ELSEVIER

Sleep Medicine 4 (2003) 147–152

SLEEP MEDICINE

www.elsevier.com/locate/sleep

Original article

Different sleep characteristics in restless legs syndrome and periodic limb movement disorder

Ilonka Eisensehr[a,*], Bruce L. Ehrenberg[b], Soheyl Noachtar[a]

[a]*Department of Neurology, Klinikum Grosshadern, Ludwig-Maximilians, University of Munich, Marchioninistrasse 15, 81377 Munich, Germany*
[b]*Department of Neurology, Tufts University, 750 Washington St, Boston, MA 02111, USA*

Received 21 August 2002; received in revised form 20 September 2002; accepted 23 December 2002

Abstract

Objective: Periodic limb movements in sleep (PLMS) may or may not be associated with restless legs syndrome (RLS). The number of PLMS is commonly used to assess the clinical severity and sleep quality of patients with RLS. It is still unclear whether the sleep disorder of periodic limb movement disorder (PLMD) is different from the sleep disorder in RLS. **Methods**: We compared the polysomnograms (PSGs) of 27 prospectively recruited RLS patients and 26 retrospectively recruited age- and sex-matched PLMD patients without RLS symptoms. **Results**: The PLM index and the index of arousal-associated PLMS (PLMAI) were significantly higher in PLMD, whereas the index of EEG arousals not associated with any sleep-related event was significantly higher in RLS. In PLMD patients, the PLMI correlated negatively with the percentage of PLMS associated with an arousal, whereas this correlation was positive in RLS patients. Further, RLS patients spent significantly more time in wake-after-sleep onset, had more rapid eye movement sleep (REM) and less sleep stage I. **Conclusions**: We conclude that the sleep disorder in RLS differs from that in PLMD. Spontaneous, not PLM associated EEG arousals should be included in the assessment of the sleep structure of patients with RLS, particularly in studies concerned with drug-efficacy.

Keywords: Restless legs syndrome; Periodic limb movement disorder; Polysomnography

1. Introduction

Restless legs syndrome (RLS) is a condition in which patients at rest, especially in the evening and during the night, report leg paresthesias accompanied by an urge to move their legs [1]. According to the International Restless Legs Syndrome Study Group (IRLSSG) [2], obligatory features of RLS are: (1) a desire to move the extremities usually associated with some definable discomfort; (2) motor restlessness; (3) worsening of symptoms at rest with at least temporary relief by activity and (4) worsening of symptoms later in the day or at night. Non-obligatory features of RLS are involuntary movements including periodic limb movements in sleep (PLMS), which commonly occur in patients with idiopathic RLS [1], but sometimes are absent [3]. Isolated PLMS may further occur as periodic limb movement disorder (PLMD) without complaints of RLS [4]. There is controversy in the literature about whether PLMD leads to severe sleep disturbance or excessive daytime somnolence [5–8]. However, there is an interesting association of PLMD and RLS with attention deficit/hyperactivity disorder [9], and it has also been suggested that PLMD is associated with the age related decline in renal function and related to several highly specific symptoms of geriatric insomnia [10]. Increased PLMS are also seen in otherwise healthy individuals [11]. Cross-sectional questionnaire studies revealed a 3.9% prevalence of PLMD and a 5.5%prevalence of RLS [12]. The etiology of PLMS has not been elucidated, but their occurrence in patients with complete spinal cord injury indicates that spinal mechanisms are involved [13], whereas dysfunction in the diencephalospinal system is discussed with RLS [14].

It is unclear whether PLMD represents a clinically less

Abbreviations: RLS, restless legs syndrome; *P*, level of significance; PLMD, periodic limb movement disorder; PLMAI, periodic limb movement associated arousal index; TAI − PLMAI, spontaneous arousal index (total arousal index − periodic limb movement associated arousal index); *, statistically significant.

* Corresponding author. Tel.: +49-89-7095-3904; fax: +49-89-7095-3677.

E-mail address: eisen@nefo.med.unio-muenchen.de (I. Eisensehr).

1389-9457/03/$ - see front matter © 2003 Elsevier Science B.V. All rights reserved.
doi:10.1016/S1389-9457(03)00004-2

severe form of RLS – in other words whether PLMD represents the sleep disorder of RLS without limb paresthesias. The present study investigated whether the polygraphic measured sleep disorder in PLMD is different from the sleep disorder in RLS.

2. Methods

2.1. Study population

Patients were diagnosed to have PLMD if they had more than five periodic limb movements per hour of sleep, occurring independent of arousals, without any complaint of RLS but with complaints of insomnia and/or daytime sleepiness. The diagnosis of PLMD was based exclusively on the results of the polysomnography (PSG) and additional clinical complaints of insomnia or daytime sleepiness in the absence of other sleep disorders.

Twenty-seven patients with RLS (RLS patients) and 26 patients with PLMD but no RLS (PLMD patients), examined by a neurologist, experienced in sleep studies, were included in the study. The RLS patients were recruited prospectively and consecutively. PLMD patients were matched retrospectively according to age and sex (Table 1). PLMD patients were recruited consecutively from a 3-year time period if they fulfilled the inclusion and exclusion criteria.

PLMD was diagnosed if patients did not complain of RLS symptoms but reported problems with nocturnal sleep or daytime sleepiness, and if their PSG showed more than five PLMS per hour of sleep in the absence of any other significant sleep disorder. PLMD patients were initially referred to the sleep lab because of difficulties in maintaining sleep: frequent nocturnal awakenings without difficulties initiating sleep (69.3%), daytime sleepiness without insomnia (19.2%) and daytime sleepiness associated with insomnia (11.5%), where insomnia relates to difficulties initiating and maintaining sleep. Therefore, all PLMD patients were suffering from clinical correlates to PLMS. Two PLMD patients with complaints about sleep maintenance had been treated with continuous positive airway pressure (CPAP) at the time of the study because of previously diagnosed obstructive sleep apnea. Patients who received sleep- or PLMD-influencing medications (benzodiazepines, anticonvulsants, antidepressants, dopaminergics, clonidine, opiates) within 1 week prior to the sleep study or had an untreated sleep-related respiratory disorder (i.e. snoring, sleep apnea syndrome) were excluded.

Patients were diagnosed with RLS if they fulfilled the four criteria proposed by IRLSSG [2]. After the initial PSG, patients with RLS have been treated with dopaminergic medications and are examined every 6 months in our RLS outpatient service.

2.2. Sleep studies

Digital PSG recording systems (Telefactor Corporation, West Conshohocken, PA, USA; Brainlab, Schwarzer, Munich, Germany) were used. Recording began around 10 p.m. and ended at 6 a.m. The PSG included six channels of electroencephalogram (EEG, two paracentral, two frontal, two occipital), electro-oculogram (EOG) and mental and submental electromyogram (EMG). The surface EMGs of both anterior tibial muscles were recorded as described by Coleman [15]. Oro-nasal airflow was recorded with thermistors mounted over the nose and mouth, and thoracic and abdominal respiratory movements were recorded by impedance plethysmography. A microphone attached near the larynx recorded snoring. Arterial oxygen saturation was measured continuously via a non-invasive infrared finger probe. Electrocardiogram was recorded continuously between the forearms. Sleep staging followed the recommendations of Rechtschaffen and Kales [16]. An apnea was defined as a cessation of airflow lasting at least 10 s, accompanied by a drop of SaO_2 by more than 2% below the

Table 1
Comparison of sociodemographics and sleep variables in RLS patients vs. PLMD patients

	RLS	PLMD	Difference between RLS and PLMD (*P*-value)
Age (years)	52.1 ± 2.2	46.0 ± 2.6	NS
Sex (% of men)	33.3	53.8	NS
St I (% of TST)	19.4 ± 2.6	27.5 ± 1.7	0.004
St II (% of TST)	38.7 ± 3	39.4 ± 2	NS
St III and IV (SWS, % of TST)	18.1 ± 2.0	21.2 ± 1.7	NS
REM (% of TST)	19.1 ± 1.7	11.9 ± 1.3	0.002
Wake-after sleep-onset (min)	78.6 ± 10.4	49.4 ± 6.9	0.037
TST (h)	7 ± 3.3	5.5 ± 1.4	NS
Sleep stage I latency (min)	23.9 ± 7.8	25.6 ± 5.4	NS
Sleep stage II latency (min)	46 ± 11.6	40.7 ± 6	NS
Sleep stage REM latency (min)	130.9 ± 15.4	164.4 ± 16.5	NS
Sleep efficiency (%)	73.3 ± 3.3	79.3 ± 3.1	NS
Total number of patients	$N = 27$	$N = 26$	

h, hour; min, minutes; NS, not statistically significant; PLMD, periodic limb movement disorder; REM, rapid eye movement sleep; RLS, restless legs syndrome; sleep efficiency, total sleep time/time in bed; St, sleep stage; SWS, slow wave sleep; TST, total sleep time.

immediately preceding baseline. A combination of criteria widely used in ASDA-accredited sleep labs in the USA, according to Moser et al. was applied for hypopnea scoring [17]. Hypopnea was defined as a decrease of the airflow by 50% or more below the waking baseline, accompanied by a drop of SaO_2 by more than 2% below the immediately preceding baseline. Arousal scoring followed the guidelines suggested by the Atlas Task Force of the American Sleep Disorders Association [18], which describe a visual scoring method based on EEG and additional EMG of the chin during REM sleep.

2.3. Data presentation and statistics

Data were analyzed using the SPSS statistical package for Windows 7.5. They are presented as mean and standard error of the mean (SEM) if not stated otherwise. The data were tested for normal distribution with the Kolmogorow Smirnov test. Data points between the two study groups (RLS and PLMD) were compared using the Chi-square test, Mann–Whitney *U*-test, Wilcoxon rank sum *W*-test and *t*-test for normally distributed data. Data were analyzed for correlation by the Pearson correlation test if normally distributed and the Spearman correlation test if not normally distributed. A $P < 0.05$ was considered significant.

3. Results

3.1. Study population

The RLS patients were slightly older than PLMD patients (Table 1, not statistically significant). The mean duration of restless legs complaints in the RLS group was 11.9 ± 2.2 years.

3.2. Sleep stages

RLS patients had significantly more REM sleep and time spent awake after sleep onset but before final awakening (WASO) but less stage (st) 1 sleep than PLMD patients (Table 1). Total sleep time (TST), sleep latencies and sleep efficiency (SE, total sleep time divided by total time in bed, expressed as percent) were similar in both groups (Table 1).

3.3. PLMS and PLM arousals (Table 2, Fig. 1)

The PLM index (PLMI, number of periodic limb movements per hour of sleep) was higher in PLMD. Eight of the 27 RLS patients had a PLMI lower than 5/h. The index of arousal-associated PLMS (PLMAI, number of arousal-associated PLMS per hour of sleep) was higher in PLMD.

In PLMD patients, the PLMI correlated negatively with the percentage of PLMS associated with an arousal (Spearman's correlation coefficient = −0.462, $P = 0.017$), whereas this correlation was positive in RLS patients (Spearman's correlation coefficient = 0.432, $P = 0.024$). The PLMI correlated positively with the PLMAI only in RLS (RLS: Spearman's correlation coefficient = 0.922, $P < 0.0001$, PLMD: Spearman's correlation coefficient = 0.360, $P = 0.071$).

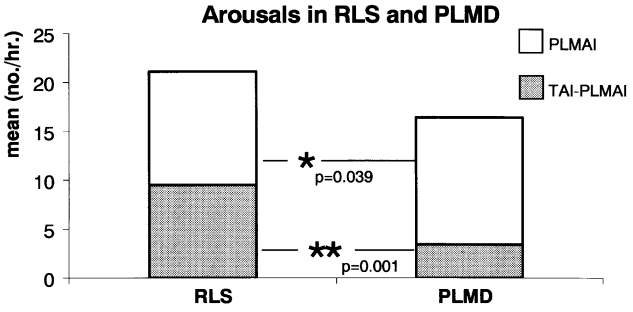

Fig. 1. Frequency of spontaneous and PLM-associated arousals in RLS and PLMD patients. The total arousal index per hour of total sleep time does not differ significantly between groups. However, the number of spontaneous arousals per hour of total sleep time is significantly higher in the RLS group whereas the number of PLM-associated arousals per hour of total sleep time is significantly lower than in the PLM group.

3.4. Non-specific arousals (Table 2, Fig. 1)

The index of EEG arousals not associated with any sleep-related event (total arousal index (TAI) − PLMAI, number of EEG arousals not associated with any other sleep-related event per hour of sleep) was higher in RLS patients compared to pure PLMD patients.

When the eight RLS patients without PLMS were excluded from the statistical analysis, we obtained similar PLMIs and WASOs in both groups. The results regarding EEG arousals, sleep stage percentages, sleep latencies and sleep efficiency remained unchanged. The positive correlation between PLMI and the percentage of PLMS-associated EEG arousals was no longer significant in the RLS group. When re-explored 1–2 years after the initial PSG, none of the RLS patients were complaining about daytime sleepiness after being successfully treated for the RLS symptoms. Patients with PLMD who reported daytime sleepiness ($n = 8$) had a mean TAI − PLMAI of 2.1/h (range: 0–9.4/h).

4. Discussion

Unlike RLS, pure PLMD is not usually associated with motor abnormalities or complaints during the waking state. We investigated similarities in sleep structure and motor phenomena during sleep in RLS and pure PLMD. Our results show that several polysomnographic features in RLS differ from those in PLMD. Some selection bias is possible, since PLMD patients were age-matched 'retrospectively' to the 'prospectively' recruited RLS patients, but our intention

Table 2
Comparison of PLM and arousal indices in patients with RLS and patients with PLMD

	RLS	PLMD	Difference between RLS and PLMD (*P*-value)
TAI (No/h)	21.0 ± 2.6	16.4 ± 1.9	(NS)
PLMI (No/h)	26.4 ± 7.1	30.9 ± 4.0	(0.041)
PLMAI (No/h)	9.5 ± 2.0	13.0 ± 1.5	(0.039)
TAI − PLMAI (No/h)	11.6 ± 1.8	3.4 ± 0.7	(0.001)
PLMAI/PLMI (%)	35.4 ± 5.8	51.8 ± 5.6	(0.050)

PLMAI/PLMI, percentage of periodic limb movements which is associated with arousals; PLMAI, index of periodic limb movement associated arousals (number of periodic limb movement associated arousals per hour of total sleep time); PLMI, periodic limb movement index (number of periodic limb movements per hour of total sleep time); TAI–PLMAI, index of spontaneous arousals (number of spontaneous arousals per hour of total sleep time); TAI, total arousal index (number of arousals per hour of total sleep time).

was only to compare the sleep structures of RLS and PLMD patients.

4.1. Arousals

RLS patients have more EEG arousals occurring independent of PLMS than PLMD patients. Drewes et al. [19] showed that pain stimuli during sleep resulted in electroencephalographic arousal responses. RLS patients reported pain or crawling and creeping sensations in the legs or arms mainly while at rest in the evening, before sleep onset and after nocturnal awakening. These paresthesias or painful sensations probably persist during sleep because RLS patients often report them on waking at night. The work of Drewes et al. [19] suggests that the typical RLS pain could cause the EEG arousals not associated with PLMS or paresthesias during sleep.

Frequent non-specific EEG arousals (usually more than 10/h) also occur in upper airway resistance syndrome [20], which is characterized by periodically increased esophageal negative pressure, frequent snoring and daytime sleepiness. Despite the low number of spontaneous EEG arousals per hour of sleep (never more than 10/h) among PLMD patients who complained of daytime sleepiness, we cannot exclude the possibility that some PLMD patients had an underlying upper airway resistance syndrome. Although we did not employ esophageal balloon or catheter to detect simultaneous decreases of esophageal pressure with each breath, we never observed snoring in the sensitive microphone channel of the PSG or in the audio of the videotape. After successful treatment of RLS symptoms with dopaminergic agents (pergolide and levodopa) administered exclusively in the evening, no RLS patient complained about daytime sleepiness. This observation is contrary to some clinical observations that sleepiness may be a common adverse effect of dopaminergic therapy. However, our evening use of L-dopa and pergolide, both known to have a short half-life and, therefore, a potential low-risk of side effects during the daytime, may explain this. Moreover, daytime sleepiness was not observed as an adverse effect in randomized controlled trials of pergolide and levodopa in RLS [21–23]. Dopaminergic medications are also reported to fragment sleep, which may result in daytime sleepiness, but effective dopaminergic therapy with pergolide and levodopa in RLS usually improves sleep quality, even if normal sleep is not reached. Since dopaminergic agents are not effective in upper airway resistance syndrome, it is very unlikely that upper airway resistance syndrome contributed to the non-PLM associated EEG arousals.

Although we did not score autonomic arousals or perform spectral analyses on EEGs, and, therefore, can only comment on the visually detectable EEG arousals (which indicated differences between RLS and PLMD), there is vast literature about the relevance of autonomic arousals unreflected by changes in the spectral analysis of EEG and microarousals detected only by spectral analysis. PLMS without EEG arousal have been associated with tachycardia and increased delta and theta activity in RLS and PLMS patients [24–26]. Autonomic activation not associated with EEG arousals was shown to affect daytime vigilance in normal individuals [27]. Further investigation is needed to determine whether sleep structure of pure PLMD, in terms of autonomic, delta and theta arousals, is different from that of RLS.

4.2. Periodic limb movements of sleep

PLMS varied considerably from night to night in PLMD patients, possibly influencing our results. However, the night-to-night variations did not reach statistical significance in earlier studies [28,29]. The inter-scorer reliability, not assessed in this study, could also have somewhat influenced our results.

A PLMI of more than 5 or 10/h is commonly used as a supportive criterion of RLS. However, PLMD is seen in a large number of people, especially the elderly, who have no RLS complaints [30]. Montplaisir et al. [3] found that about 20% of 133 RLS patients had a PLMI lower than 5/h. Slightly (not significantly, by Chi-square test) more number of patients in our study than in Montplaisir et al. ($n = 8$; 30%) reported typical RLS complaints without PLMS during PSG. The increased rate of RLS patients without PLMS in our study could be due to differences in RLS severity, although this was not adequately assessed in either study. Our findings confirm the low sensitivity of PLMS for diagnosing RLS. However, the higher the PLMI in RLS

patients, the greater was the percentage of PLMS associated with an EEG arousal. On the other hand, we found a negative correlation of PLMI with the percentage of arousal-associated PLMS in PLMD. Thus, in addition to non-specific EEG arousals, PLMS indicate to some extent the arousability and sleep disruption in RLS, but not in PLMD.

4.3. Sleep stages

We found that RLS patients had more REM sleep than PLMD patients, who had increased stage 1 sleep. The administration of L-dopa reduces REM sleep in rats [31]. Thus, it can be speculated that increased REM sleep in RLS could be the result of reduced L-dopa in the striatal area, supporting the results of some imaging studies that reveal mild striatal dopaminergic deficit in RLS patients [32–35]. There are, however, contradictory studies that found no alteration of the striatal dopaminergic system in RLS [36,37].

5. Conclusion

RLS and PLMD are two polysomnographically distinct disturbances of sleep patterns opposing the hypothesis that PLMD might be a less severe form of RLS. To the best of our knowledge, this is the first study to compare the sleep structure of RLS with that of pure PLMD. Our findings suggest that different pathophysiological mechanisms may influence sleep in RLS and pure PLMD. Our results further suggest that non-specific EEG arousals may be a potential discriminative polysomnographic characteristic between RLS and pure PLMD, pointing to the inclusion of spontaneous EEG-arousals in the evaluation of sleep disorders and drug therapy in RLS patients.

References

[1] Ambrosetto C, Lugaresi E, Coccagna G, Tassinari CA. Clinical and polygraphic remarks in the restless legs syndrome. Riv Patol Nerv Ment 1965;86:244–51.

[2] The International Restless Legs Syndrome Study Group (Walters AS, Group Organizer and Correspondent), Toward a better definition of the restless legs syndrome. Mov Disord 1995;10:634–42.

[3] Montplaisir J, Boucher S, Poirier G, et al. Clinical, polysomnographic, and genetic characteristics of restless legs syndrome: a study of 133 patients diagnosed with new standard criteria. Mov Disord 1997;12: 61–5.

[4] Bixler EO, Kales A, Velo-Bueno A, et al. Nocturnal myoclonus and nocturnal myoclonic activity in a normal population. Res Commun Mol Pathol Pharmacol 1982;36:129–40.

[5] Lugaresi E, Coccagna G, Montavani M, Lebrun R. Some periodic phenomena arising during drowsiness and sleep in man. Electroenceph clin Neurophysiol 1972;32:701–5.

[6] Karadeniz D, Ondze B, Besset A, Billiard M. Are periodic leg movements during sleep (PLMS) responsible for sleep disruption in insomnia patients? Eur J Neurol 2000;7:331–6.

[7] Guilleminault C, Raynal D, Weitzman ED, Dement WC. Sleep related periodic myoclonus in patients complaining of insomnia. Trans Am Neurol Assoc 1975;100:19–21.

[8] Coleman RM. Periodic movements in sleep (Nocturnal myoclonus) and restless legs syndrome. In: Guilleminault C, editor. Sleeping and waking disorders. Menlo Park, CA: Addison-Wesley; 1982 p. 265–95.

[9] Chervin RD, Archbold KH, Dillon JE, et al. Association between symptoms of inattention, hyperactivity, restless legs, and periodic leg movements. Sleep 2002;25:213–8.

[10] Bliwise D, Petta D, Seidel W, Dement W. Periodic leg movements during sleep in the elderly. Arch Gerontol Geriatr 1985;4:273–81.

[11] Hening WA, Allen RP, Walters AS, Chokroverty S. Motor functions and dysfunctions during sleep. In: Chokroverty S, editor. Sleep disorders medicine: basic science, technical considerations, and clinical aspects. Boston, MA: Butterworth-Heinemann, 1999. p. 441–507.

[12] Ohayon MM, Roth T. Prevalence of restless legs syndrome and periodic limb movement disorder in the general population. J Psychosom Res 2002;53:547–54.

[13] Yokota T, Hirose K, Tanabe H, Tsukagoshi H. Sleep-related periodic leg movements (nocturnal myoclonus) due to spinal cord lesion. J Neurol Sci 1991;104:13–18.

[14] Bucher SF, Seelos KC, Oertel WH, et al. Cerebral generators involved in the pathogenesis of the restless legs syndrome. Ann Neurol 1997; 41:639–45.

[15] Coleman RM. Periodic movements in sleep (nocturnal myoclonus and restless legs syndrome). In: Guilleminault C, editor. Sleeping and waking disorders. Menlo Park, CA: Addison-Wesley, 1982. p. 265–95.

[16] Rechtschaffen A, Kales A, editors. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Bethesda, MD: US Department of Health, Education, and Welfare, Public Health Service – National Institutes of Health, National Institute of Neurological Diseases and Blindness, Neurological Information Network, 1968.

[17] Moser NJ, Phillips BA, Berry DTR, Harbison L. What is hypopnea, anyway? Chest 1994;105:426–8.

[18] The Atlas Task Force of the American Sleep Disorders Association. EEG arousals: scoring rules and examples. A preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. Sleep 1992;16:174–84.

[19] Drewes AM, Nielsen KD, Arendt-Nielsen L, et al. Pain and sleep. The effect of cutaneous and deep pain on the electroencephalogram during sleep – an experimental study. Sleep 1997;20:632–40.

[20] Guilleminault C, Stoohs R, Clerk A, et al. A cause of excessive daytime sleepiness: the upper airway resistance syndrome. Chest 1993;104:781–7.

[21] Stiasny K, Wetter TC, Winkelmann J, et al. Long-term effects of pergolide in the treatment of restless legs syndrome. Neurology 2001; 56:1309–42.

[22] Wetter TC, Stiasny K, Winkelmann J, et al. A randomized controlled study of pergolide in patients with restless legs syndrome. Neurology 1999;52:944–50.

[23] Collado-Seidel V, Kazenwadel J, Wetter TC, et al. A controlled study of additional sr-L-dopa in L-dopa-responsive restless legs syndrome with late night symptoms. Neurology 1999;52:285–90.

[24] Sforza E, Nicolas A, Lavigne G, et al. EEG and cardiac activation during periodic leg movements in sleep. Support for a hierarchy of arousal responses. Neurology 1999;52:786–91.

[25] Sforza E, Juony C, Ibanez V. Time-dependent variation in cerebral and autonomic activity during periodic leg movements in sleep: implications for arousal mechanisms. Clin Neurophysiol 2002;113: 883–91.

[26] Winkelman JW. The evoked heart rate response to periodic leg movements of sleep. Sleep 1999;22:575–80.

[27] Martin SE, Wraith PK, Deary IJ, Douglas NJ. The effect of nonvisible

sleep fragmentation on daytime function. Am J Respir Crit Care Med 1997;155:1596–601.
[28] Bliwise DL, Carskadon MA, Dement WC. Nightly variation of periodic leg movements in sleep in middle aged and elderly individuals. Arch Gerontol Geriatr 1988;7:273–9.
[29] Mosko SS, Dickel MJ, Ashurst J. Night-to-night variability in sleep apnea and sleep-related periodic leg movements in the elderly. Sleep 1988;11:340–8.
[30] Ancoli Israel S, Kripke DF, Klauber MR, et al. Periodic limb movements in sleep in community-dwelling elderly. Sleep 1991;14: 496–500.
[31] Galarraga E, Corsi Cabrera M, Sangri M. Reduction in paradoxical sleep after L-Dopa administration in rats. Behav Neural Biol 1986;46: 249–56.
[32] Ruottinen HM, Partinen M, Hublin C, et al. A FDOPA PET study in patients with periodic limb movement disorder and restless legs syndrome. Neurology 2000;54:502–4.
[33] Staedt J, Stoppe G, Kogler A, et al. Nocturnal myoclonus syndrome (periodic movements in sleep) related to central dopamine D2-receptor alteration. Eur Arch Psychiatry Clin Neurosci 1995;245: 8–10.
[34] Turjanski N, Lees AJ, Brooks DJ. Striatal dopaminergic function in restless legs syndrome. 19F-dopa and 11C-raclopride PET studies. Neurology 1999;52:932–7.
[35] Michaud M, Soucy JP, Chabli A, et al. SPECT imaging of striatal pre- and postsynaptic dopaminergic status in restless legs syndrome with periodic leg movements in sleep. J Neurol 2002;249:164–70.
[36] Trenkwalder C, Walters AS, Henning WA, et al. Positron emission tomographic studies in restless legs syndrome. Mov Disord 1999;14: 141–5.
[37] Eisensehr I, Wetter TC, Linke R, et al. Normal IPT and IBZM SPECT in drug-naive and levodopa-treated idiopathic restless legs syndrome. Neurology 2001;57:1307–9.