LETTER TO THE EDITOR

# Periodic Limb Movements During Sleep and White Matter MRI Hyperintensity in Minor Stroke or TIA

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The study by Boulos et al. reports, in a relatively small group of patients with first-ever minor ischemic stroke or transient ischemic attack (TIA), that the amount of periodic leg movements during sleep (PLMS) is positively associated with the volume of white matter hyperintensity (WMH) at MRI.[1] This finding is in line with the increasing amount of data indicating a possible role for PLMS in the risk for cardio- and cerebrovascular diseases.[2]

This interesting paper stimulated us in replicating this analysis in a larger series of patients recruited in the context of a multicenter, international prospective polysomnographic (PSG) study in patients with ischemic stroke and TIA (SAS-CARE).[3]

We selected, from the whole group of 255 patients enrolled (the relative complete set of data will be published independently), those with clinical features comparable to those of the patients reported by Boulos et al.[1]; in this way, we were able to collect data from a total of 68 patients (56 males and 13 female, mean age 59.8 years, range 29.8–78.6 years). The inclusion criteria were: no previous clinical acute cerebrovascular event, unilateral symptoms, diagnosis of TIA or ischemic stroke, NIH Stroke Scale (NIHSS) ranging between 0 and 3 at discharge from hospital. All subjects underwent a full-night PSG recording and a brain MRI within 1 week from the event, followed by the quantification of the volume of the stroke and of WMH over the nonaffected hemisphere. An additional PSG recording was available for 67 out of these 68 patients, obtained approximately 3 months after the acute event.

We then subdivided the patients into two subgroups, based on the amount of PLMS found in their first PSG, with the same cutoff used by Boulos et al.,[1] that is, patients with PLMS index <5/h ($n$ = 35) and patients with PLMS index ≥5/h ($n$ = 33). Subsequently, a comparison was carried out between age, body mass index, WMH and stroke volume, and several PSG parameters found in these two groups. Age, in particular, was not different (59.3 years with interquartile range 51.2–66.3 in patients with PLMS index <5/h vs. 59.7 years with interquartile range 56.2–66.2 in patients with PLMS index ≥5/h, respectively), as well as WMH (1.3 $cm^3$ with interquartile range 0.4–3.6 vs. 1.8 $cm^3$ with interquartile range 0.7–5.2, respectively) and stroke volumes (1.8 $cm^3$ with interquartile range 0.3–8.0 vs. 0.9 $cm^3$ with interquartile range 0.4–10.8, respectively) which were very similar. Only apnea/hypopnea index and arousal index were significantly higher in the patients with more PLMS. We repeated the same comparison by considering a PLMS index cutoff value of ≥15/h instead of ≥5/h and obtained some additional differences between the two subgroups ($n$ = 53 vs. $n$ = 15, respectively) indicating, besides higher apnea/hypopnea index and arousal index, also higher body mass index, increased sleep stages 1 and 2 and decreased sleep stage 3 in patients with more PLMS but, again age and WMH or stroke volumes were not significantly different (see Supplementary Tables).

Three months after stroke/TIA, based on the PLMSI ≥5/h cutoff, only 44 patients could be classified in the same group of the first recording (21 positive and 23 negative), while 13 who were negative at the first recording (PLMSI < 5) became positive (PLMSI ≥ 5) at the second one, and 10 who were positive in the acute phase became negative after 3 months. Moreover, considering the PLMSI ≥15/h cutoff, 58 patients continued to present the same level of PLMS (10 continued to reach it and 48 continued to have less) while only 6 that had not reached the cutoff at the first recording reached it after 3 months and only 3 that had PLMSI ≥15/h in the acute phase did not have it anymore after 3 months.

We then repeated the same analysis described above with the data obtained at 3 months and were, again, unable to find differences in WMH or stroke volumes (measured in the acute phase). Furthermore, differences in the other parameters appeared to be less than in the acute phase, with none of them being significantly different with the PLMSI ≥5/h cutoff; only sleep duration was shorter and BMI higher in the subgroup of patients with PLMSI ≥15/h than in those without (see Supplementary Tables).

Based on these results, and applying an almost identical analysis, we were unable to replicate the findings by Boulos et al.[1] in a larger series of comparable patients. Indeed, it is difficult to interpret the different results because of methodological reasons. Cause/effect relationships remain speculative when obtained from cross-sectional studies on an overall limited number of patients and in the absence of knowledge about the situation preceding the cerebrovascular event, especially regarding the duration of the presence of PLMS. As shown also in our analysis, the night-to-night variability of PLMS[4] is an additional factor that increases the complexity of the problem. Thus, the duration of the presence of PLMS is an elusive but probably important factor to take into consideration when assessing long-term consequences of their associated heart rate[5] and blood pressure rises,[6–8] as suggested by studies in restless legs syndrome.[9,10] Finally, as shown by our analysis, the choice of a cutoff of PLMSI ≥15/h, lead to more stable results in repeated measurements.

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## SUPPLEMENTARY MATERIAL

Supplementary data are available at *SLEEP* online.

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## SUBMISSION & CORRESPONDENCE INFORMATION

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## DISCLOSURE STATEMENT

None declared.