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SCIENTIFIC INVESTIGATIONS

Polysomnographic features of idiopathic restless legs syndrome: a systematic review and meta-analysis of 13 sleep parameters and 23 leg movement parameters

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Study Objectives: This study aims to explore the polysomnographically measured sleep and leg movement differences between idiopathic restless legs syndrome (RLS) patients and healthy controls.

Methods: An electronic literature search was conducted in EMBASE, MEDLINE, all EBM databases, CINAHL, and PsycINFO. Only observational case-control studies were included in the meta-analysis. The differences in 13 sleep parameters and 23 leg movement parameters between RLS patients and healthy controls were explored.

Results: Thirty-eight studies were identified for systematic review, 31 of which were used for meta-analysis. Meta-analyses revealed significant reductions in total sleep time, sleep efficiency, stage N2 and rapid eye movement (REM) sleep percentages, and increases in wake time after sleep onset, stage shifts per hour, stage N1 percentage, REM latency, arousal index, and apnea-hypopnea index. Some leg movement parameters, such as periodic limb movement during sleep (PLMS) index, PLMS sequence duration, number of PLMS sequence, and periodicity index, were higher in RLS patients compared with healthy controls. Further, our meta-analysis revealed a higher PLMS index during non-REM sleep compared with that during REM sleep.

Conclusions: RLS patients manifest a lightening of sleep, increased sleep fragmentation, and greater sleep-related breathing disruption and limb movements during sleep relative to healthy normal individuals. The distributions of PLMS during a night's sleep may provide more information to clarify the specific characteristics of leg movements in RLS. PLMS in RLS are concentrated in non-REM sleep. The periodicity index may be a more sensitive and specific marker of RLS than the PLMS index.

Keywords: restless legs syndrome, sleep, polysomnography, leg movements

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Studies exploring polysomnographic changes in idiopathic restless legs syndrome have not established the extent and type of changes in sleep associated with the disease. We performed a meta-analysis that explored the polysomnographic changes in idiopathic restless legs syndrome compared with controls.

Study Impact: This study showed that polysomnographic abnormalities (ie, decreased total sleep time, sleep efficiency, N2 and rapid eye movement sleep percentages, and increased wake time after sleep onset, stage shifts per hour, N1 percentage, rapid eye movement latency, arousal index, apnea-hypopnea index, and some leg movement parameters) are present in idiopathic restless legs syndrome. Our findings underscore the need for a comprehensive polysomnographic assessment of sleep and leg movement changes in idiopathic restless legs syndrome.

INTRODUCTION

Restless legs syndrome (RLS), a somatosensory network disorder, is characterized by an urge to move the legs, usually associated with unpleasant leg sensations; symptom relief with activity; induction or exacerbation of symptoms by rest; and diurnal fluctuations with symptoms worsening in the evening and at night.[1] These symptoms can contribute to sleep disturbances, with a 75.5% prevalence in RLS patients,[2] which negatively impact general health and decrease quality of life.[3–5] Thus, comprehensive sleep assessments are necessary and clinically important for optimizing the managements of RLS.[6]

Polysomnography (PSG), the gold standard to objectively assess sleep quantity and quality, provides quantitative sleep measures that can allow practitioners to macroscopically distinguish non–rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep, stage N1 to N3 of NREM sleep, and wakefulness. PSG is also required to record leg movements (LM) scored as periodic leg movements during sleep (PLMS), which is very often associated with RLS that have different clinical picture across the lifespan,[7,8] based on the electromyographic signals of tibialis anterior.[9,10] PSG-determined alterations in sleep and LM parameters have high clinical relevance and importance for understanding the neurobiology of RLS. For instance, while RLS severity is traditionally evaluated by

using questionnaires such as the International RLS Study Group (IRLSSG) rating scale,[11] PSG-measured PLMS, sleep efficiency (SE), and sleep latency (SL) provide more objective parameters reflecting RLS severity and are less susceptible to report bias compared with methods that depend on patients' estimates of severity,[12–14] and therefore are commonly used to quantify the severity of disease and efficacy of RLS treatment.[15–18] In addition to these macroscopic measures of sleep, alterations in sleep microstructural data, seen in measurement of cyclic alternating patterns (CAP) and power spectral analysis (PSA), have been reported in RLS. Alteration of CAP in RLS has been suggested to reflect an excess of sleep instability/discontinuity,[19] and Ferri et al reported that PSA revealed increased electroencephalogram (EEG) activity in the alpha and beta bands and/or increased beta/delta ratio during the sleep onset period and wakefulness preceding sleep in RLS compared with healthy controls (HCs), suggesting a hyperarousal state in RLS during the sleep onset period.[20]

Previous studies have examined PSG parameters in attempts to characterize the objective sleep profile of RLS, but the exact PSG changes in RLS compared to HCs have not been clearly established. Variations in findings across different studies may involve heterogeneity in demographic characteristics (ie, sex and age), clinical variables (ie, RLS severity and medication status), and experimental methodology (ie, differences in PSG recording and/or scoring methods, use or absence of adaptation nights, etc). Meta-analytic techniques can help resolve discrepancies across studies and quantify the impact of potential moderators. To our knowledge, no meta-analytic study of PSG-measured sleep and LM in RLS has been conducted to date. To fill this gap, we systematically reviewed previous case-control studies and, by using meta-analytic procedures wherever possible, estimated the pooled effect sizes for the differences in PSG-measured sleep and LM variables between idiopathic RLS patients and HCs. We also explored the impact of potential moderators that could contribute to heterogeneity of PSG findings across studies.

METHODS

Protocol and registration

We registered the protocol of this study (PROSPERO ID: CRD42021228355) following the meta-analysis of observational studies in epidemiology (MOOSE) and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statements.[21–23]

Eligibility criteria according to the Population, Intervention, Comparison, Outcomes and Study (PICOS) approach

Population (P)

Participants were patients diagnosed with idiopathic RLS according to established criteria such as the International Restless Legs Syndrome Study Group (IRLSSG) criteria.[1] Studies unrelated to RLS and animal studies were excluded.

Intervention (I)

This element was not applicable as this is a systematic review of observational studies.

Comparison (C)

Comparisons were to HCs. Studies not using HCs were excluded from the main analyses.

Outcomes (O)

The primary outcomes were alterations in PSG-measured sleep and LM parameters in idiopathic RLS patients compared with HCs. The detailed PSG parameters are listed following in the section "Data collection process." Studies containing no information on the outcomes of interest were excluded.

Study design (S)

Only case-control studies were included. Statements, editorials, case series, case reports, guidelines, review papers, and comments were excluded. Other eligibility criteria required that the studies be published in peer-reviewed journals in English. If the same patients were used in more than one publication, then only the dataset including the most relevant information for our meta-analysis was used to avoid data duplication.

Information sources, search, and study selection

We searched MEDLINE via OVID; EMBASE via OVID; all EBM databases via OVID; CINAHL via EBSCO; and PsycINFO via EBSCO (search strategies are provided in the supplemental material, **Table S1, Table S2, Table S3, Table S4, and Table S5**). The reference lists of all primary studies were also screened for additional study candidates. The literature search was performed on January 7, 2021. We reran the literature search on May 6, 2022 to identify newly published studies. Two reviewers (R.R. and Y.Z.) independently selected relevant studies. Discrepancies were resolved by discussion with the senior author (X.D.T.).

Data collection process and quality assessment of included studies

Y.Z. and R.R. independently extracted the data from the reviewed studies using a predesigned form. The extracted data were entered by Y.Z. and verified by the above 2 reviewers. The PSG variables examined in this review include sleep macrostructure: total sleep time (TST), SE, SL, wake time after sleep onset (WASO), and percentage of N1, N2, N3, and REM sleep, REM latency, stage shifts per hour (SS/h), and awakenings number per hour. In American Academy Sleep Medicine (AASM) scoring rules, N3 represents slow wave sleep and also replaces stage 3 and stage 4 in the Rechtschaffen and Kales (R&K) nomenclature.[9] Therefore, the data for stage 3 + stage 4 in the included studies were also extracted to form slow wave sleep wherever possible. Additional PSG-measured sleep parameters include arousal index, apnea-hypopnea index (AHI), PSA data (ie, alpha, beta, delta, theta, and gamma frequency activity), as well as CAP parameters, sleep spindles, and K-complex data.

The extracted LM parameters included bilateral LM index, isolated LM duration (during REM, NREM, and total sleep, respectively), isolated LM index (during REM, NREM, and

total sleep, respectively), monolateral LM index, periodicity index (PI) (during REM, NREM, and total sleep, respectively), PLMS associated with arousal index (PLMAI), PLMS index (during REM, NREM, and total sleep, respectively), PLMS duration (during REM, NREM, and total sleep, respectively), PLMS sequence duration, PLMS sequence number, and total LM index (during REM, NREM, and total sleep, respectively). Among the various LM parameters, the PI, which is not routinely deemed to be a standard index, was computed as the ratio between the number of intermovement intervals contained in regular uninterrupted sequences of at least 4 LMs, separated by 10- to 90-s intervals (onset-to-onset), and the total number of intermovement intervals recorded.[24–26]

Demographic, clinical, and methodological variables extracted included the number of participants and their mean age, sex (male percentage), IRLSSG criteria rating score, including patients taking psychoactive medications (Yes vs No), whether excluding obstructive sleep apnea (OSA) (Yes vs No), adaptation night (Yes vs No), and PSG scoring methods (R&K vs AASM). These variables were examined as potential moderators which impact sleep changes in RLS in our analysis.

R.R. and Y.Z. independently assessed the risk of bias of the included studies by using the adapted version of the National Institute for Health and Care Excellence (NICE) checklist[27] with discrepancies resolved by discussion with the senior author (X.D.T.).

Statistical analysis

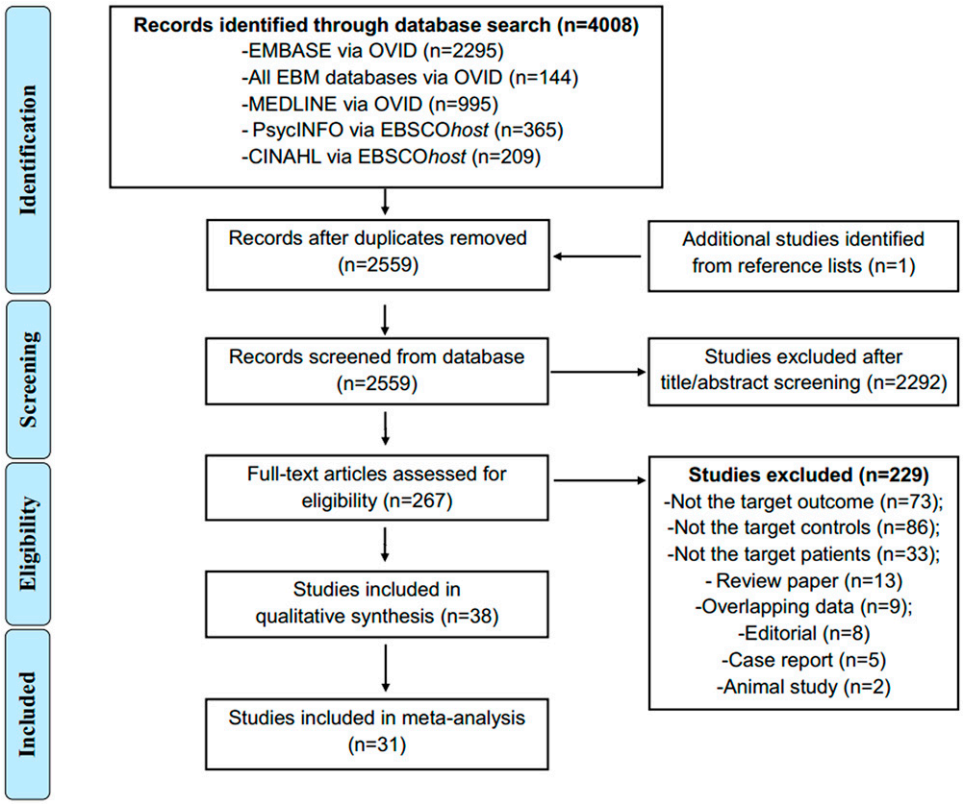
In our meta-analysis, we applied a random effects model to ensure relatively conservative findings. The sample size, mean, and standard deviation for idiopathic RLS patients and HCs were entered for calculating the standardized mean difference for PSG-measured nighttime sleep between groups. For the global effect-size estimate of PSG-measured sleep parameters, the Q-statistic and I^2 were calculated to test the magnitude of heterogeneity, and to inform on the degree of overlap between the 95% confidence intervals (CIs) of different studies. Publication bias for our meta-analytic findings were evaluated by the Egger regression method,[28] with P values < 0.05 suggesting the presence of bias. The Duval and Tweedie's trim and fill test was performed to estimate the adjusted effect sizes when publication bias was detected.[29] Depending on the variable type (continuous or categorical) of potential moderators, a meta-regression or subgroup analysis was conducted to estimate the potential source of heterogeneity of effect sizes between studies. All analyses in our meta-analysis were conducted using Comprehensive Meta-Analysis software (Biostat Inc., Englewood, NJ).

RESULTS

Study selection

Our search yielded 4008 publications (**Figure 1**). After removing the duplicates, the title/abstract of the remaining 2559

Figure 1—PRIMSA flow chart used for the identification of eligible studies.



articles were screened. A total of 267 studies were selected for full text review. Of these, 38 articles[18–20,24,30–63] were found to meet inclusion criteria of our systematic review (**Table 1**), and 31[18–20,24,32,34–39,41–43,46–49,51–63] of the 38 studies were used in our meta-analysis. The excluded studies with reasons for their exclusion are listed in **Table S6**.

Description of the included studies

As shown in **Table 1**, the sample sizes of the 38 studies ranged from 12 participants (6 RLS patients and 6 controls)[40] to 209 participants (141 RLS patients and 68 controls).[30] Mean age of RLS patients and controls ranged from 29 to 67.8 years (reported in 37 studies). Males as percentages of RLS patients and HCs ranged from 0%–100% (reported in 38 studies). Mean disease duration of RLS patients ranged from 9.3 to 20 years (reported in 9 studies). All included studies performed PSG in a sleep lab. Ten studies[34,36,44,49–53,57,62] used AASM PSG criteria and 25 studies used R&K criteria for scoring sleep (3 studies[33,55,63] did not specify which scoring criteria were used). Twenty-two studies[18–20,24,30–32,36,38–40,42,43,46–48,54,56,59–62] utilized an adaptation night, 14 studies did not, and 2 studies[55,63] left this unspecified. For the medication status of the patients, 37 of the 38 studies reported that their patients were drug naïve or a wash out period was included before PSG examinations; 1 study[40] did not report the medication status of their patients. Thirty-six of the 38 studies utilized an OSA exclusion criterion, while one[50] did not utilize an OSA exclusion criterion and one[58] did not report whether they used an OSA exclusion criterion. The quality assessments of the included studies are provided in **Table S7**.

Comparison between RLS patients and controls: the whole sample

In the whole sample, meta-analysis revealed significantly decreased TST, SE, N2 percentage, REM sleep percentage, and increased WASO, stage shifts per hour, N1 percentage, REM latency, AHI, and arousal index in RLS patients compared with HCs (**Table 2**). There were no significant differences in SL, awakenings number per hour, and slow wave sleep percentage between RLS patients and HCs ($P > .05$).

For the LM parameters, RLS patients showed statistically significant higher PI during NREM sleep, PI (total), PLMAI, PLMS index, PLMS index during NREM sleep, PLMS index during REM sleep, PLMS sequence duration, PLMS sequence number, total LM index, total LM index during NREM sleep, and total LM index during REM sleep compared with those in HCs.

Across all study findings, publication bias was only detected by Egger's test for the difference in PLMS index but not in any other variable (**Figure S1, Figure S2, Figure S3, Figure S4, Figure S5, Figure S6, Figure S7, Figure S8, Figure S9, Figure S10, Figure S11, Figure S12, Figure S13, Figure S14, Figure S15, Figure S16, Figure S17, and Figure S18** in the supplemental material). After adjusting for publication bias with the trim-and-fill method, there was still statistically significant increased PLMS index (standardized mean difference = 1.654, 95% confidence interval: 1.094 to 2.214) in RLS patients compared with HCs. It should be noted that, for LM parameters, we only performed Egger's test for PLMS index, PLMAI, PLMS sequence duration, PLMS sequence number, and total LM index. Publication bias for the other LM parameters was not estimated because of limited available data.

Moderator analysis

As shown in **Table 3**, moderator analyses revealed that sex (male percentage), mean age, mean disease duration, mean IRLSSG rating score, and mean PLMS index of the patients, use of an adaptation night (Yes vs No), and PSG scoring methods (R&K vs AASM) did not significantly impact the differences in sleep architecture between RLS patients and controls ($P > .05$). For LM parameters, moderator analyses were only conducted for PLMS index and PLMAI because of limited available data for other LM parameters.

All 31 included studies in the meta-analysis stated that their patients were drug naïve or had a wash out period before PSG examinations. Thus, there were no drug effects on our meta-analysis findings. After restricting the analyses only to studies having an OSA exclusion criterion, the meta-analytic findings in the whole sample analysis remained and did not show any significant changes ($P > .05$).

Other parameters with insufficient data for meta-analysis

For LM parameters, some parameters were only reported in 1 study. For instance, Ferri et al reported that bilateral LM index,[46] monolateral LM index,[46] and duration of monolateral LM[31] were statistically significantly higher compared with those in HCs.

Ferri et al[30] divided the LMs into 3 groups: LMs with intervals < 10, 10–90, or > 90 seconds. The number of LMs included in each group was significantly increased in RLS patients compared with HCs. The LMs with an interval of > 90 seconds steadily occurred during the nighttime sleep, whereas the hourly distribution of LMs with intervals of 10–90 seconds or < 10 was bell-shaped or decreasing in RLS patients or HCs, respectively.[30] In addition, LMs with an interval of < 10 seconds tended to show constituted shorter sequences and shorter duration compared with LMs with intervals of 10–90 or > 90 seconds.[30]

PSA data,[20,45,51] CAP parameters,[19] sleep spindles,[53] and K-complexes[40] were also explored for possible differences between RLS patients and HCs (**Table S8**). The number of studies in these areas is limited and findings are inconsistent between studies. For instance, Choi et al[51] reported that the delta-band power was significantly increased in RLS patients compared to HCs, while Hornyak et al[45] reported that spectral power of all sleep epochs did not differ between groups. Furthermore, Ferri et al[19] reported that CAP rate is significantly increased in RLS patients compared with HCs.

DISCUSSION

Summary of findings

To our knowledge, this is the first systematic review and meta-analysis to report PSG changes in idiopathic RLS patients. The results showed significantly decreased TST, SE, and REM

Table 1—Study characteristics.

Study	Sample Size	Percentage Male	Mean Age	IRLSSG Score	Disease Duration (years)	Includes Criterion to Exclude OSA	Adaptation	PSG Scoring Methods
Allen et al, 2013[61]	18 RLS	44.4%	62.9 ± 10.6	NR	NR	Yes	Yes	R&K
	14 controls	50%	60.1 ± 8.2			Yes	Yes	R&K
Boehm et al, 2009[54]	95 RLS	51.6%	54.6 ± 11.1	NR	16.4 ± 13.4	Yes	Yes	R&K
	31 controls	48.4%	59.3 ± 9.4			Yes	Yes	R&K
Cha et al, 2020[53]	15 RLS	13.3%	45.73 ± 11.78	30.38 ± 5.18	NR	Yes	No	AASM
	15 controls	0	49.00 ± 7.55			Yes	No	AASM
Chenini et al, 2019[52]	84 RLS	47.0%	55.14 ± 12.32	NR	NR	Yes	No	AASM
	64 controls	NR	NR			Yes	No	AASM
Choi et al, 2017[51]	12 RLS	8.3%	47.92 ± 9.41	29.92 ± 4.98	NR	Yes	No	AASM
	16 controls	6.3%	48.38 ± 9.04			Yes	No	AASM
Dauvilliers et al, 2018[50]	108 RLS	39.81%	61.54 (24.10–85.03)	28	NR	No	No	AASM
	45 controls	37.78%	53.91 (23.00–74.87)			No	No	AASM
Earley et al, 2011[60]	36 RLS	30.6%	59.2	NR	NR	Yes	Yes	R&K
	34 controls	47.1%	59.2			Yes	Yes	R&K
Eisensehr et al, 2001[59]	14 RLS	14.3%	67.2 ± 8.5	NR	19.8 ± 14.7	Yes	Yes	R&K
	10 controls	70%	66.4 ± 7.3			Yes	Yes	R&K
Elena et al, 2020[49]	42 RLS	35.7%	58.56 ± 9.65	NR	NR	Yes	No	AASM
	30 controls	33.3%	58 ± 9			Yes	No	AASM
Ferri et al, 2006a[46]	22 RLS	59.1%	29.0 ± 8.62	25.1 ± 5.35	NR	Yes	Yes	R&K
	22 controls	54.5%	30.9 ± 6.18			Yes	Yes	R&K
Ferri et al, 2006b[24]	43 RLS	39.5%	60.8 ± 9.10	NR	NR	Yes	Yes	R&K
	22 controls	54.5%	30.9 ± 6.18			Yes	Yes	R&K
Ferri et al, 2009[48]	20 RLS	65.0%	47.6 ± 12.01	NR	NR	Yes	Yes	R&K
	12 controls	25%	46.7 ± 15.21			Yes	Yes	R&K
Ferri et al, 2010[19]	34 RLS	32.3%	56.67	26.0	NR	Yes	Yes	R&K
	13 controls	33.3%	60.7 ± 12.51			Yes	Yes	R&K
Ferri et al, 2012[47]	90 RLS	41.1%	57.55	26.2	NR	Yes	Yes	R&K
	28 controls	42.9%	53.1 ± 19.55			Yes	Yes	R&K
Ferri et al, 2014[20]	27 RLS	55.6%	53.6 ± 14.90	NR	NR	Yes	Yes	R&K
	14 controls	50%	50.3 ± 15.83			Yes	Yes	R&K
Ferri et al, 2017a[30]	141 RLS	44.7%	55.2 ± 14.26	25.4 ± 5.36	NR	Yes	Yes	R&K
	68 controls	44.1%	52.9 ± 18.91			Yes	Yes	R&K

(continued on following page)

Table 1—Study characteristics. (*Continued*)

Study	Sample Size	Percentage Male	Mean Age	IRLSSG Score	Disease Duration (years)	Includes Criterion to Exclude OSA	Adaptation	PSG Scoring Methods
Ferri et al, 2017b[31]	111 RLS	44.1%	56.0 (45–65)	NR	NR	Yes	Yes	R&K
	42 controls	47.6%	60.0 (30.3–66.0)			Yes	Yes	R&K
Garcia-Borreguero et al, 2004[58]	12 RLS	41.7%	54.9 ± 11.2	20.6 ± 4.2	15.8 ± 9.9	NR	No	R&K
	12 controls	41.7%	53.8 ± 8.5			NR	No	R&K
Hornyak et al, 2005[45]	20 RLS	50%	50.4 ± 9.6	27.6 ± 5.3	NR	Yes	No	R&K
	20 controls	50%	51.8 ± 7.7			Yes	No	R&K
Hornyak et al, 2007[18]	45 RLS	35.6%	47.4 ± 10.9	24.0 ± 6.2	NR	Yes	Yes	R&K
	45 controls	35.6%	47.3 ± 10.5			Yes	Yes	R&K
Jin et al, 2020[62]	32 RLS	43.8%	59.0 ± 9.3	25.9 ± 6.3	NR	Yes	Yes	AASM
	21 controls	23.8%	56.3 ± 8.2			Yes	Yes	AASM
Kim, 2014[44]	13 RLS	15.4%	52.0 (37.5–58.0)	32.0 (26.5–35.5)	20.0(11.0–30.0)	Yes	No	AASM
	13 controls	7.7%	52.0 (45.0–54.5)			Yes	No	AASM
Manconi et al, 2007[42]	37 RLS	45.9%	67.8 ± 5.3	25.4 ± 6.31	NR	Yes	Yes	R&K
	14 controls	42.9%	66.5 ± 5.9			Yes	Yes	R&K
Manconi et al, 2011[43]	13 RLS (pram)	NR	NR	NR	NR	Yes	Yes	R&K
	10 RLS (placebo)	NR	NR	NR	NR	Yes	Yes	R&K
	10 controls	40%	58.9 ± 13.36			Yes	Yes	R&K
Michaud et al, 2002[41]	100 RLS	40%	48.8 ± 11.5	NR	NR	Yes	No	R&K
	50 controls	42%	48.4 ± 9.2			Yes	No	R&K
Montplaisir et al, 1996[40]	6 RLS	50%	51.3 ± 12.4	NR	NR	Yes	Yes	R&K
	6 controls	50%	51.6 ± 12.8			Yes	Yes	R&K
Montplaisir et al, 1998[39]	16 RLS	50%	50.6 ± 10.4	NR	NR	Yes	Yes	R&K
	16 controls	50%	50.9 ± 11.6			Yes	Yes	R&K
Park et al, 2021[63]	30 RLS	26.7%	46.3 ± 13.0	29.9 ± 7.6	9.4 ± 8.5	Yes	NR	NR
	31 controls	25.8%	44.1 ± 12.0			Yes	NR	NR
Pearson et al, 2006[38]	16 RLS	68.8%	65.3 ± 9.2	NR	NR	Yes	Yes	R&K
	15 controls	40%	59.4 ± 7.2			Yes	Yes	R&K
Plazzi et al, 2012[37]	17 RLS	35.3%	42.8 ± 16.95	22.1 ± 6.62	NR	Yes	No	R&K
	17 controls	41.2%	44.1 ± 17.25			Yes	No	R&K
Rassu et al, 2020[57]	15 RLS (*S*-SIT−)	26.67%	60.54 ± 10.05	27.40 ± 6.49	17.51 ± 12.19	Yes	No	AASM
	17 RLS (*S*-SIT+)	35.29%	60.33 ± 11.36	28.06 ± 5.45	14.19 ± 13.71	Yes	No	AASM
	17 controls	11.76%	58.82 ± 11.68			Yes	No	AASM
Salas et al, 2018[36]	35 RLS	42.9%	59.23 ± 9.82	25.41 ± 6.51	NR	Yes	Yes	AASM
	31 controls	38.7%	57.90 ± 8.35			Yes	Yes	AASM

(continued on following page)

Table 1—Study characteristics. (*Continued*)

Study	Sample Size	Percentage Male	Mean Age	IRLSSG Score	Disease Duration (years)	Includes Criterion to Exclude OSA	Adaptation	PSG Scoring Methods
Saletu et al, 2000[35]	12 RLS	33.3%	57.2 ± 11.7	NR	NR	Yes	No	R&K
	12 controls	33.3%	59.0 ± 15.9			Yes	No	R&K
Schilling et al, 2010[56]	72 RLS	37.0%	54.8 ± 13.2	NR	9.3 ± 9.2	Yes	Yes	R&K
	34 controls	32.4%	49.7 ± 8.3			Yes	Yes	R&K
Sieminski et al, 2016[34]	30 RLS	40%	49.0 ± 14.9	NR	NR	Yes	No	AASM
	27 controls	44.4%	44.3 ± 16.3			Yes	No	AASM
Thireau, 2017[33]	64 RLS	46.9%	58.9 ± 12.5	25.0 ± 4.0	NR	Yes	No	NR
	38 controls	23.7%	44.9 ± 13.1			Yes	No	NR
Wetter et al, 2002[32]	10 RLS	100%	56 ± 6	NR	15 ± 10	Yes	Yes	R&K
	8 controls	100%	57 ± 5			Yes	Yes	R&K
Winkelman et al, 2014[55]	18 RLS	44.4%	44.4 ± 15	23.3 ± 8.6	18.2 ± 16.1	Yes	NR	NR
	17 controls	41.2%	43.5 ± 14.3			Yes	NR	NR

AASM = American Academy of Sleep Medicine, IRLSSG = International Restless Legs Syndrome Study Group, NR = not reported, OSA = obstructive sleep apnea, Pram = pramipexole, RLS = restless legs syndrome, R&K = Rechtschaffen and Kales = S-SIT − = patients with RLS without sensory component, S-SIT+ = patients with RLS and sensory component. Empty table cells indicate data not available in original study.

sleep percentage, and increased WASO, stage shifts per hour, N1 percentage, rapid eye movement sleep latency (REML), AHI, arousal index, and various LM parameters in RLS patients compared with HCs. We also explored the effects of some demographic, clinical, and methodological characteristics (ie, sex, age, disease duration, IRLSSG rating score, PLMS index, use of an adaptation night, and PSG scoring method used) on sleep changes in RLS, and the results did not reveal any significant effects of these factors on our pooled effect sizes. Microstructure measures (ie, CAP) and sophisticated analyses (ie, PSA) also have been used to define the sleep profile of RLS, but the exact changes of CAP and EEG power spectra could not be fully established due to the limited number of studies and the methodological differences across studies.

LM characteristics of RLS

Our meta-analysis confirmed the increased PLMS index in RLS patients compared with HCs. However, increased PLMS index is also commonly seen in patients with other sleep disorders, such as rapid eye movement sleep behavior disorder (RBD)[42] and narcolepsy.[46] These findings suggested that, despite being highly sensitive for RLS, the PLMS index might not be a unique marker of RLS. The distributions of PLMS during a night's sleep may provide more information to clarify the specific characteristics of LM in RLS.[26] Comparing the PLMS index between RLS patients and HCs during REM and NREM sleep, respectively, our meta-analysis revealed a higher PLMS index (41.41 vs 19.50) during NREM sleep compared with that during REM sleep, suggesting that PLMS in RLS are concentrated in NREM sleep. This is consistent with previous studies which also reported that RLS patients are most likely to show PLMS during the first half of their usual sleep period, in which NREM sleep is dominant.[26,64–66] By comparison, PLMS in RBD and narcolepsy are mainly concentrated in REM sleep.[26,42,46] The REM preponderance of PLMS in narcolepsy and RBD compared with NREM may reflect a more pathological condition in narcolepsy and RBD, although previous studies have demonstrated that dopaminergic transmission impairment abnormalities may be responsible for the presence of PLMS in the 3 diseases (RLS, narcolepsy, and RBD).[67–70] The REM preponderance of PLMS in narcolepsy and RBD has been suggested to be due to the impaired mechanism responsible for motor inhibition during REM sleep in these diseases.[68,69] On the other hand, clinically, there were reduced responses to dopamine agonists in narcolepsy and RBD compared with those in RLS,[71–73] suggesting the strategy of management of PLMS in RLS should be different from that of narcolepsy and RBD, a possibility that might drive future study.

Although PLMS is very commonly seen (80.2%) in patients with primary RLS, nearly 20% of primary RLS patients do not show PLMS,[17] suggesting the absence of association between RLS and PLMS is not unusual. Recently, Bliwise et al[74] also reported no association between RLS and PLMS in patients with Parkinson disease. These findings suggest that the PLMS is not always a reliable indicator of RLS. Furthermore, the PLMS index shows high night-to-night variability[75] indicating that more stable LM parameters are needed. PI, a LM parameter

Table 2—Summary of meta-analysis results comparing RLS patients and controls.

	No. of Comparisons	No. of RLS/ Controls	Means of RLS	Means of Controls	SMD (95%CI)	Q	I^2
Sleep Architecture							
TST min	29	978/658	358.057	385.561	–0.405 (–0.582 to –0.228)***	74.995***	62.664
SE %	30	978/664	75.429	84.035	–0.634 (–0.782 to –0.486)***	53.242**	45.532
SL min	26	921/612	21.144	16.801	0.132 (–0.023 to 0.288)	49.290**	49.280
WASO min	13	365/317	81.290	53.654	0.644 (0.417 to 0.871)***	23.216*	48.312
AWN/h	8	256/136	4.603	3.539	0.365 (–0.165 to 0.896)	38.339***	81.742
SS/h	8	256/136	11.763	10.119	0.412 (0.115 to 0.710)**	12.334	43.244
N1%	24	777/527	10.304	8.014	0.404 (0.215 to 0.592)***	55.794***	58.777
N2%	24	777/527	47.095	51.175	–0.398 (–0.538 to –0.259)***	31.422	26.803
SWS%	24	777/527	13.899	14.433	–0.096 (–0.275 to 0.083)	51.080**	54.973
REM%	24	777/527	17.310	18.786	–0.219 (–0.432 to –0.005)*	73.111***	68.541
REML min	7	163/134	104.937	72.815	0.589 (0.351 to 0.827)***	4.157	0
AHI (events/h)	8	248/232	4.092	2.944	0.269 (0.088 to 0.450)**	6.518	0
AI (events/h)	11	440/328	20.190	13.994	0.574 (0.359 to 0.789)***	18.762*	46.700
LM Parameters							
PLMS index (events/h)	29	999/657	36.550	5.083	1.260 (1.067 to 1.453)***	78.108***	64.152
PLMS index during NREM sleep (events/h)	4	96/65	41.413	5.763	1.676 (1.131 to 2.221)***	6.273	52.178
PLMS index during REM sleep (events/h)	5	191/96	19.495	2.612	0.584 (0.284 to 0.884)***	5.136	22.118
PLMAI (events/h)	11	441/297	10.568	1.562	0.875 (0.637 to 1.112)***	19.296*	48.176
PLMS duration (NREM), s	4	169/74	2.343	1.984	0.485 (–0.160 to 1.130)	13.829**	78.306
PLMS duration (REM), s	4	169/74	2.024	1.687	0.353 (–0.037 to 0.743)	5.224	42.577
PLMS duration (TST), s	4	144/88	2.734	2.493	0.286 (–0.292 to 0.865)	13.147**	77.182
PLMS sequence duration, s	7	324/146	85.170	4.926	0.576 (0.286 to 0.866)***	11.302	46.911
PLMS sequence, number	7	324/146	14.735	4.939	1.296 (0.888 to 1.703)***	19.475**	69.192
Bilateral LM index (events/h)	1	22/22	111.100	20.000	2.176 (1.431 to 2.922)***	0.000	0.000
Isolated LM duration (NREM), s	3	74/43	2.532	2.402	0.111 (–0.289 to 0.512)	2.160	7.395
Isolated LM duration (REM), s	3	74/43	2.020	2.246	–0.178 (–0.562 to 0.207)	0.568	0.000
Isolated LM duration (TST), s	3	102/58	2.732	2.575	0.133 (–0.242 to 0.507)	2.565	22.025
Isolated LM index (events/h)	6	229/115	8.353	6.816	0.426 (0.006 to 0.847)*	15.241**	67.193
Isolated LM index during NREM sleep (events/h)	4	96/65	8.051	6.265	0.442 (–0.140 to 1.024)	9.250*	67.567
Isolated LM index during REM sleep (events/h)	4	96/65	11.315	8.898	0.390 (–0.176 to 0.956)	8.803*	65.921
Monolateral LM index (events/h)	1	22/22	171.600	35.500	2.348 (1.580 to 3.116)***	0.000	0.000
Periodicity index during NREM sleep (events/h)	2	37/29	0.680	0.368	1.206 (0.675 to 1.738)***	0.029	0.000
Periodicity index during REM sleep (events/h)	2	37/29	0.492	0.265	0.750 (–0.178 to 1.679)	3.272	69.436

(continued on following page)

Table 2—Summary of meta-analysis results comparing RLS patients and controls. (*Continued*)

	No. of Comparisons	No. of RLS/ Controls	Means of RLS	Means of Controls	SMD (95%CI)	Q	I^2
Periodicity index (total) (events/h)	2	37/29	0.658	0.402	1.078 (0.554 to 1.602)***	0.079	0
Total LM index (events/h)	6	229/115	46.349	11.693	1.654 (1.094 to 2.214)***	21.156**	76.367
Total LM index during NREM sleep (events/h)	4	96/65	49.434	12.835	1.813 (1.095 to 2.531)***	10.380*	71.097
Total LM index during REM sleep (events/h)	4	96/65	34.537	11.803	0.670 (0.093 to 1.247)*	8.831*	66.028

*$P < .05$, **$P < .01$, ***$P < .001$. AHI = apnea-hypopnea index, AI = arousal index, AWN = awakenings number, LM = leg movement, NREM = non–rapid eye movement sleep, PLMAI = periodic leg movements during sleep associated with arousal index, PLMS = periodic limb movements during sleep, Q = Cochran's Q-statistic, REM = rapid eye movement sleep, REML = rapid eye movement sleep latency, RLS = restless legs syndrome, SE = sleep efficiency, SL = sleep latency, SMD = standardized mean difference, SS = stage shifts, SWS = slow wave sleep, TST = total sleep time.

reflecting LM periodicity, has been shown to have lower night-to-night variability and more stability compared to the PLMS index.[75] Our meta-analysis found increased PI in RLS patients compared with HCs. PI in patients with RLS has also been shown to be higher than that seen in narcolepsy and RBD,[26,42,46] supporting the potential of PI to be a more sensitive and specific marker of RLS than the PLMS index. However, this does not mean that other LM parameters are not clinically useful. A recent study has highlighted the changes in heart rate associated with different types of LMs (ie, short-interval LMs during sleep, PLMS, and isolated LMs during sleep) at all ages in RLS, which might constitute an essential piece of knowledge in the ongoing scientific debate around the possibility and opportunity of treating PLMS.[76]

Sleep macrostructure changes in RLS

Based on patient self-reports, previous studies have indicated that a majority of RLS patients (94%) report sleep-onset insomnia or numerous nocturnal awakenings.[17] Objectively, PSG changes in our study focused on quantitative sleep parameters and further demonstrated disturbed objective sleep parameters (eg, decreased N2, TST, and REM sleep, and increased N1 and WASO), clearly showing fragmented sleep with deterioration of both REM and NREM sleep in RLS. The effects of chronic sleep loss on health outcomes have always been given great attention. For instance, chronic sleep deprivation, as in untreated RLS, could result in an increased risk of hypertension and diabetes or result in an impairment of sleep-dependent memory consolidation.[18,77–79] Prefrontal cognitive deficits similar to those reported for 1 night of sleep loss have also been demonstrated in RLS patients.[18,38] These suggested that the sleep loss in RLS should be carefully monitored.

The mechanisms underlying the PSG changes in RLS are unclear. Given the high prevalence of PLMS in RLS, it could be that the increased PLMS index may also impact sleep in RLS patients. It has been suggested that PLMS in RLS may be associated with a generalized EEG oscillatory pattern during sleep, such as the CAP,[19] an EEG marker of arousal instability that recurs in NREM sleep.[80] PLMS in RLS may contribute to disturbed sleep by generating arousal instability, especially during NREM sleep. DelRosso et al reported increased awakening time following movements in RLS patients compared with HCs.[81] Surprisingly, our meta-regression analysis did not reveal any significant relationship between PLMS index and any changes of sleep parameters in RLS (while the associations between other LM parameters and sleep changes could not be explored due to limited available data). This lack of an observed association between the PLMS index and sleep changes may have several explanations. First, PLMS occur mainly during NREM sleep in RLS and CAP occurs only in NREM sleep. If PLMS actually has an impact on sleep in RLS, then PLMS during NREM sleep, but not during REM sleep, are those that result in sleep changes in RLS. In our analysis, we examined PLMS during overnight sleep (which merged components of PLMS during NREM and REM sleep) to explore its associations with sleep parameters. The addition of PLMS during REM may have confounded the PLMS during NREM

Table 3—Moderator analyses.

Moderators	TST	WASO	SE	SL	N1 Percentage	N2 Percentage	SWS Percentage	REM Percentage	REM Latency	AWN/h	SS/h	PLMS Index	PLMAI	AI	AHI
Sex (Male%)															
No. of comparisons	27	13	28	24	22	22	22	22	7	6	6	27	11	11	8
No. of RLS/controls	955/638	365/317	955/644	898/592	754/507	754/507	754/507	754/507	163/134	233/116	233/116	976/637	441/297	440/328	248/232
Point estimate	1.147	0.593	–0.692	–0.839	–0.235	0.205	–1.037	–0.165	0.588	–0.578	–1.200	–0.154	0.500	0.925	–0.933
SE	0.562	1.082	0.514	0.629	0.641	0.502	0.576	0.701	0.788	3.676	1.978	0.678	0.664	0.872	0.805
P	0.041	0.584	0.178	0.182	0.713	0.683	0.072	0.814	0.456	0.875	0.544	0.821	0.451	0.289	0.246
Mean Age															
No. of comparisons	27	13	28	24	22	22	22	22	7	6	6	27	11	11	8
No. of RLS/controls	955/638	365/317	955/644	898/592	754/507	754/507	754/507	754/507	163/134	233/116	233/116	976/637	441/297	440/328	248/232
Point estimate	–0.028	0.028	–0.010	–0.018	–0.018	–0.017	0.017	0.008	–0.014	–0.020	–0.022	–0.005	0.031	0.019	–0.019
SE	0.011	0.018	0.010	0.011	0.014	0.010	0.013	0.016	0.013	0.033	0.014	0.013	0.034	0.024	0.018
P	0.013	0.110	0.314	0.099	0.201	0.086	0.191	0.622	0.264	0.534	0.126	0.723	0.365	0.421	0.297
Disease Duration (y)															
No. of comparisons	7	—	9	8	7	7	7	7	—	—	—	9	—	—	—
No. of RLS/controls	251/150	—	283/177	269/167	251/150	251/150	251/150	251/150	—	—	—	283/177	—	—	—
Point estimate	–0.027	—	–0.012	–0.027	–0.009	0.001	–0.023	0.023	—	—	—	0.012	—	—	—
SE	0.053	—	0.043	0.073	0.044	0.079	0.031	0.031	—	—	—	0.030	—	—	—
P	0.603	—	0.784	0.713	0.842	0.987	0.472	0.458	—	—	—	0.680	—	—	—
IRLSSG Rating Score															
No. of comparisons	13	8	13	12	11	11	11	11	—	—	—	14	—	—	—
No. of RLS/controls	376/285	154/156	362/281	347/266	309/233	309/233	309/233	309/233	—	—	—	396/285	—	—	—
Point estimate	–0.008	–0.054	0.026	–0.054	–0.109	0.039	0.062	0.023	—	—	—	–0.036	—	—	—
SE	0.054	0.040	0.033	0.046	0.042	0.035	0.050	0.040	—	—	—	0.044	—	—	—
P	0.886	0.177	0.426	0.245	0.009	0.256	0.220	0.558	—	—	—	0.413	—	—	—
PLMS Index															
No. of comparisons	25	12	26	24	22	22	22	22	6	7	7	—	11	11	8
No. of RLS/controls	888/586	330/286	888/592	859/567	738/501	738/501	738/501	738/501	151/122	229/122	229/122	—	441/297	440/328	248/232
Point estimate	–0.005	–0.003	0.003	–0.004	0.008	–0.003	–0.001	0.010	–0.0007	–0.063	–0.046	—	–0.002	0.009	–0.010
SE	0.005	0.007	0.006	0.006	0.010	0.007	0.009	0.011	0.007	0.053	0.024	—	0.013	0.011	0.007
P	0.388	0.707	0.633	0.505	0.418	0.659	0.902	0.336	0.914	0.234	0.055	—	0.868	0.437	0.152
Adaptation Night															
No															
No. of comparisons	10	7	10	8	9	9	9	9	2	1	1	11	7	7	6
No. of RLS/controls	314/247	185/168	314/247	287/220	214/197	214/197	214/197	214/197	24/28	17/17	17/17	389/310	298/229	273/206	173/156
SMD	–0.591***	0.595***	–0.642***	0.073	0.427**	–0.340**	–0.054	0.031	0.557	0.795*	0.903*	1.084***	0.889***	0.503***	0.147
Q	17.530*	6.947	16.411	23.360**	15.061	3.191	3.403	10.646	0.063	0	0	8.293	17.895**	8.699	2.608
I^2	48.660	13.630	45.159	70.034	46.884	0	0	24.853	0	0	0	0	66.471	31.028	0
Yes															
No. of comparisons	18	4	18	16	14	14	14	14	5	7	7	16	3	3	1
No. of RLS/controls	634/380	132/101	616/369	586/344	533/299	533/299	533/299	533/299	139/106	239/119	239/119	562/299	125/51	137/91	45/45

(continued on following page)

Table 3—Moderator analyses. (*Continued*)

Moderators	TST	WASO	SE	SL	N1 Percentage	N2 Percentage	SWS Percentage	REM Percentage	REM Latency	AWN/h	SS/h	PLMS Index	PLMAI	AI	AHI
SMD	–0.289*	0.825**	–0.654***	0.142	0.411**	–0.488***	–0.127	–0.319*	0.598***	0.304	0.346*	1.465***	0.881***	0.728*	0.523*
Q	55.353***	13.077**	35.328**	23.643	39.455***	18.037	47.281***	51.295***	4.077	36.780***	9.855	64.737***	1.314	9.099*	0
I^2	69.288	77.059	51.879	36.555	67.051	27.925	72.505	74.656	1.898	83.687	39.117	76.829	0	78.019	0
Between Group Difference															
Q	2.664	0.511	0.005	0.115	0.006	1.196	0.167	3.121	0.017	1.102	2.021	3.777	0.001	0.422	2.429
P	0.103	0.475	0.945	0.735	0.938	0.274	0.683	0.077	0.896	0.294	0.155	0.052	0.975	0.516	0.119
PSG Scoring Methods															
AASM															
No. of comparisons	8	7	7	6	6	6	6	6	1	—	—	8	4	6	6
No. of RLS/controls	240/208	208/187	208/187	193/172	173/156	173/156	173/156	173/156	12/16	—	—	247/207	141/122	173/156	173/156
SMD	–0.573***	0.555***	–0.539***	–0.145	0.195	–0.324**	–0.012	0.197	0.491	—	—	1.200***	0.686***	0.588***	0.147
Q	3.731	3.789	3.982	15.824**	1.139	0.721	1.808	4.437	0	—	—	10.158	1.153	5.992	2.608
I^2	0	0	0	68.403	0	0	0	0	0	—	—	31.091	0	16.551	0
R&K															
No. of comparisons	20	4	21	18	17	17	17	17	6	—	—	19	6	4	1
No. of RLS/controls	708/419	109/82	722/429	680/392	574/340	574/340	574/340	574/340	151/118	—	—	704/402	282/158	237/141	45/45
SMD	–0.316*	0.984**	–0.684***	0.218**	0.515***	–0.482***	–0.143	–0.329*	0.600***	—	—	1.352***	1.117***	0.585*	0.523*
Q	67.955***	14.850**	47.344**	22.614	49.507***	20.606	48.305***	52.415***	4.085	—	—	65.572***	15.692**	12.209**	0
I^2	72.040	79.798	57.756	24.826	67.681	22.352	66.877	69.474	0	—	—	72.549	68.137	75.427	0
Between Group Difference															
Q	2.564	1.277	0.972	2.750	3.419	1.298	0.594	9.029	0.072	—	—	0.615	2.969	0	2.429
P	0.109	0.258	0.324	0.097	0.064	0.255	0.441	0.003	0.789	—	—	0.433	0.085	0.922	0.119

With the exception of PLMS index and PLMAI, Analyses for the effects of potential moderators on the pooled effect sizes of differences in other leg movement parameters between RLS patients and healthy controls were not performed because of limited available data. *P < .05, **P < .01, ***P < .001. AASM = American Academy of Sleep Medicine, AHI = apnea-hypopnea index, AI = arousal index, AWN = awakenings number, Q = Cochran's Q-statistic, REM = rapid eye movement sleep, RLS = restless legs syndrome, IRLSSG = International Restless Legs Syndrome Study Group, PLMAI = periodic leg movements during sleep associated with arousal index, PLMS = periodic limb movements during sleep, R&K = Rechtschaffen and Kales, SE = sleep efficiency, SMD = standardized mean difference, SS = stage shifts, SWS = slow wave sleep, TST = total sleep time.

association with disturbed sleep in RLS. Thus, a better parameter that should be used to test this association is the PLMS index during NREM sleep, rather than that of NREM and REM combined. Second, the possible association between the PLMS index and sleep changes was impacted by the intermovement intervals (IMI) of LM. Emerging evidence suggests that LM with IMI < 10 s were possibly associated with the level of sleep disruption, while LMs with IMI ranging from 10 to 90 s informed mainly on the sensorimotor component of RLS.[30] In the current systematic review, we did not explore a meta-regression to test the associations of the PLMS index during NREM with sleep changes or the effects of IMI on the associations between the PLMS index and sleep changes in RLS because of limited available data.

PSA and CAP

Previous studies also explored changes in EEG frequency components, which tried to provide important neurobiological insight into RLS and its clinical relevance. Ferri et al[20] reported increased EEG alpha and beta bands and/or beta/delta ratio in RLS compared with HCs during the sleep onset period (the 10-minute period centered with the occurrence of the first sleep spindle in the EEG), supporting a hypothesis regarding the presence of a hyperarousal state in RLS during this period.

Furthermore, Choi et al[51] reported increased delta-band power in RLS patients compared to HCs, and the delta-band power was significantly associated with the RLS severity score in RLS patients prior to treatment. This seems counterintuitive because of our prior conceptualized notions of increased presence of PLMS during light NREM sleep, and not necessarily during deeper "slow wave" sleep in RLS.[26,42,46] However, it should be noted that the delta rhythm, especially during the deep NREM sleep stage, has been suggested to be an important indicator of the sleep homeostatic process.[82] Generally, a compensatory increase in slow wave activity is found after a period of sustained wakefulness and a decrease after sleep.[83–85] Therefore, the increased delta-band power in RLS and its associations with RLS severity score found by Choi et al[51] may reflect an increased demand for homeostatic regulation because of cortical hyperexcitability during wakefulness resulting from RLS symptoms.[51]

These findings suggested that exploring changes in EEG frequency components in RLS may be useful for understanding the underlying electrophysiological mechanisms of the disease, and for exploring possible biomarkers and potential targets for more effectively treating RLS. However, at present, due to the limited number of available studies and methodological differences across studies, it cannot be determined which EEG frequency component may be a unique marker of RLS.

In addition to macroscopic changes in sleep, microscopic changes (ie, CAP) are also promising parameters for examination.[86] Emerging evidence suggests that CAP parameters, may be better associated with self-reported RLS symptoms compared to traditional sleep architecture variables,[19] and may have a role in the cognitive dysfunction reported in patients with RLS.[19,38] However, only 1 study has reported on CAP in RLS.[19] The limited evidence makes it impossible to draw conclusions with confidence.

Limitations

The present review has limitations. First, some factors, such as depression and anxiety, which potentially could influence PSG changes in RLS, could not be explored due to limited available data. Second, although almost all of the included studies utilized an OSA exclusion criterion, the exact criterion varied across studies (eg, AHI > 5 or 15 events/h, etc.) with some studies failing to include any detail beyond stating that OSA was excluded. This may potentially bias our findings. Third, although many LM parameters were meta-analyzed to reveal LM features, some parameters (ie, PI during NREM and REM sleep, and isolated LM duration) were not always reported, with the result that meta-analyses for these parameters may be underpowered. These specific and potentially informative parameters deserve future attention for the valuable information they may provide about the nature of RLS. Fourth, other factors, such as discomfort wearing PSG devices and variations in sleep recording schedule across sleep labs may also potentially contribute to heterogeneity across studies and impact our pooled effect sizes.

In conclusion, the current meta-analysis demonstrates multiple significant PSG-determined sleep and LM abnormalities in patients with idiopathic RLS compared with HCs. Surprisingly, the PLMS index was not associated with sleep changes in RLS. The present systematic review also suggested that studies using more stable LM parameters (ie, PI, IMI of LM, and time distribution of LM throughout the night) are warranted to provide more reliable objective measure of PLMs in RLS, facilitate better understanding of the natural/characteristics of LM in RLS, and optimize management of the disorder. Finally, current evidence is too limited to make meaningful statements about PSA and CAP in RLS despite their potential to reflect the underlying neurobiology of the disease.

ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
CAP, cyclic alternating pattern
EEG, electroencephalogram
IMI, inter-movement intervals
IRLSSG, International Restless Legs Syndrome Study Group
LM, leg movement
NREM, non–rapid eye movement
OSA, obstructive sleep apnea
PI, periodicity index
PLM, periodic leg movements
PLMAI, periodic leg movements during sleep associated with arousal index
PLMS, periodic limb movement during sleep
PSA, power spectral analysis
PSG, polysomnography
R&K, Rechtschaffen and Kales
RBD, REM sleep behavioral disorder
REM, rapid eye movement
RLS, restless legs syndrome
SE, sleep efficiency
SL, sleep latency

SS, stage shift
TST, total sleep time
WASO, wake time after sleep onset

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