *J Clin Sleep Med* 2012;8(2):231-232.

REFERENCES

1. Jambhekar SK, Com G, Jones E, et al. Periodic limb movements during sleep in children with narcolepsy. *J Clin Sleep Med* 2011;7:597-601.
2. Iber C, Ancoli-Israel S, Chesson AL, Quan SF, eds. *The AASM manual for the scoring of sleep and associated events: rules, terminology, and technical specifications*. 1st ed. Westchester, IL: American Academy of Sleep Medicine, 2007.
3. Ferri R, Zucconi M, Manconi M, Plazzi G, Bruni O, Ferini-Strambi L. New approaches to the study of periodic leg movements during sleep in restless legs syndrome. *Sleep* 2006;29:759-69.
4. Ferri R. The time structure of leg movement activity during sleep: the theory behind the practice. *Sleep Med* 2012 <http://dx.doi.org/10.1016/j.sleep.2011.10.027>.
5. Ferri R, Zucconi M, Manconi M, et al. Different periodicity and time structure of leg movements during sleep in narcolepsy/cataplexy and restless legs syndrome. *Sleep* 2006;29:1587-94.
6. Ferri R, Franceschini C, Zucconi M, et al. Sleep polygraphic study of children and adolescents with narcolepsy/cataplexy. *Dev Neuropsychol* 2009;34:523-38.
7. Plazzi G, Ferri R, Franceschini C, et al. Periodic leg movements during sleep in narcoleptic patients with or without restless legs syndrome. *J Sleep Res* 2011;20:2869.

8. Plazzi G, Ferri R, Antelmi E, et al. Restless legs syndrome is frequent in narcolepsy with cataplexy patients. *Sleep* 2010;33:689-94.
9. Pennestri M-H, Whittom S, Benoit A, Petit D, Carrier J, Montplaisir J. PLMS and PLMW in healthy subjects as a function of age: Prevalence and interval distribution. *Sleep* 2006;29:1183-7.
10. Ferri R, Manconi M, Plazzi G, et al. Leg movements during wakefulness in Restless Legs Syndrome: Time structure and relationships with periodic leg movements during sleep. *Sleep Med* 2012;13:433-41.
11. Ferri R, Manconi M, Lanuzza B, et al. Age-related changes in periodic leg movements during sleep in patients with restless legs syndrome. *Sleep Med* 2008;9:790-8.
12. Walters AS, Rye DB. Review of the relationship of restless legs syndrome and periodic limb movements in sleep to hypertension, heart disease, and stroke. *Sleep* 2009;32:589-97.
13. Walters AS, Rye DB. Evidence continues to mount on the relationship of restless legs syndrome/ periodic limb movements in sleep to hypertension, cardiovascular disease, and stroke. *Sleep* 2010;33:287.
14. Winkelman JW, Redline S, Baldwin CM, Resnick HE, Newman AB, Gottlieb DJ. Polysomnographic and health-related quality of life correlates of restless legs syndrome in the Sleep Heart Health Study. *Sleep* 2009;32:772-8.
15. Zucconi M, Ferri R, Allen R, et al. The official World Association of Sleep Medicine (WASM) standards for recording and scoring periodic leg movements in sleep (PLMS) and wakefulness (PLMW) developed in collaboration with a task force from the International Restless Legs Syndrome Study Group (IRLSSG). *Sleep Med* 2006;7:175-83.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication December, 2011

Accepted for publication January, 2012

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DISCLOSURE STATEMENT

Dr. Ferri has consulted for Merck and Sapio-Life. Prof. Bruni has consulted for Sapio-Life. Prof. Plazzi and Dr. Zucconi have indicated no financial conflicts of interest.