Periodic leg movements of sleep in narcoleptic patients with or without restless legs syndrome

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Background

Compared to age-matched normal controls, periodic and non periodic limb movements of sleep (PLMS and LM respectively), are higher in both REM and nonREM sleep in narcolepsy with cataplexy (NC), and these motor activities are particularly intense in REM sleep. Also, restless legs syndrome (RLS) is significantly more frequent in individuals with NC (approximately 15%) than in control subjects. To our knowledge, the amount and characteristics of PLMS in NC, associated or not with the presence of RLS, remains unknown. In this new study, we analyzed PLMS features in NC patients with or without RLS in comparison to matched idiopathic RLS and control subjects, with the aim to assess if the presence of RLS influences the polysomnographic and daytime sleepiness phenotypes of NC.

Methods

For this study, 100 consecutive NC patients (67 males and 33 females, mean age 40.6 years, 17.07 S.D., range 12-80.6) were recruited. All patients underwent a face-to-face interview covering different aspects including a detailed description of RLS symptoms when present. After this process, RLS was diagnosed in 17 NC patients (NC/RLS+).

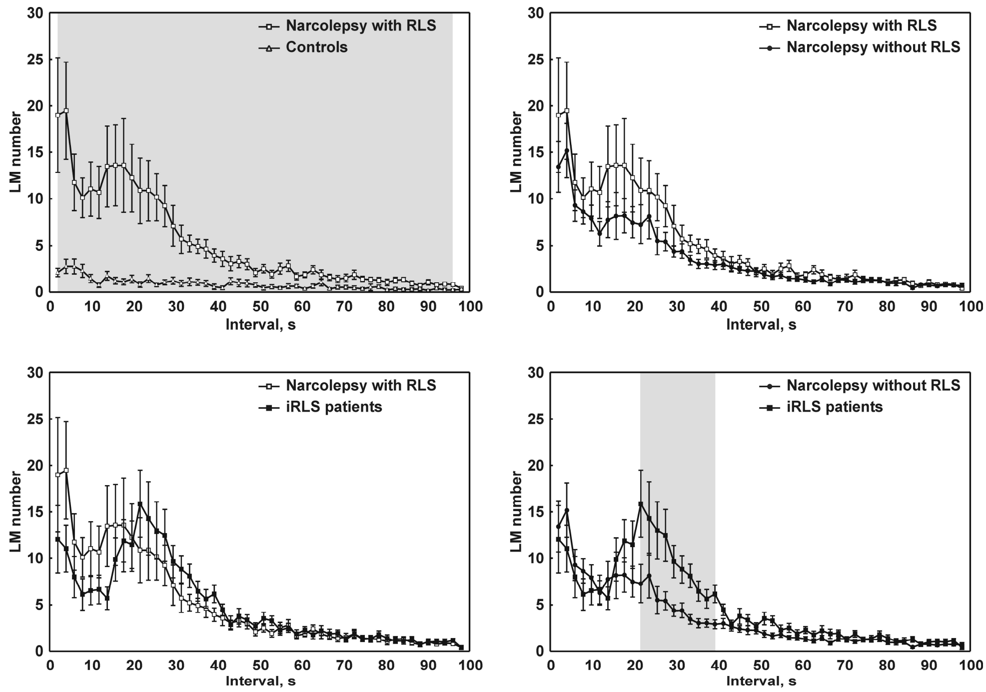
Given the well-known age and gender influences on sleep and especially PLMS, we compared the 17 NC/RLS+ subjects to gender- and age- matched patients with NC without RLS (NC/RLS-). We selected within the initial group of 100 consecutive NC patients, 2 NC/RLS- patients matched for age and gender per each NC/RLS+ subject. We also selected from the available polysomnographic recording database, 17 normal controls and 17 patients affected by idiopathic RLS (iRLS) matched for age and gender.

All subjects (NC/RLS+, NC/RLS-, iRLS and normal controls) underwent a nocturnal polysomnography in a sleep lab. A multiple sleep latency test (MSLT) was performed for all NC in the sleep laboratory the following day. Sleep stages and PLMS were rescored following standard criteria.

Results

Overall, all LM indexes (total, PLMS and isolated LMs) were highest in iRLS patients and lowest in controls, with those of NC/RLS+ very close to iRLS, but slightly higher than those of NC/RLS–. Differently, when NREM and REM sleep are considered separately, LM indexes predominated in NREM sleep for iRLS and in REM sleep for NC/RLS+, respectively. Also the periodicity indexes calculated in this study show the same decreasing trend along the groups, with the highest value found in iRLS, followed by NC/RLS+. Figure 1 depicts the comparison of the distribution histogram of inter-LM intervals during sleep in patients with NC/RLS+ and normal controls (top left panel), patients with NC/RLS– (top right panel), and patients with iRLS (bottom left panel). Also the comparison between NC/RLS– and iRLS patients is shown in the bottom right panel.

Fig. 1. Distribution histograms of inter-LM intervals during sleep of all subject groups included in this study.



Discussion: The main scope of this study was to understand to what extent the presence of RLS in NC increased the amount of PLMS and related findings. The results indicate that RLS in NC is characterized by PLMS with a time structure similar, but not identical, to that of PLMS in iRLS. These findings confirm the specificity of these features of PLMS for RLS and NC, with patients with both conditions showing an intermediate PLMS pattern. Our periodicity index analysis was reliable and sensitive.

In addition to LM analysis, our study also compares for the first time sleep structure in NC and iRLS: NC patients seem to have a worse sleep architecture when compared to both controls and iRLS, presenting a higher number of awakenings and of sleep stage shifts, a reduction in sleep stage two and an increase in sleep stage one. Moreover, RLS also seems to influence sleep onset in NC, with NC/RLS+ patients having an increased sleep onset latency when compared to NC/RLS– cases, but shorter than iRLS. Our data also confirm that NC patients, as a whole, display increased motor activity during sleep. In particular, while iRLS present the highest LM number in NREM sleep, NC/RLS+ patients show the highest LM indexes in REM sleep and the overall indexes in total sleep are very close in iRLS and NC/RLS+, with a remarkable gap from NC/RLS- values.

RLS also seems to determine an increase of LM periodicity in NC/RLS+ compared to NC/RLS–. Moreover, the overnight distribution of PLMS displays an interesting finding, different in NC from iRLS cases. In fact, while iRLS patients show the typical "homeostatic shape" of the PLMS time course, NC subjects present a stable overnight representation of PLMS. This intriguing difference probably indicates a different motor dyscontrol modulation in these two different conditions, possibly related to the hypocretin deficit. We can speculate that the lack of such a circadian distribution of PLMS in patients affected by both NC and RLS might be due to the interference exerted by the deficiency of hypocretin on iron and or DA activities.

In terms of daytime sleepiness, the lack of differences in the MSLT results between these two groups indicates that narcoleptic syndrome is the most important clinical aspect of these patients, EDS and cataplexy being the most frequent and disabling complaints. In contrast, RLS symptoms are usually detected only after a careful and targeted interview of the patients. Excessive daytime sleepiness and cataplexy are the main concerns of these patients. On this basis, it is not easy to suggest to treat RLS in these patients; however, it is not sufficiently known if this might be an issue after a successful treatment of narcolepsy.