Εργαστήριο Μελέτης Ύπνου

Πανεπιστημιακό Γενικό Νοσοκομείο ΑΤΤΙΚΟΝ

Βλάμη Αικατερίνη

Πνευμονολόγος
Somnologist Expert in Sleep Medicine
(ESRS board 2014)

ΑΙΘΟΥΣΑ ΣΑΝΤΟΡΙΝΗ

16:00-17:30 **Στρογγύλη Τράπεζα**

Αποφρακτική άπνοια στον ύπνο και άλλες διαταραχές του ύπνου: τι πρέπει να γνωρίζουμε

Προεδρείο: *Π. Στειρόπουλος - Σ. Σχίζα*

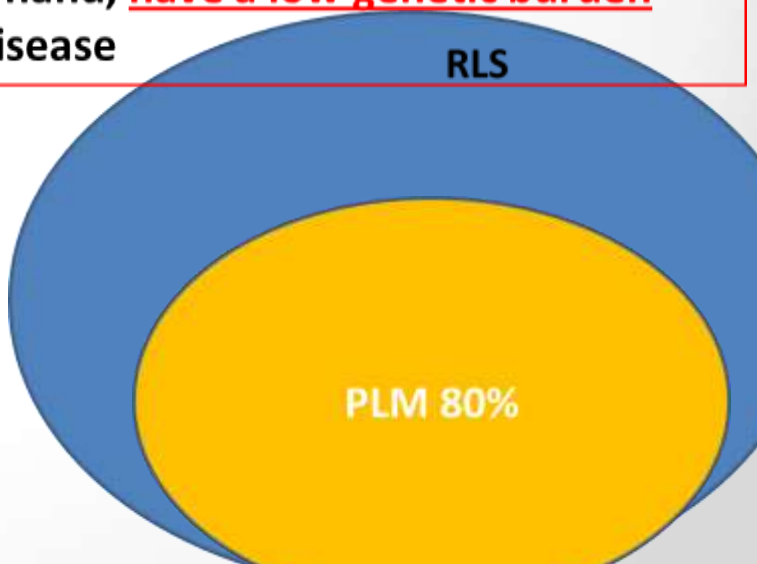
- ΣΑΥ και αϋπνία
  Γ. Τρακαδά
- ΣΑΥ και PLMs
  Κ. Βλάμη
- ΣΑΥ Κλινική διαγνωστική προσέγγιση
  Α. Πατάκα
- Ετήσια κλινική ανασκόπηση
  Χ. Μερμίγκης

- ΣΑΥ και PLMs
  Κ. Βλάμη

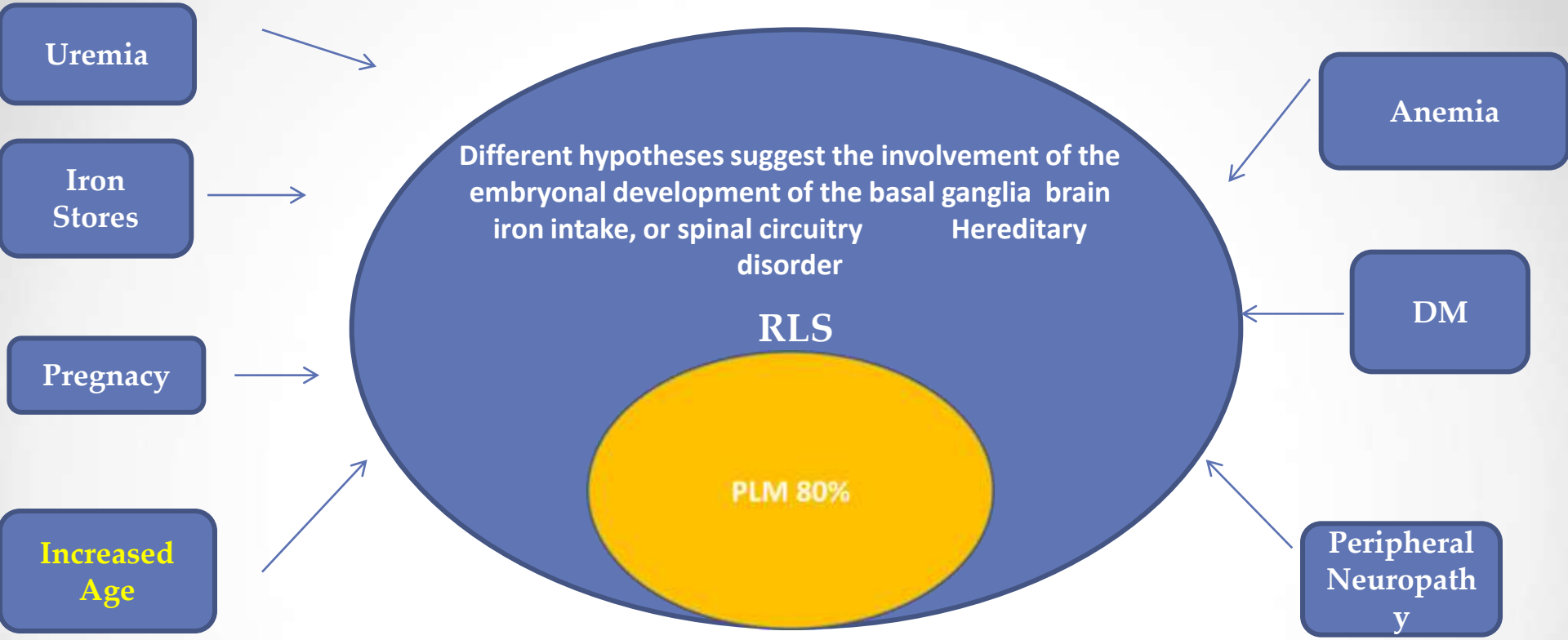
Experts and patients alike describe Restless Leg Syndrome(RLS) both as a miserably impairing disorder and as "the most common disorder you have never heard of." Critics do not regard RLS as a disorder at all but, rather, as the fabrication of an omnivorous pharmaceutical industry

RLS is a waking sensorimotor disturbance.Those afflicted describe an intensely uncomfortable, overwhelming urge to move the legs (often accompanied by dysesthesias), predominantly in the evening or at night, that is present at rest and relieved only temporarily by movement.

The susceptibility of an individual to RLS is dependent on both environmental and genetic influences, in a way where early onset familial cases have a high genetic burden but lower environmental burden.
RLS in patients with multiple comorbidities, on the other hand, have a low genetic burden but require higher environmental burden to trigger the disease



Periodic Limb Movements (PLM) in sleep, which was originally called "nocturnal myoclonus" consist of recurrent involuntary dorsiflexion of the foot and lower



Effect of a probable impaired supraspinal dopaminergic control of gait

There is striking ethnic disparity in reported prevalence of RLS 5 to 15% in Western Europe (Clinically significant RLS, requiring daily treatment, has a prevalence of 2.7% in European and North American populations) 0.1% in Singapore,2% in native Ecuador, 3.2% in Turkey, 4.6% in elderly Japanese, unknown prevalence in Africa

Forty-seven years ago, Ekbom reported that 25% of people with RLS have low serum iron levels and that 24% of those with iron deficiency anemia have RLS

Table 12 Diagnostic criteria for restless legs syndrome (RLS; adapted from ICSD-3)

Criteria A–C must be met

A. An urge to move the legs, usually accompanied by or thought to be caused by uncomfortable and unpleasant sensations in the legs. These symptoms must:

1. Begin or worsen during periods of rest or inactivity such as lying down or sitting;
2. Be partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues; and
3. Occur exclusively or predominantly in the evening or night rather than during the day

B. The above features are not solely accounted for as symptoms of another medical or a behavioural condition (e.g. leg cramps, positional discomfort, myalgia, venous stasis, leg oedema, arthritis, habitual foot-tapping)

C. The symptoms of RLS cause concern, distress, sleep disturbance or impairment in mental, physical, social, occupational, educational behavioural or other important areas of functioning

Table 1. Summary of the pharmaceutical therapeutical options for RLS

Substance	Effective dose	Application	Approv RLS	Notes
Levodopa/benserazide	100/25–200/50 mg/day	Oral	Parts of (100– mg/d	Only recommended for intermittent RLS
Pramipexole	0.25–0.75 mg/day	Oral	EU, USA (0.25- mg/d	Requires monitoring for augmentation
Ropinirole	0.5–4.0 mg/day	Oral	EU, USA (0.5–4 mg/d	Requires monitoring for augmentation
Rotigotine	1.0–3.0 mg/day	Transdermal	EU, USA (1.0–3 mg/d	Requires monitoring for augmentation
Pregabalin	150–300 mg/day	Oral	Off-labe	
Gabapentin enacarbil	600–1200 mg/day	Oral	USA, Jap (600 r	
Oxycodone-naloxone	2 × 5–2 × 20 mg/day	Oral	EU (2 × 5 mg/d	
Ferric carboxymaltose	1000 mg	IV	Off-label	Effective in iron-insufficient RLS patients

Periodic Leg Movement Disorder (PLMD) is a PSG

Disorder

- PLMS are present in up to 6% of the general population *(Res Commun*
- *Chem Pathol Parmacol 1982)*
- PLMS are present in 45% of adults aged 65 years or older *(Sleep 1991)*
- PLMS can be detected in asymptomatic individuals

PLMs cutoff values as high as >15/h

Table 13 Diagnostic criteria for periodic limb movement disorder (PLMS; adapted from ICSD-3)

Criteria A–D must be met

A. Polysomnography demonstrates PLMS, as defined in the latest version of the American Academy of Sleep Medicine (AASM) Manua for the Scoring of Sleep and Associated Events

B. The frequency is >5 h^{-1} in children or >15 h^{-1} in adults

C. The PLMS cause clinically significant sleep disturbance or impairment in mental, physical, social, occupational, educational, behavioural or other important areas of functioning

D. The PLMS and the symptoms are not explained more clearly by another current sleep disorder, medical or neurological disorder or mental disorder (e.g. PLMS occurring with apnoeas or hypopnoeas should not be scored)

Data suggest a partial overlap of PLMS Index values between symptomatic and asymptomatic individuals, emphasizing the importance of clinical context over an absolute cutoff value.

PLMS

Table 1
Examples of conditions in which an increased PLMS index has been reported.

		PLMS index (PLMSI = number/hour of sleep)
(a)	Normal subjects >40 years	>10/h [35]
(b)	RLS	>5/h in 80.2% of patients [85]; 30.4/h, 36.7/h [39]
(c)	Narcolepsy	>5/h in 25–70% of patients [86]; 17.3/h [45]
(d)	OSAS	>5/h in 27.3–61.5% of patients (average 16.9/h) [87,88]
(e)	RBD	>10/h in 70% of patients [89]; >15/h in 85% [46]
(f)	Parkinson disease	68.3/h [90,91]
(g)	L-dopa-responsive hereditary dystonia	50% of subjects with PLMS [92]
(h)	Multiple system atrophy	33.7/h [91]
(i)	Corticobasal degeneration	Single case reports [93–95]
(j)	Spinal cord lesions and anesthesia	17–114/h (unclear results) [96,97]
(k)	Attention deficit-hyperactivity disorder	>5/h in 64–66.7% of patients recorded [65,98]
(l)	Radiculopathies	Single case report [99]
(m)	Motor neuron diseases (syringomyelia and syringobulbia)	PLMSI 3.1–61.0/h (17.9 ± 24.4 S.D.): >5/h in 61.5% of patients [100]
(n)	Stiff man syndrome	Single case report [101]
(o)	Uremia	>5/h in 85.4% of patients [102]
(p)	Pregnancy	PLMSI 3.7–49.7/h [103]
(q)	Insomnia	PLMSI 17.9 ± 24.62 S.D. [47]
(r)	Nightmares	PLMSI 8.8 ± 8.9 S.D. [104]
(s)	Post-traumatic stress-disorder	PLMSI 11.2 ± 10.6 S.D. [105]
(t)	Beta-thalassemia and congenital dyserythropoietic anemia	PLMSI 13.9 ± 12.1 S.D. and 7.3 ± 11.1 S.D., respectively [106]
(u)	Fibromyalgia	>5/h in 38% of patients [107]

Pathophysiology of PLMs

- The pathogenesis of PLMs is not clear
- There is **neuronal hyperexcitability** with involvement of brain stem and spinal cord structures, in particular the central pattern generator for gait and **decreased dopaminergic transmission**

- **It is supported that PLMS are generated in the spinal cord. In particular, de Mello et al. observed PLMS in patients with complete spinal cord lesions; thus, the spinal cord seems to be sufficient to produce periodic activity of the legs**

- Dopaminergic agonists regarded as first line treatment

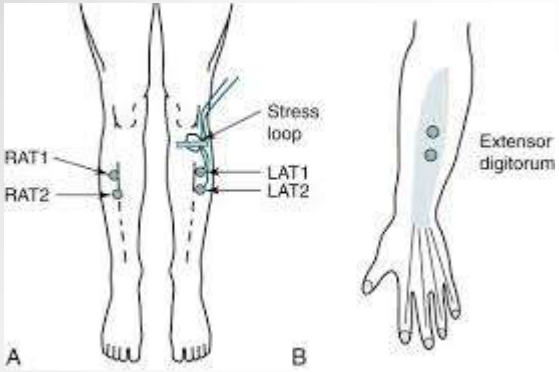
PSG gold standard test for PLMs

PLMS

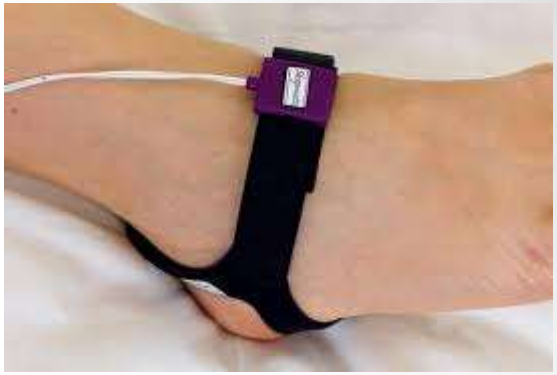
Typically **recorded from the tibialis anterior (TA) muscle**, which extends, proximally, from the lateral condyle and superior two thirds of the anterolateral surface of the tibia (interosseous margin) to, distally, the medial and plantar surfaces of the medial cuneiform and the base of the 1st metatarsal. **Its main function is to dorsiflect the foot and ankle**. It receives direct innervation from the L4, L5, and S1 spinal segments through the deep peroneal nerve

Variability of PLMs through nights

World Association of Sleep Medicine/ IRLSSG/AASM



Leg Movements-PSG



- Surface electrodes must be placed at 2–3 cm apart or 1/3 of the length of the anterior tibialis
- Impedance should be ≤10 K for clinical studies but ≤5 K is recommended for research studies
- Bilateral recordings are required. Two channels, one for each leg are strongly recommended for all studies and required for research
- Recording LM activity from other muscles is recommended only for research purposes or for special clinical conditions (eg, arm restlessness, bruxism, RBD, painless legs moving toes syndrome)

World Association of Sleep Medicine (WASM) 2016 Standards for Recording and Scoring Leg Movements in Polysomnograms Developed by a Joint Task Force from the International and the European Restless Legs Syndrome Study Groups (IRLSSG and EURLSSG)

Sleep Medicine 2016

Leg Movements-PSG

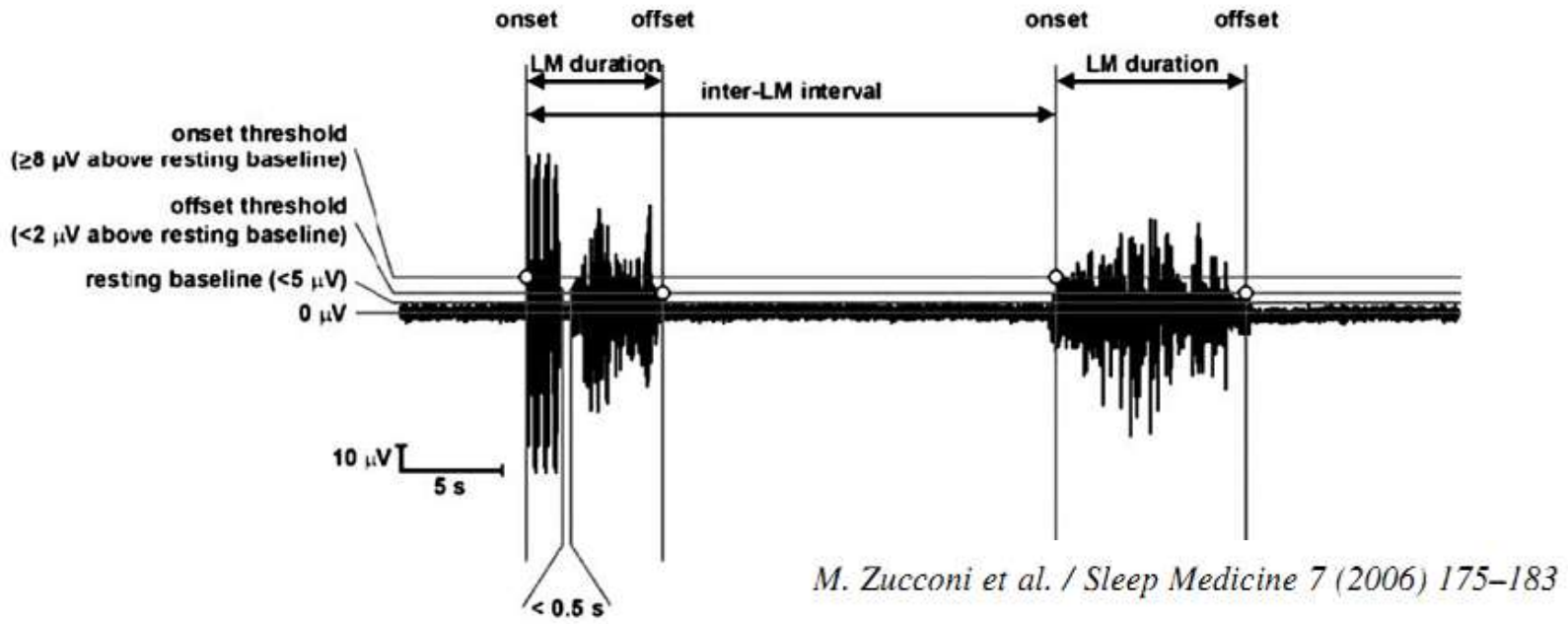


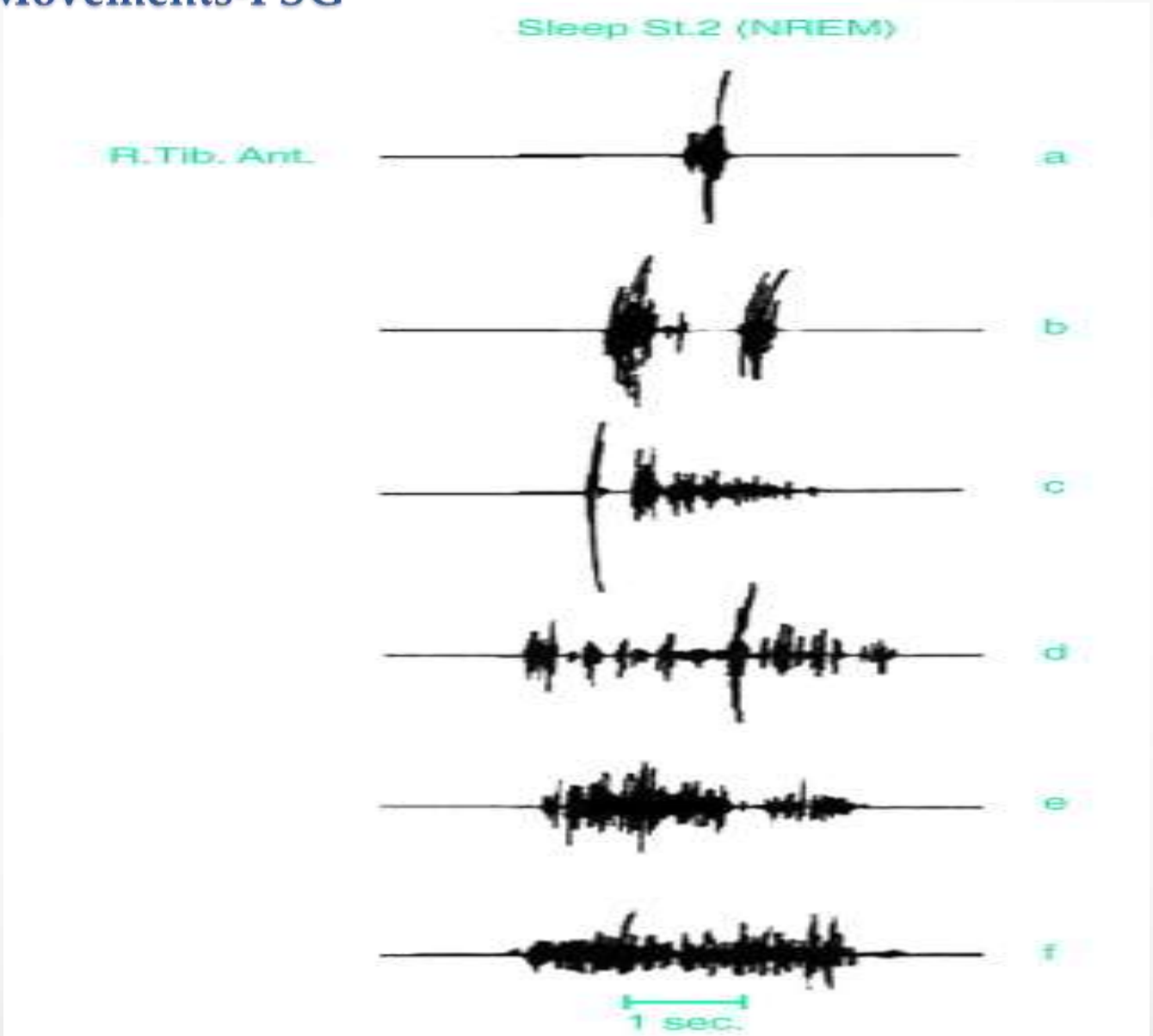
Fig. 4. Overview of the detection parameters for candidate PLM.

PLMs cutoff values as high as >15/h

- Onset of a leg movement event is defined as the point at which there is an 8μV increase in EMG voltage above resting EMG;
- Ending of a leg movement event is defined as the start of a period lasting at least 0.5 during which the EMG does not exceed 2μV above resting EMG
- **Leg movements occurring during a period from 0.5 s preceding a respiratory event to 0.5 s following are not scored according to AASM criteria**
- Periodic limb movements (PLM) are defined as repetitive leg movements lasting from 0.5 to 10 s, separated by an intermovement interval (defined as the time between onsets of consecutive leg movements) ranging from 5 to 90 s, organized in series of at least 4 leg movements

American Academy of Sleep Medicine; 2012.

Leg Movements-PSG



PLMs / OSA

- PLMs are found in 24-48% of patients with OSA
- The current criteria for the scoring of a leg movement as a PLMS excludes those associated with respiratory events (Respiratory Related Leg Movement-RRLM)
- RRLM are provoked by respiratory-related arousals
- **"Genuine" PLMS can occur in OSA as part of the phenotypic spectrum of RLS**

The occurrence of RRLM might be influenced by at least three main factors

- **Presence of PLMS not related to respiratory events**
- **Presence of RLS**
- **Severity of the respiratory disturbance**

Table 13 Diagnostic criteria for periodic limb movement disorder (PLMS; adapted from ICSD-3)

Criteria A–D must be met

A. Polysomnography demonstrates PLMS, as defined in the latest version of the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events

B. The frequency is >5 h^{-1} in children or >15 h^{-1} in adults

C. The PLMS cause clinically significant sleep disturbance or impairment in mental, physical, social, occupational, educational, behavioural or other important areas of functioning

D. The PLMS and the symptoms are not explained more clearly by another current sleep disorder, medical or neurological disorder or mental disorder (e.g. PLMS occurring with apnoeas or hypopnoeas should not be scored)

Data suggest a partial overlap of PLMS Index values between symptomatic and asymptomatic individuals, emphasizing the importance of clinical context over an absolute cutoff value.

OSA-PLMs

OSA	PLM
• Respiratory events	• **Leg movements**
• Periodicity of the events	• Periodicity of the events
• Respiratory arousals	• Arousals
• Autonomic arousals	• Autonomic arousals
• **Respiratory related leg movements**	• Fragmented sleep/Autonomic activation
• Fragmented sleep/Autonomic activation	• Daytime sleepiness/fatigue
• Daytime sleepiness/fatigue	• Cardiovascular morbidity
• Cardiovascular morbidity	

Physiopathology of

RLS/PLMS in sleep-disordered breathing

- **Intermittent hypoxia** associated with apnoeic events has also been linked with **dysfunction of the dopaminergic pathway** suggestive of a possible relationship between OSA and RLS (*Sleep. 2005*)
- **Dysfunctional dopaminergic pathway** is implicated in the genesis of **RLS**, which seems to be **affected in obese people** (lower dopamine D2 receptor availability in the striatum of obese people) *Neurolog y 2009*

Two different scoring criteria for Respiratory Related Leg Movement

are available

- **WASM/IRLSSG**: **RRLM** are consider leg movements as respiratory related when a **leg movement occurs at the end (± 0.5 s) of an apnea or hypopnea**
- **AASM**: **RRLM** any movement occurring **within 0.5 sec preceding the start of an apnea event, and during 0.5 sec following the end** of a breathing episode
- These criteria are based on consensus and empiric experience and have not been addressed with analytic approaches
- LM very rarely occur at the beginning or during the apnea, but many follow the end of the apnea, often exceeding the time window of 0.5 sec and are not picked up by either method

3.4.2 Respiratory events

Candidate leg movements that are associated with respiratory events are called respiratory event associated leg movements (CLMr). There is not a general consensus on the best rules defining CLMr. It is recommended that in a clinical context for patients with significant obstructive sleep-related breathing disorders extreme caution is exercised in interpreting the PLMS index with CLMr excluded. The rules used for defining CLMr should be explicitly stated.

CLMr are defined as CLM that:

A. have some part overlapping within an interval of 2.0 s before to 10.25 s after the end of a respiratory event (recommended for obstructive sleep apnea syndromes)
Level of evidence: B [19]

OR

B. have some part overlapping with an interval of 0.5 s before to 0.5 s after the end of a respiratory event (alternative) Level of evidence: C [1]

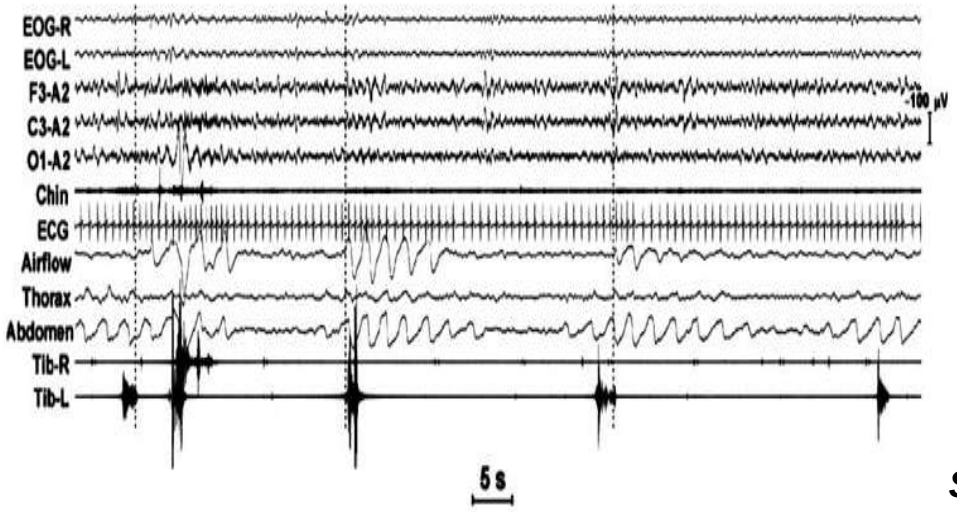


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Fig. 5. Sequence of leg movements overlapping with or occurring within ±0.5 s of breathing resumption of sleep apnea events (vertical dashed lines).

Respiratory Related Leg Movements/Arousals

3.4.1 Arousals

An arousal and a leg movement are associated with each other when they are overlapping or when there is less than 0.5 s between the end of one event and the onset of the other

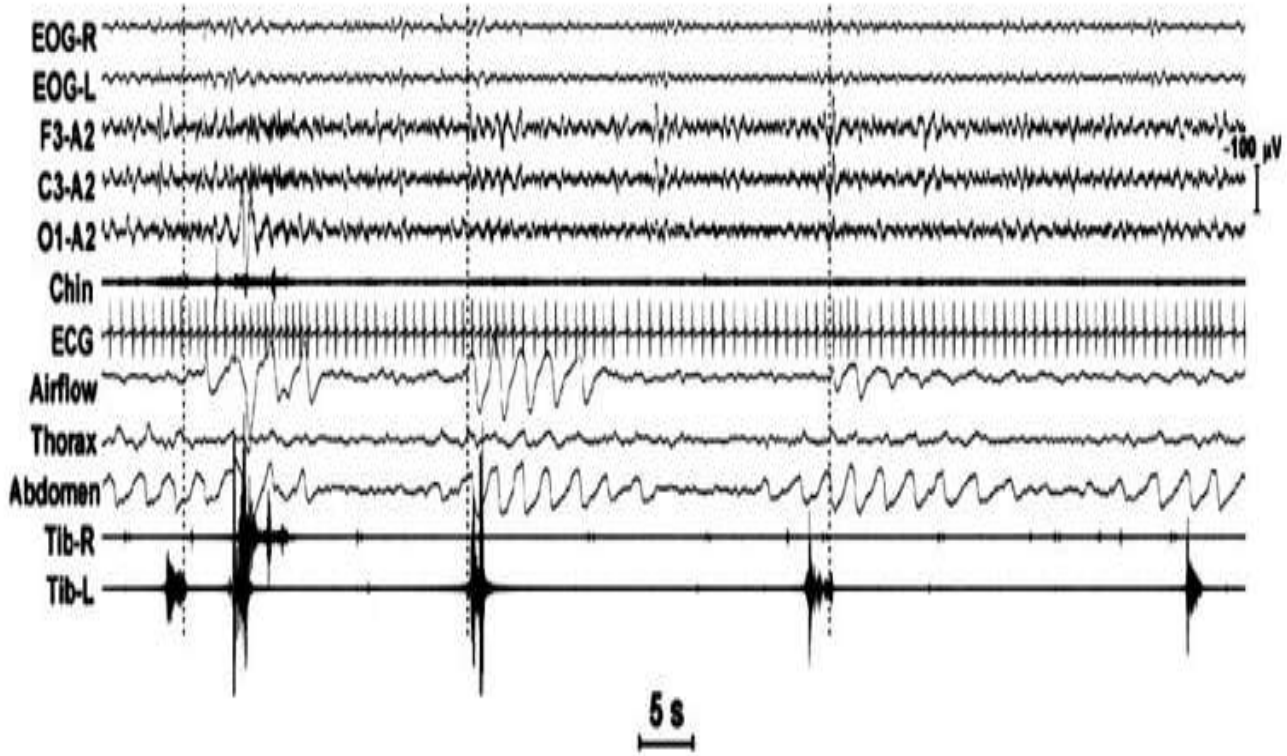

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Fig. 5. Sequence of leg movements overlapping with or occurring within ±0.5 s of breathing resumption of sleep apnea events (vertical dashed lines).

RESPIRATORY-RELATED LEG MOVEMENTS RELATIVE TO PLM DURING SLEEP

http://dx.doi.org/10.5665/sleep.3484

Respiratory-Related Leg Movements and Their Relationship with Periodic Leg Movements During Sleep

SLEEP 2014;

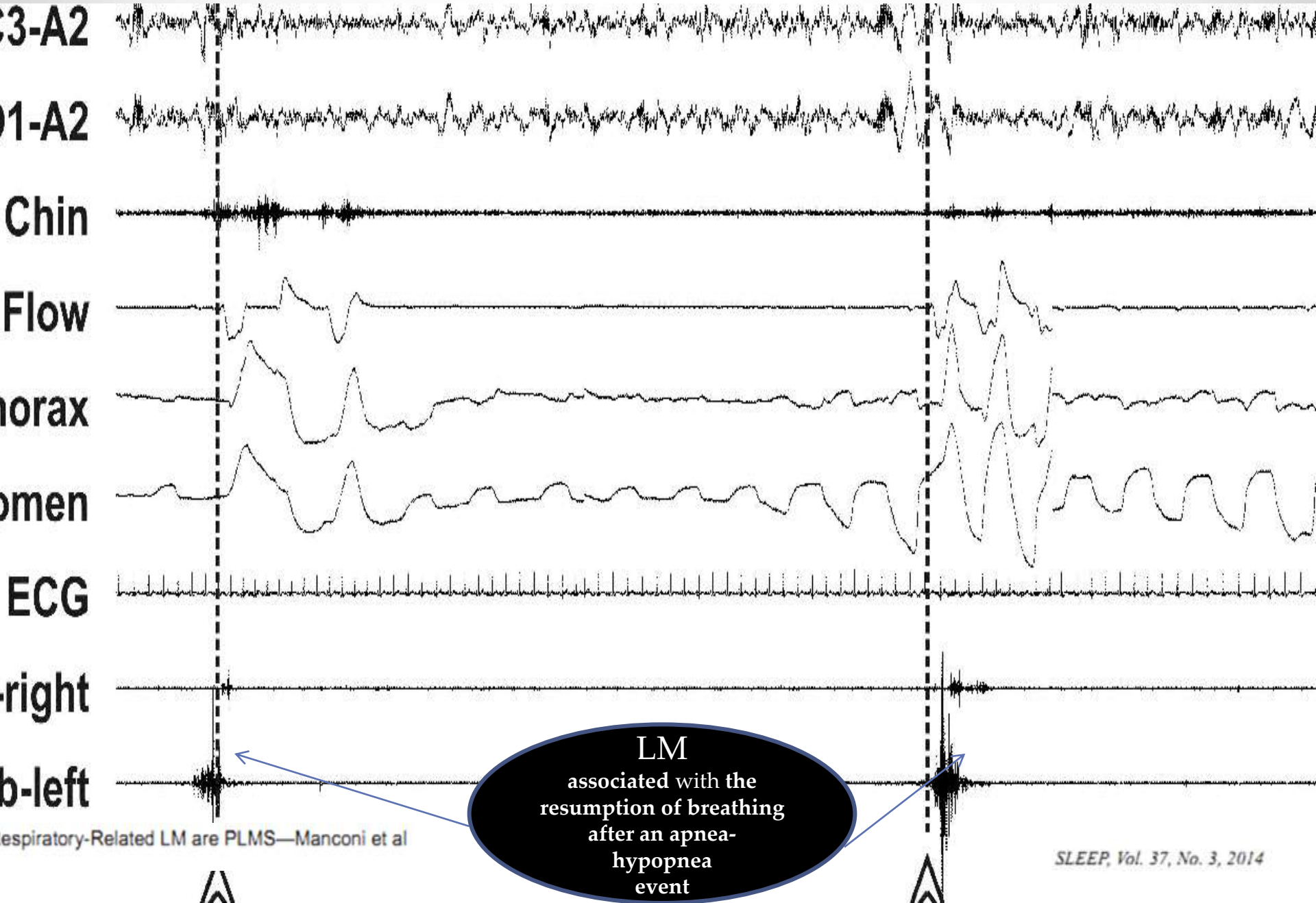
Mauro Manconi, MD, PhD[1]; Irina Zavalko, MD[1,2]; Claudio L. Bassetti, MD[3]; Elisabetta Colamartino, RPSGT[1]; Marco Pons, MD[4]; Raffaele Ferri, MD[5]

Retrospective chart review with OSA and RLS

This study shows that individuals with RRLM consistently have NRLM with features typical for "genuine" PLMS

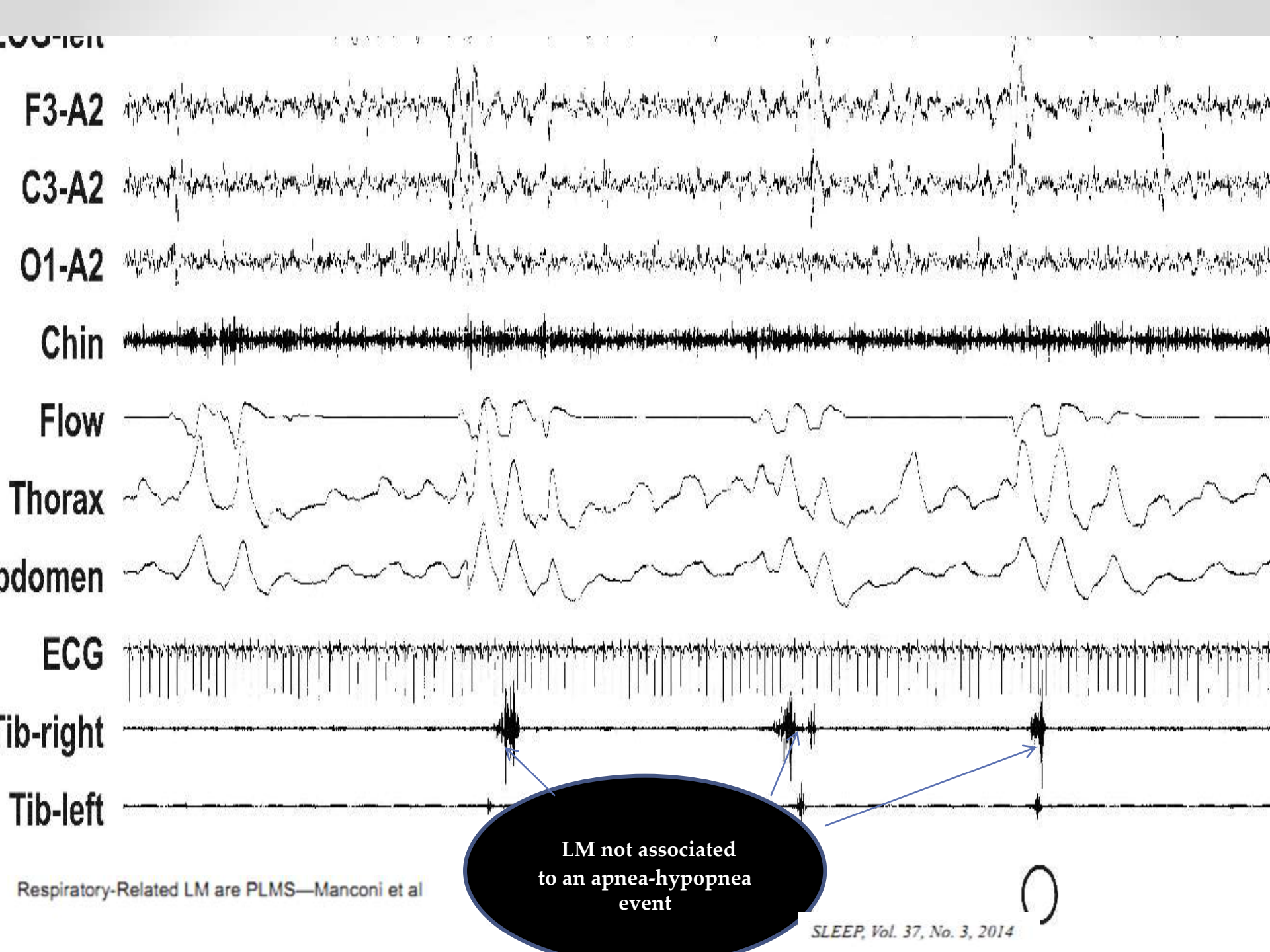
In the current study, patients with OSA in whom these "genuine" PLMS are not observed, RRLM also were not observed.

Subjective sleepiness was found to be similar in the two groups



espiratory-Related LM are PLMS—Manconi et al

SLEEP, Vol. 37, No. 3, 2014



Respiratory-Related LM are PLMS—Manconi et al

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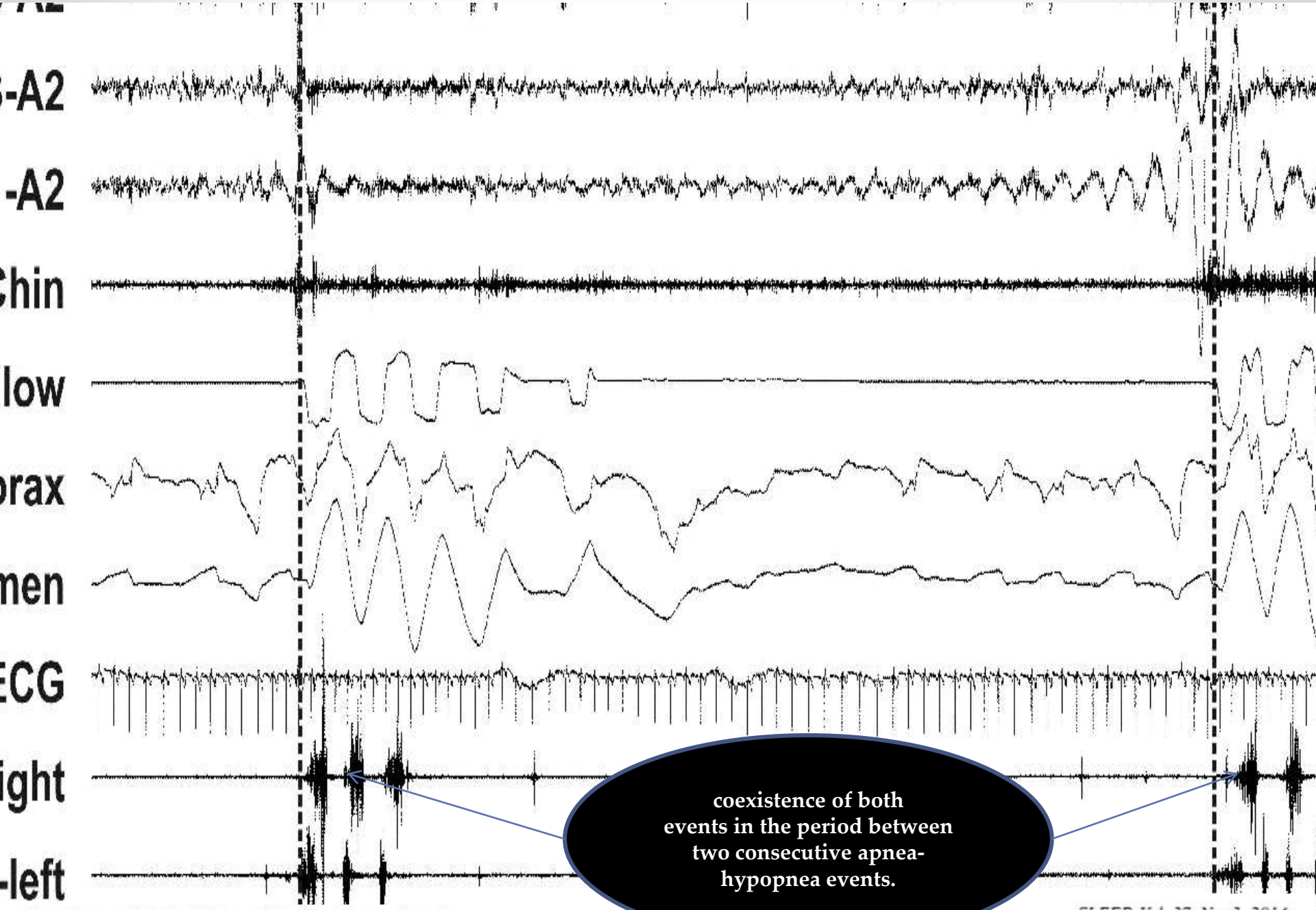


Respiratory-Related LM are PLMS—Manconi et al

SLEEP, Vol. 37, No. 3, 2014

Table 1—Comparison between clinical features, respiratory parameters, sleep architecture in patients with obstructive sleep apnea without (OSA LM-) leg movement > 15/h

	OSA LM+ (n = 64)		OSA LM- (n = 20)		Mann-Whitney
	Mean	SD	Mean	SD	P <
Age, y	55.8	11.28	53.1	7.11	NS
Body mass index	33.1	6.43	31.1	9.30	0.03[a]
Epworth Sleepiness Scale	9.7	4.73	11.2	4.89	NS
Apnea-hypopnea index	59.5	25.44	37.6	10.63	**0.0003**
Oxygen desaturation index	49.1	23.87	31.7	18.26	**0.0015**
Average oxygen saturation, %	91.4	3.29	92.0	4.67	0.035[a]
Lowest oxygen saturation, %	75.3	8.55	79.0	10.15	0.026[a]
Oxygen saturation < 90% time, %	22.4	26.21	14.4	27.80	**0.007**
Time in bed, min	457.8	43.62	465.1	34.27	NS
Sleep period time, min	435.5	54.73	441.5	45.84	NS
Total sleep time, min	370.8	58.89	369.8	68.20	NS
Sleep latency, min	16.0	14.49	14.5	13.14	NS
First REM period latency, min	130.3	64.29	140.1	69.14	NS
Stage shifts/h	17.4	7.13	14.7	3.86	NS
Awakenings/h	7.6	4.21	7.0	2.90	NS
Sleep efficiency, %	81.0	10.17	79.7	13.52	NS
Wakefulness after sleep onset, %	14.8	8.02	16.2	13.18	NS
Sleep stage N1, %	13.2	8.42	6.6	3.62	**0.002**
Sleep stage N2, %	44.3	12.78	46.2	12.27	NS
Sleep stage N3, %	15.4	9.51	17.5	6.89	NS
Sleep stage R, %	12.2	4.85	13.5	7.60	NS
Arousal Index	44.3	19.82	31.1	15.21	**0.006**

Table 2—Comparison between clinical features, respiratory parameters, sleep architecture and leg motor activity during sleep in patients with obstructive sleep apnea with or without respiratory-related leg movement

	RRLM+ (n = 39)		RRLM- (n = 25)		Mann-Whitney	Effect size
	Mean	SD	Mean	SD	P <	Cohen d
Sleep stage N1, %	14.1	8.52	11.9	8.26	NS	0.252
Sleep stage N2, %	42.7	13.13	46.9	12.02	NS	-0.338
Sleep stage N3, %	15.8	9.40	14.7	9.85	NS	0.116
Sleep stage R, %	12.2	4.85	12.3	4.94	NS	-0.011
Arousal Index	44.6	19.67	43.9	20.45	NS	0.032
Total sleep						
Total, index	59.7	34.87	33.8	19.53	**0.00006**	**0.915**
PLMS, index	49.4	37.31	22.0	19.33	**0.00009**	**0.920**
Isolated, index	10.3	3.48	11.8	3.33	NS	-0.429
NREM sleep						
Total, index	63.4	36.30	34.7	22.29	**0.00002**	**0.955**
PLMS, index	53.2	38.81	23.3	21.96	**0.00008**	**0.947**
Isolated, index	10.3	3.73	11.4	4.09	NS	-0.283
REM sleep						
Total, index	39.7	31.81	29.1	15.24	NS	0.423
PLMS, index	28.6	33.56	14.8	12.94	NS	0.545
Isolated, index	11.0	5.34	14.4	6.07	0.024[a]	-0.581
PLMS sequence number	20.4	8.73	13.3	6.54	**0.0006**	**0.921**
PLMS sequence duration, sec	107.5	94.23	66.6	84.98	0.035[a]	0.455
PLMS duration in REM, sec	2.3	0.89	2.6	1.10	NS	-0.306
PLMS duration in NREM, sec	2.4	0.53	2.3	0.47	NS	0.236
Isolated LM duration in REM, sec	2.3	1.15	1.9	0.69	NS	0.470
Isolated LM duration in NREM, sec	2.4	0.67	2.2	0.53	0.036[a]	0.493
Periodicity index	0.473	0.235	0.460	0.199	NS	0.060

Conclusions

- **RRLM might represent part of a phenotypic spectrum that also includes "genuine" PLMS** because they cluster clearly in the patients who also have typical PLMS not correlated with the respiratory events
- It is possible that the **same genetic background** might predispose the individuals to **present typical PLMS**, when no other strong synchronizing mechanisms are at work, **or RRLM**, when the more powerful respiratory rhythm takes the lead and forces LM to synchronize with it accordingly
- This might also suggest that in **discussion of future scoring criteria, RRLM should not be excluded from the analysis of PLMS**
- The definition of RRLM is based on WASM/IRLSSG3 similar to those indicated by the AASM, which are consensus based
- There is need to **explore in more detail the time structure of LM**, **apnea**, and **arousals** that might provide important hints for a better understanding of **how these phenomena interact with each other**

The NEW ENGLAND JOURNAL of MEDICINE

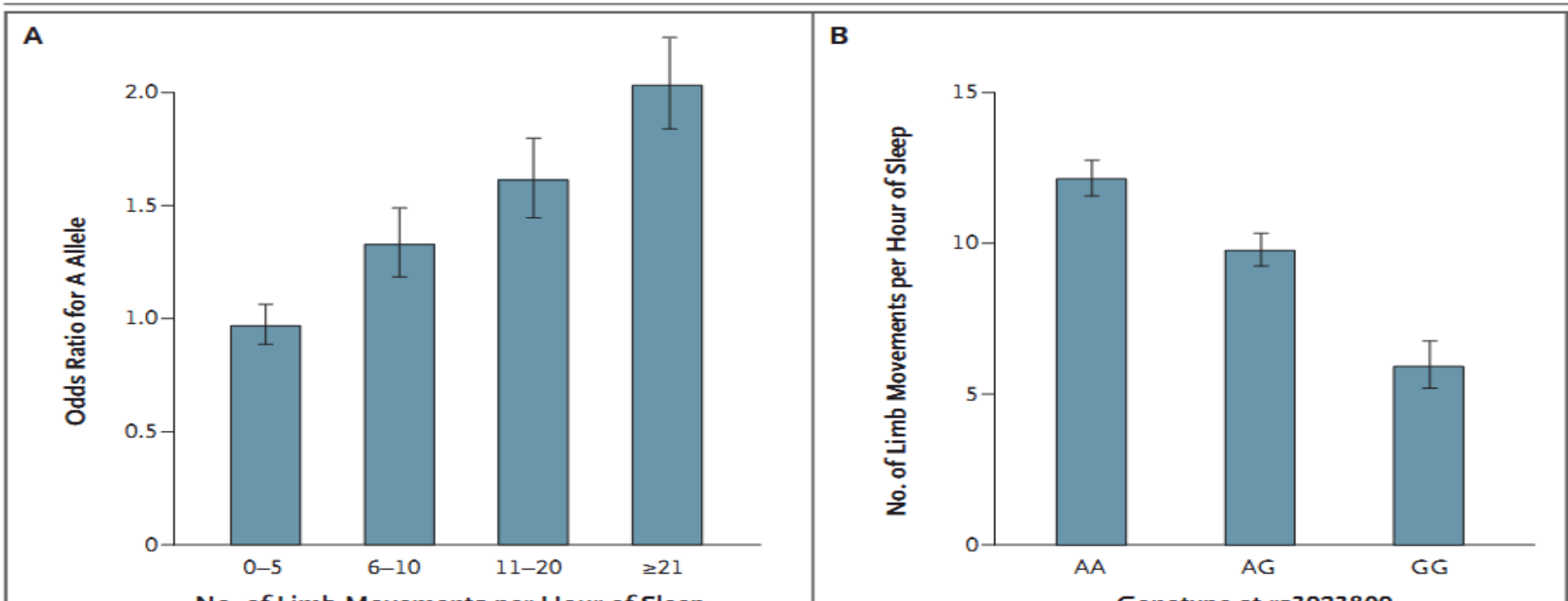
AUGUST 16, 2007

- We found that the frequency of periodic limb movements in sleep correlated with the presence of allele A of marker rs3923809
- AA homozygotes had almost twice as many limb movements per hour of sleep as did non-carriers (P<0.001)

Further study is required to determine whether the A allele of marker rs3923809 is associated with periodic limb movements outside the context of RLS

A Genetic Risk Factor for Periodic Limb Movements in Sleep

GENETIC RISK FOR SLEEP-RELATED LEG MOVEMENT



The NEW ENGLAND JOURNAL of MEDICINE

A Genetic Risk Factor for Periodic Limb Movements in Sleep

AUGUST 16, 2007

This sequence variant does not appear to be a gene for RLS but, rather, for periodic limb movements in sleep

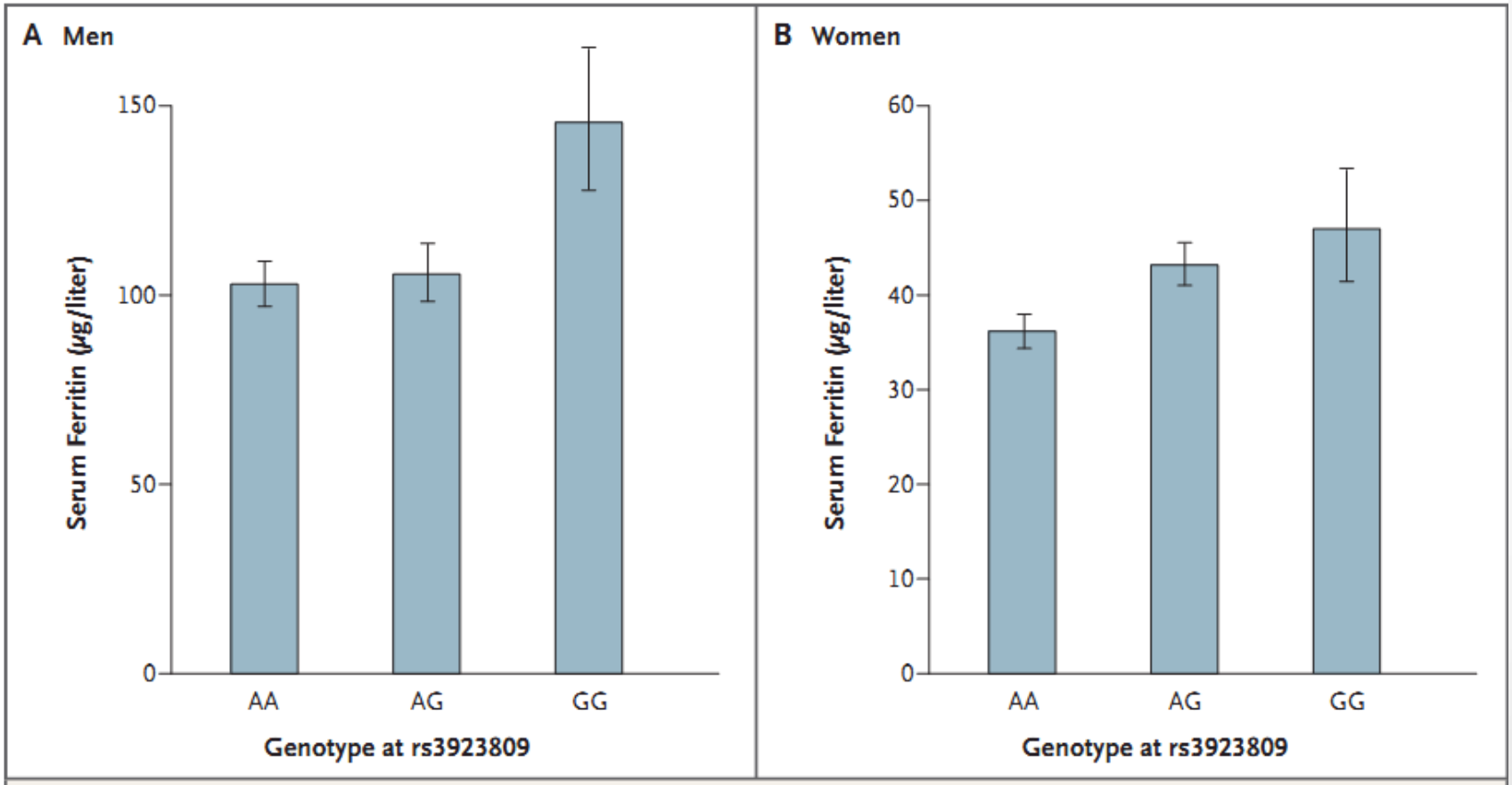
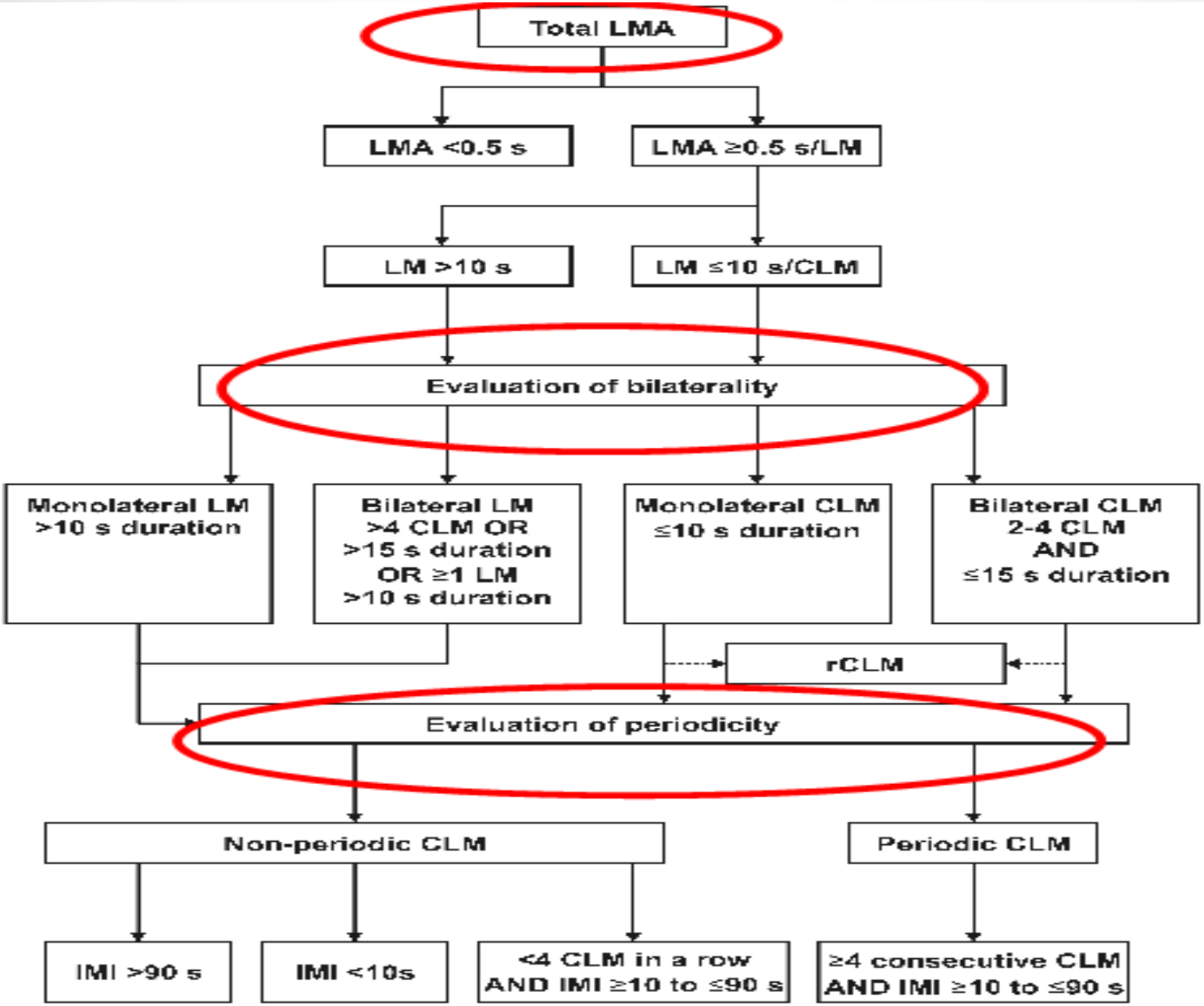


Figure 3. Serum Ferritin Levels in Subjects with RLS and Their Relatives.

Among 362 men (Panel A) and 603 women (Panel B), serum ferritin levels decreased by 13% per A allele at marker rs3923809 (95% CI, 5 to 20; P=0.002).


Total LMA
LMA <0.5 s
LMA ≥0.5 s/LM
LM >10 s
LM ≤10 s/CLM
Evaluation of bilaterality
Monolateral LM >10 s duration
Bilateral LM >4 CLM OR >15 s duration OR ≥1 LM >10 s duration
Monolateral CLM ≤10 s duration
Bilateral CLM 2-4 CLM AND ≤15 s duration
rCLM
Evaluation of periodicity
Non-periodic CLM
Periodic CLM
IMI >90 s
IMI <10s
<4 CLM in a row AND IMI ≥10 to ≤90 s
≥4 consecutive CLM AND IMI ≥10 to ≤90 s

Movement Disorders, Vol. 20, No. 4, 2005

Clinically Significant But Unsuspected Restless Legs Syndrome in Patients With Sleep Apnea

Sowmya Lakshminarayanan, MD,[1,2]
Kanchana Devi Paramasivan, MD,[1,2]
Arthur S. Walters, MD,[1,2]* Mary L. Wagner, PharmD,[3]
Shivani Patel, BA,[3] and Vandna Passi, BA[3]

TABLE 1. *MEMO questionnaire recommended by the NIH consensus conference on RLS*

Question	Circle one
a) Do you have unpleasant sensations like creepy, crawly or other feelings in your legs combined with an urge or need to move your legs?	Yes/No
b) Do these feelings occur mainly or only at rest, for example lying or sitting, and do they improve with movement?	Yes/No
c) Are these feelings worse in the afternoon, evening or night than in the morning?	Yes/No
d) How often do these feelings occur?	Less than one time per year At least one time a year but less than one time per month One time per month 2–4 times per month 2–3 times per week 4–5 times per week 6–7 times per week.

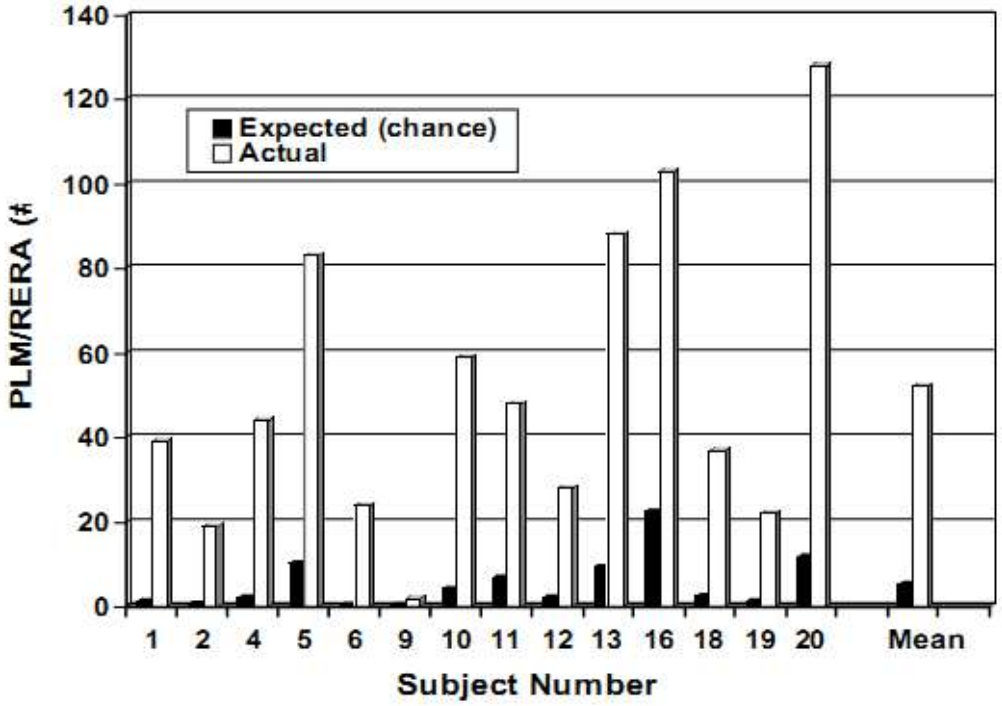
Patients were only considered positive for RLS if they answered affirmatively to all 3 primary questions (a–c).
NIH, National Institutes of Health; RLS, restless legs syndrome.

Clinically significant RLS occurred in 8.3% of OSA patients compared with 2.5% in the control group

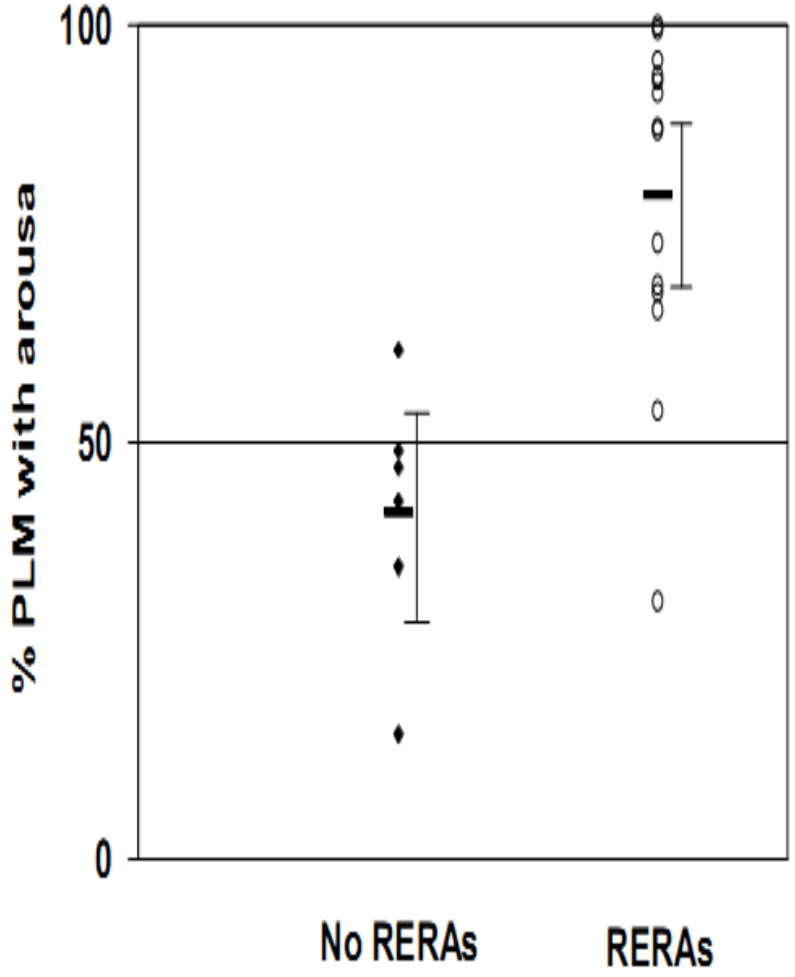
The Association of Upper Airway Resistance with Periodic Limb Movements

SLEEP, Vol. 24, No. 2, 2001

Elliott N. Exar and Nancy A. Collop



gure 1—Total number of PLM/RERA events per overnight study for each s
ct who demonstrated both events (actual), with corresponding number
ents that would be expected per overnight study by chance alone (expecte
e equation for prediction of expected concomitant events given a rand
sociation of PLMs and RERAs is given in methods section. The mean act
M/RERAs for the group was 51.7+36.2; the mean expected PLM/RERAs v
4+6.3. PLM = periodic limb movement; RERA = respiratory effort rela



Change in Periodic Limb Movement Index During Treatment of Obstructive Sleep Apnea with Continuous Positive Airway Pressure

Alp Sinan Baran, MD[1]; Allen C. Richert, MD[1]; Alan B. Douglass, MD[2]; Warren May, PhD[3]; Khalil Ansarin, MD[4]

SLEEP 2003;

The PLMs may increase in moderate to severe OSA due mainly to "unmasking" of underlying PLMD (spotaneous PLMs)

The PLMs may decrease in mild OSA post-CPAP due to resolution of PLMs associated with respiratory effort-related arousals (induced PLMs secondary to RERAs)

Unmasking of Periodic Limb Movements With the Resolution of Obstructive Sleep Apnea During Continuous Positive Airway Pressure Application

Laura C. Hedli*,†, Paul Christos†, and Ana C. Krieger†

J Clin Neurophysiol. 2012

PLM seen during CPAP titration may be related to a concurrent sleep disorder because of "unmasking" in patients with treated OSA

Prevalence of Pediatric Periodic Leg Movements of Sleep After Initiation of PAP Therapy

Pediatric Pulmonology 49:252–256 (2014)

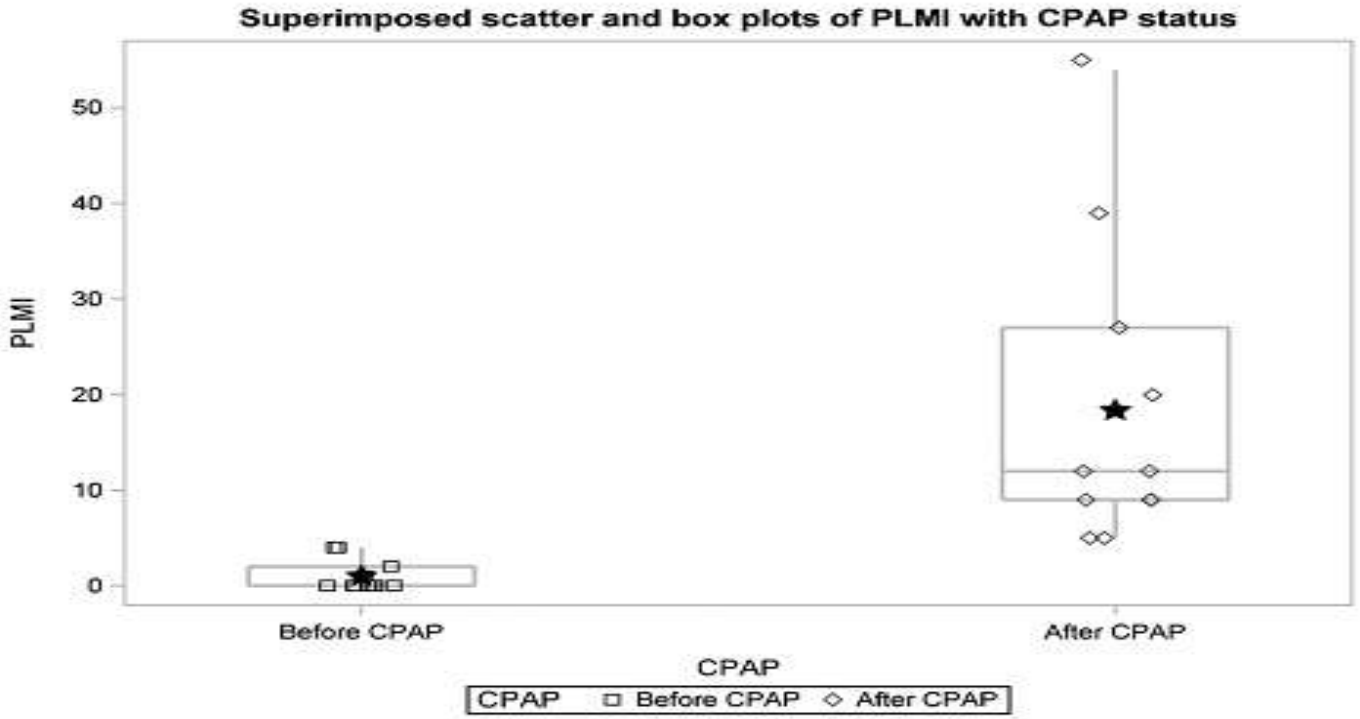
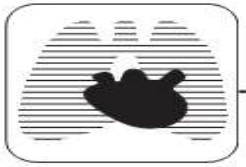


Fig. 1. Superimposed scatter and box plots of periodic limb movement index (PLMI) with positive airway pressure (PAP) status. The *X*-axis shows increasing PAP pressures on study night. The *Y*-axis is the corresponding increase in PLMI with increasing PAP pressures. Prior to initiation of CPAP, the median PLMI was 1. Following optimization of PAP therapy, PLMI rose in this series to a median of 12/hr.



CHEST

Original Research

SLEEP DISORDERS

CHEST 2012

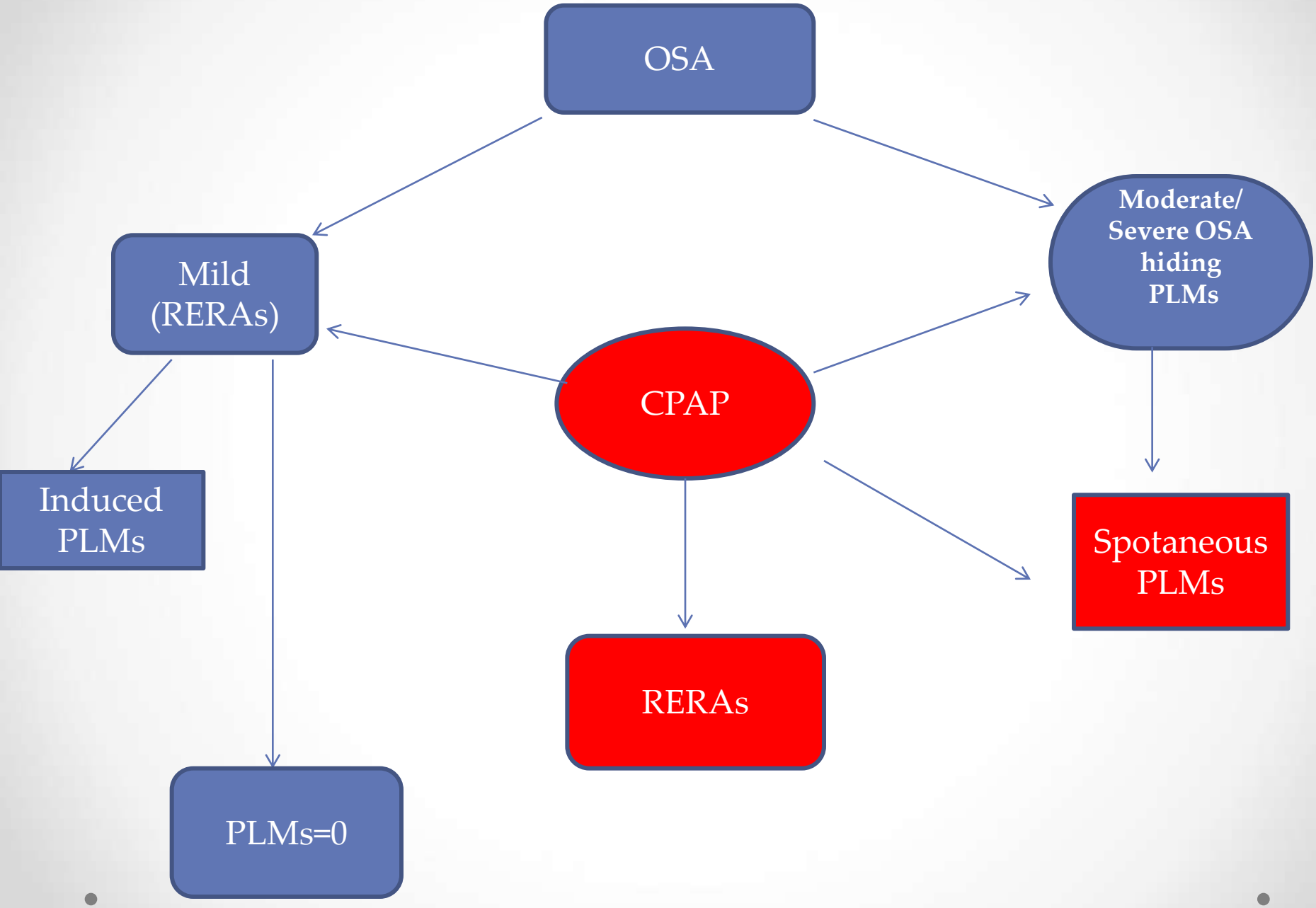
Periodic Leg Movement, Nasal CPAP, and Expiratory Muscles

Won Hee Seo, MD; and Christian Guilleminault, MD, DBiol

- This study showed that PLMs do not disappear with the elimination of AASM defined hypopnea, but with the elimination of flow limitation and the associated instability of NREM sleep (CAP)
- PLM induces "hypopnea" (ie, PLM would increase inspirations secondary leading to a compensatory physiologic pause related to the "hyperbreath" associated with some degree of CO2 depletion)
- PLMs monitored in the legs are also simultaneously seen in the abdominal muscles, and both EMG bursts disappear with optimal PAP pressure with the absence of flow limitation

Controversy CPAP-PLMs

- CPAP therapy can induce or worsen PLMS (*Chest 1989*)
- Severe OSA patients experienced an increase in the number of PLMS during CPAP treatment, whereas a decrease in PLMS was observed among mild OSA patients during CPAP therapy (*Sleep 2003*)
- PLMS decreased with CPAP treatment whether the patients had mild or severe OSA (*Respir.Med. 2002*)
- Severity of RLS symptoms has also been found to improve after 3 months of CPAP therapy in patients affected by the combination of RLS and OSA (*Sleep Med. 2006*)
- **Mandibular advancement device can also induce PLMS in OSA patients who did not have a diagnosis of PLM at baseline (*Sleep Breath. 2010*)**


OSA
Mild (RERAs)
Moderate/ Severe OSA hiding PLMs
CPAP
Induced PLMs
Spotaneous PLMs
RERAs
PLMs=0

Periodic Leg Movements and Sleepiness in Patients Evaluated for Sleep-disordered Breathing

RONALD D. CHERVIN

Am J Respir Crit Care Med Vol 164. pp 1454–1458, 2001

- This study,could not show a link between incidental PLMS and increased or subjective sleepiness
- Rates of **PLMS associated with arousals seem to provide no better prediction of sleepiness**, and in fact weakly predict alertness, perhaps because patients who are more sleepy are not able to arouse when a PLM occurs
- PLM-arousals may be less helpful than commonly thought, especially if it leads to medication for an asymptomatic polysomnographic finding
- Unless the clinical history suggests neurodegenerative disorders, or restless legs syndrome routine scoring of PLMS

ELSEVIER

Sleep Medicine 6 (2005) 225–229

www.elsevier.com/locate/sleep

Original article

Periodic limb movements and sleepiness in obstructive sleep apnea patients

José Haba-Rubio[a,*], Luc Staner[a], Jean Krieger[b], Jean P. Macher[a]

[a]*FORENAP/Centre Hospitalier, Rouffach, France*
[b]*Hôpitaux Universitaires, Strasbourg, France*

Received 13 April 2004; received in revised form 21 July 2004; accepted 25 August 2004

Conclusion: In this study we did not find a link between PLMS and increased objective or self-evaluated sleepiness in OSAS patients, before or after treatment with CPAP.

J Sleep Res. (2015) 24, 722–729

Comorbidities:PLMS and OSA

Basal sympathetic predominance in periodic limb movements in sleep with obstructive sleep apnea

There is sympathetic predominance in patients with OSA and PLMS. Therefore, comorbid OSA and PLMS may negatively affect the cardiovascular system of patients

ASSOCIATION BETWEEN PLMS AND AROUSALS IN RLS

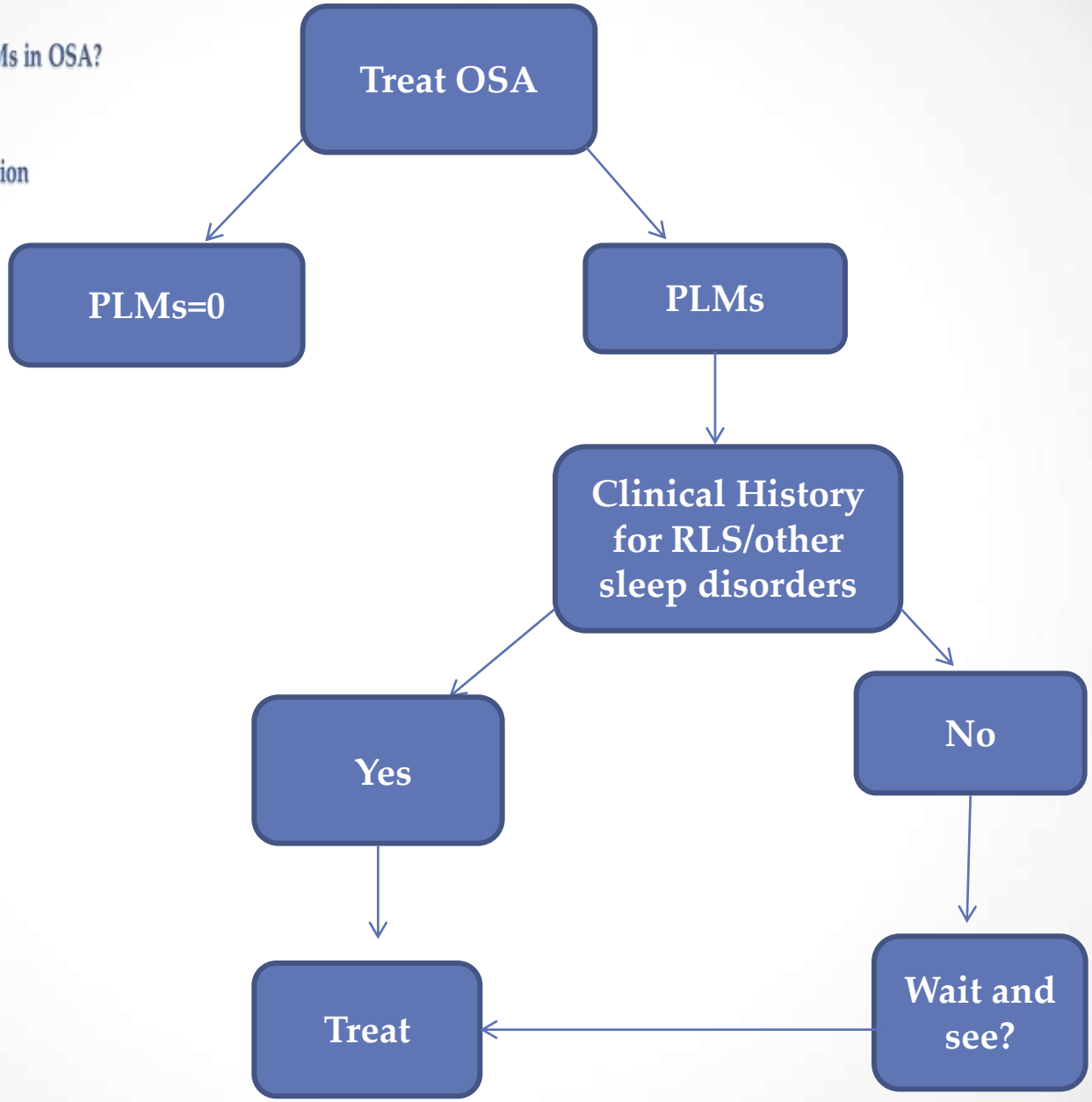
An Evidence-based Analysis of the Association between Periodic Leg Movements during Sleep and Arousals in Restless Legs Syndrome

SLEEP 2015

PLMS and arousals and their correlated durations seem to indicate that both events might be regulated by a complex mechanism, such as heart rate and blood pressure rather than being connected by a simple reciprocal cause/effect relationship

Treat or not to Treat? PLMs in OSA?

That is the Question



Conclussions

- OSA and PLMs coexist (PLMs 24-48% in OSA)
- Pathophysiologic Interactions among two disorders are complicated
- OSA, treated or not can induce PLMs
- There is a specific genetic background for PLMs. RRLMs may be a different phenotype of the same genetic disorder
- PLMs in OSA could affect sympathetic activation and cardiovascular morbidity but rather not daytime sleepiness
- PLMs in OSA should be treated only if there is another sleep disorder or PLMs are sustain
- **The main issue is the controversy of scoring rules for LMs and the relation of RRLMs with PLMs**

ΑΙΘΟΥΣΑ ΣΑΝΤΟΡΙΝΗ

16:00-17:30 **Στρογγύλη Τράπεζα**

Αποφρακτική άπνοια στον ύπνο και άλλες διαταραχές του ύπνου: τι πρέπει να γνωρίζουμε

Προεδρείο: *Π. Στειρόπουλος - Σ. Σχίζα*

- ΣΑΥ και αϋπνία
  Γ. Τρακαδά
- ΣΑΥ και PLMs
  Κ. Βλάμη
- ΣΑΥ Κλινική διαγνωστική προσέγγιση
  Α. Πατάκα
- Ετήσια κλινική ανασκόπηση
  Χ. Μερμίγκης

- ΣΑΥ και PLMs
  Κ. Βλάμη

Ευχαριστώ για την προσοχή σας