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A Polysomnographic Study on Periodic Limb Movements in Patients with Restless Legs Syndrome and Neuroleptic-induced Akathisia

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ABSTRACT

Eighteen patients with restless legs syndrome (RLS) and 4 patients with neuroleptic-induced akathisia (NIA) underwent all-night polysomnographic recordings before and during clonazepam treatment. Ten normal control subjects and 4 non-akathitic psychiatric patients treated with neuroleptics underwent polysomnographic recordings, which were compared with those of the RLS and NIA patients, respectively. Daily treatment with 0.5 to 3 mg clonazepam improved subjective complaints of 17 out of 18 patients with RLS and all the 4 patients with NIA. All the 18 patients with RLS exhibited periodic limb movements (PLM) on the polysomnograms before treatment, but only 2 of 10 control subjects exhibited PLM. Three of the 4 patients with NIA exhibited PLM, but none of the 4 controls on neuroleptics showed PLM. Clonazepam decreased the total number of PLM per hour in patients of both RLS and NIA.

Key words: *Periodic limb movement disorder, Restless legs syndrome, Akathisia*

Neuroleptic-induced akathisia (NIA) is a frequent side effect of pharmacotherapy for psychosis. Akathisia is diagnosed only by inquiring about symptoms and by observing motor restlessness in patients, as there are no specific laboratory findings. Restless legs syndrome (RLS) is characterized by severe dysesthesia, such as feeling as if ants are crawling under the skin, and by a discomfort deep inside the lower limbs, rarely including the upper limbs. Patients with RLS complain of a restlessness manifested by pacing, foot rubbing, tossing and turning in bed, and sometimes marching in place or rocking movements. Manifestations often become worse when the patient is in bed at night. The clinical picture of NIA is similar to that of RLS, but some differences are pointed out between two conditions[39)].

RLS is frequently associated with periodic limb movement disorder (PLMD)[2,9)], which is characterized by stereotyped dorsi-flexion movements at the ankle joint and flexion movements at the knee and hip joints. They usually repeat at regular 20 to 40 sec intervals during non-rapid eye movement (non-REM) sleep, and although originally called nocturnal myoclonus, they are usually not as brief as "true" myoclonus[3,7,38)]. Furthermore, it has been reported that clonazepam improves RLS[19)].

These features of RLS led us to examine whether clonazepam also improves NIA or not. In the present study, we treated patients with RLS and NIA with clonazepam and quantified PLM in polysomnographic findings.

MATERIALS AND METHODS

Eighteen patients with a prolonged history of restlessness and dysesthesias which were worse at night and were not attributable to neuroleptics, neuropathy, or other causes, were selected at the clinic of psychiatry of Ehime University Hospital (Table 1). They were 8 males and 10 females with a mean age of 71 (range 65–88). The dysesthesia in all 18 patients was identified as a discomfort deep inside the lower limbs. One patient also showed restless arms. They were classified as moderate or severe RLS according to ASDA (American Sleep Disorders Association) Criteria[2)]. The mean duration of illness was 15 years (range 2–45 years). All 18 patients also had a history of sleep disturbance. Ten control subjects, who were

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Table 1. Profiles of RLS patients and non-RLS control subjects

RLS Case	Age	Sex	Past History	Present Concurrent Illness
1	65	male	pneumonia	anemia
2	65	female	ovarian cyst	hypertension
3	66	female	(–)	(–)
4	66	female	(–)	hypertension
5	66	male	(–)	(–)
6	66	male	subarachnoid bleeding	angina pectoris
7	66	male	(–)	(–)
8	68	female	uterine cancer	(–)
9	69	female	(–)	hyperlipidemia
10	69	female	epilepsy	(–)
11	70	male	lung tuberculosis	(–)
12	70	male	(–)	angina pectoris
13	71	female	uterine myoma	(–)
14	73	male	liver disease	(–)
15	73	female	(–)	(–)
16	75	female	(–)	(–)
17	81	female	(–)	(–)
18	88	male	(–)	hypertension
non–RLS Control				
1	65	male	(–)	(–)
2	65	male	gastric ulcer	(–)
3	65	male	(–)	(–)
4	68	female	(–)	(–)
5	68	female	(–)	(–)
6	70	female	(–)	(–)
7	70	female	pneumonia	(–)
8	75	male	(–)	(–)
9	75	female	(–)	(–)
10	90	female	lung tuberculosis	(–)

without psychiatric or physical disorders and had taken medication for at least one year, were compared with the RLS patients (4 males, 6 females; mean age 70, range 65–90). No significant difference in sex and age was found between RLS patients and controls.

Four patients with schizophrenic disorder receiving neuroleptics and antiparkinsonian drugs were diagnosed as suffering from acute neuroleptic-induced akathisia (NIA)[4] at the clinic of psychiatry of Ehime University Hospital (Table 2). These patients, 2 males and 2 females (mean age 41 years), met DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, 3rd ed. revised)[1] criteria for schizophrenic disorder and had been treated with oral neuroleptics and antiparkinsonian drugs for a mean duration of 3 months. Patients with dystonia, dyskinesia, parkinsonism or other physical disorders were excluded. To compare patients with NIA, we selected 4 patients with schizophrenic disorder who also met DSM-III-R criteria, and had been taking oral neuroleptics and antiparkinsonian drugs for a mean duration of 3 months without NIA. They were 2 males and 2 females (mean age 39 years) without any extrapyramidal symptoms such as dystonia or dyskinesia. No significant difference in sex, age, and duration of neuroleptic treatment was observed between patients with NIA and without NIA.

All RLS and NIA patients and their control subjects underwent conventional all-night recording including electroencephalography using standard recording techniques (electrode pairs used: O_1–A_2, O_2–A_1, C_3–A_2, C_4–A_1), electrooculography (electrodes at left and right bilateral canthus), mentalis electromyography, spirography (nasal air flow), electrocardiography, and limbs electromyograms (surface electrodes placed on both tibialis anterior and extensor hallucis longus muscles). One PLM was counted when one leg movement resulted in at least one-half of the amplitude of maximal ankle dorsiflexion, either of the unilateral muscle or simultaneously of the

Table 2. Profiles of NIA patients and non-NIA control subjects

NIA Cases	Age	Sex	Neuroleptics (mg/day)		Antiparkinsonian Drugs (mg/day)	
1	37	female	chlorpromazine	100	biperiden	1
			haloperidol	1.5	promethazine	80
2	41	male	chlorpromazine	25	profenamine	60
			sultopride	300	promethazine	12.5
			zotepine	150		
3	42	female	chlorpromazine	12.5	biperiden	2
			haloperidol	3	promethazine	25
					trihexyphenidyl	4
4	43	male	chlorpromazine	25	biperiden	3
			haloperidol	6		
non-NIA controls						
1	33	male	chlorpromazine	50	biperiden	3
			haloperidol	3		
2	36	female	haloperidol	3	biperiden	3
			bromperidol	3	promethazine	12.5
3	41	male	haloperidol	3	biperiden	3
			sulpiride	300		
4	45	female	chlorpromazine	120	biperiden	3
			haloperidol	3	promethazine	75

bilateral muscle[7]. Additionally, a PLM was scored only when it occurred as part of a series of five or more consecutive movements lasting 0.5 to 5.0 sec, with an interval between movements of 5 to 90 sec[9]. A PLM index (number of PLM per hour of sleep) greater than 5 was considered pathologic[28]. Sleep stages were determined in 10 sec epochs, according to the standardized manual[33].

Eighteen patients with RLS received an initial dose of 0.5 mg clonazepam orally 30 min before bed time. As they reported their subjective responses, the individual dosage was adjusted in 0.5 mg steps for 15 to 34 days (mean 24 days). Adjustment stopped once a patient reported a good subjective response. Before and during clonazepam treatment, all RLS patients underwent all-night recordings. Patients were asked whether restlessness or dysesthesias changed during each phase of treatment. We compared the PLM characteristics polysomnographically before and during treatment.

Four patients with NIA were initially treated with oral clonazepam at a dose of 1.5 mg daily without changing the dose of neuroleptics and antiparkinsonian medications. The effectiveness of clonazepam was evaluated according to the complaints of the patients and objective observations using the Clinical Assessment for Akathisia designed by Yagi[41]. The dosage of clonazepam was adjusted in 0.5 mg steps to 4 mg daily. Before and during clonazepam treatment, all NIA patients underwent all-night recordings. We compared their PLM characteristics before and during treatment.

Each control subject also underwent an all-night recording. Informed consent was obtained from all patients and controls. A statistical analysis was carried out by Wilcoxon's signed rank test.

RESULTS

Therapeutic Response

Seventeen of 18 patients with RLS reported subjective improvement of restlessness, dysesthesias, and sleep disturbances within 3 days from the start of clonazepam treatment. The effective dosage of clonazepam was in the range of 0.5–1.5 mg per night (ten patients received 0.5 mg, three 1 mg, and one 1.5 mg). One patient (Case 15) who had "restless arms" reported no subjective improvement with clonazepam treatment by 0.5 mg up to 2 mg per night. All 4 patients with NIA resolved their symptoms within 8 days from the start of treatment. The effective dosage of clonazepam ranged from 1.5 to 3 mg daily (two pa-

tients received 1.5 mg, one 2.5 mg, and one 3 mg). No serious side effects were observed.

Polysomnographic Findings:

A case example (RLS Case 1)

Figure 1 shows the all-night polysomnogram of Case 1 with RLS. Periodic muscular discharges of PLM appeared repetitively in the EMGs recorded from bilateral anterior tibialis and extensor hallucis longus muscles. The intervals between the discharges were about 20 sec, with discharge periods of 3 to 4 sec. Soon after the onset of each discharge, arousal responses appeared in the mentalis EMG and EEG.

In Case 1, we counted a total number of 117 PLM in the left leg and 5 in the right before medication (Fig. 2 (a)). After clonazepam treatment for 18 days, we counted a total number of 17 PLM in the left leg and 1 PLM in the right (Fig. 2 (b)). Both the total number of PLM and the

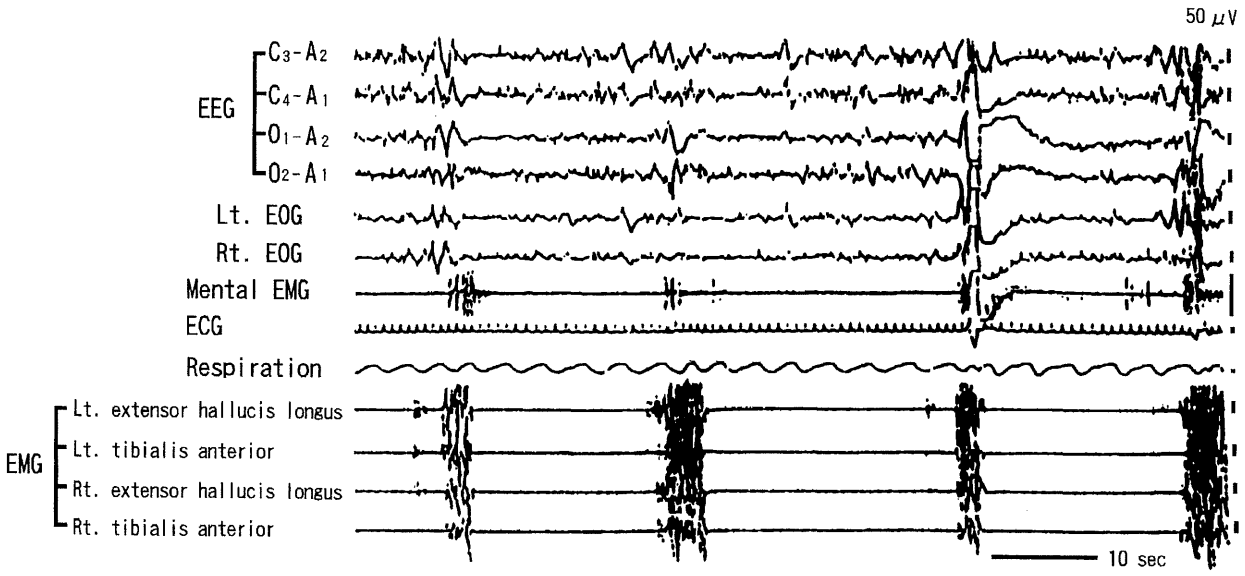

Fig. 1. PLM of RLS Case 1 (65 year-old male with sleep disturbance)
Rhythmic PLM discharges were observed bilaterally on the tibialis anterior and extensor hallucis longus muscles. The interval was about 20 seconds and duration was 3 to 4 sec.

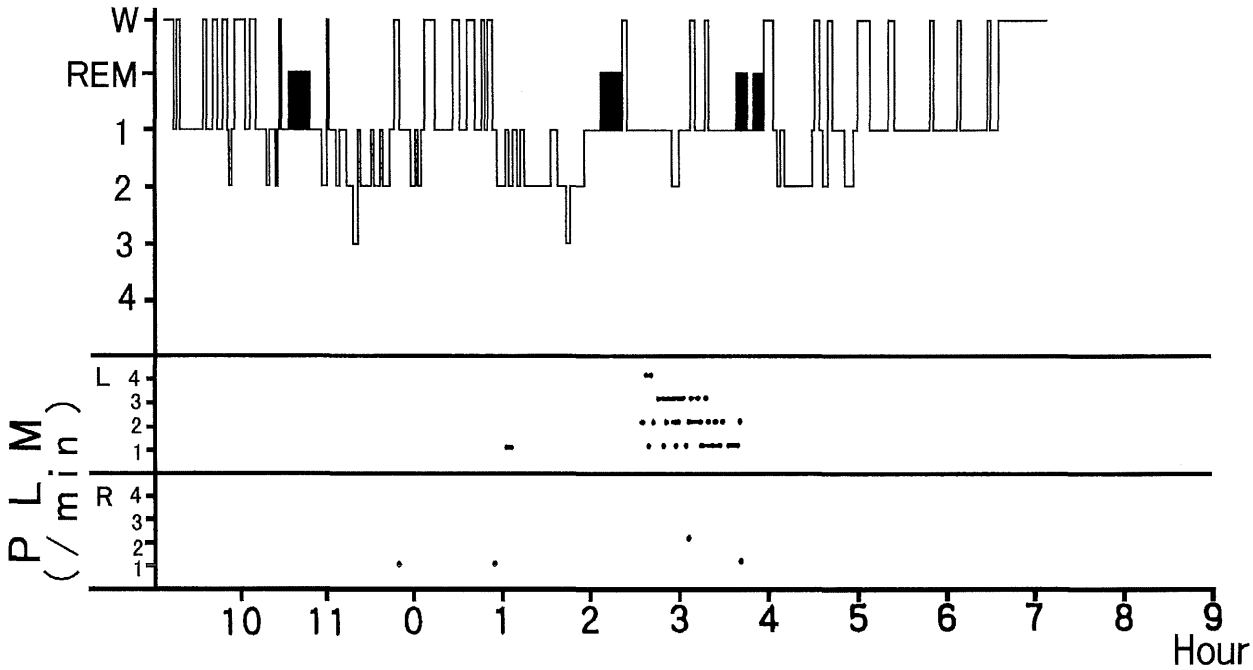

Fig. 2 (a). Sleep pattern and number of PLM per minute before treatment (RLS Case 1)
The upper part of the figure shows the sleep pattern. The number of PLM per minute in both legs is demonstrated in the lower part of the figure.

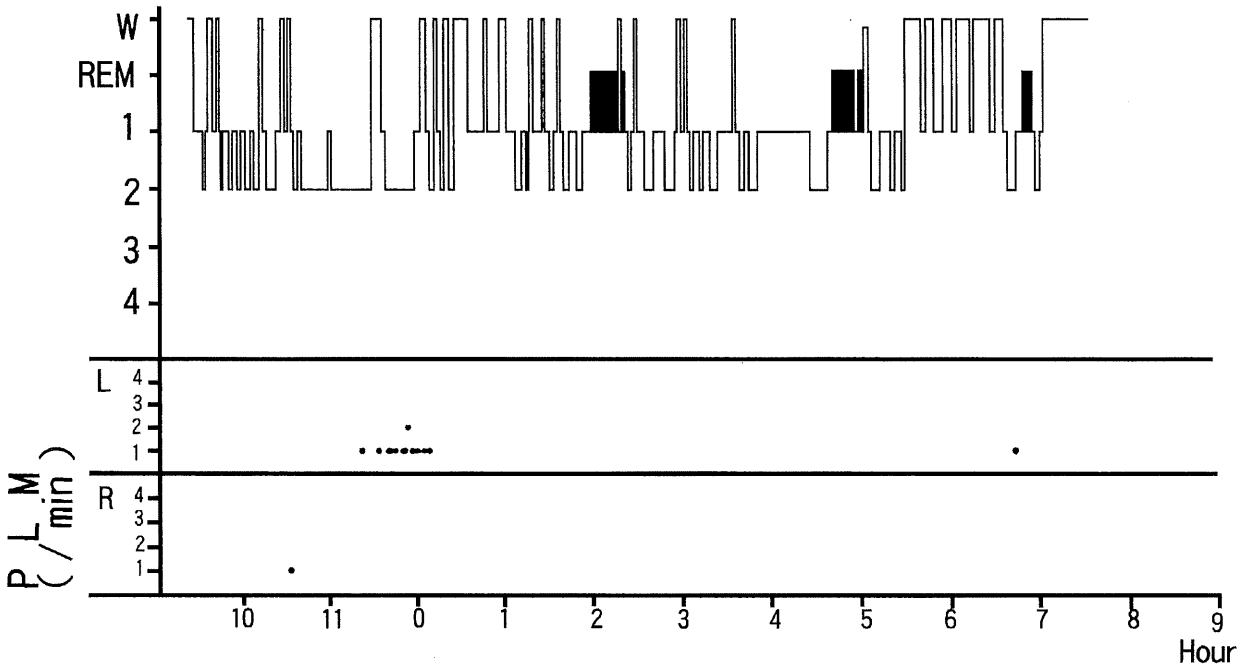

Fig. 2 (b). Sleep pattern and number of PLM per minute during treatment (RLS Case 1)
The sleep pattern is shown in the upper part of the figure. The number of PLM per minute is shown in the lower part of the figure.

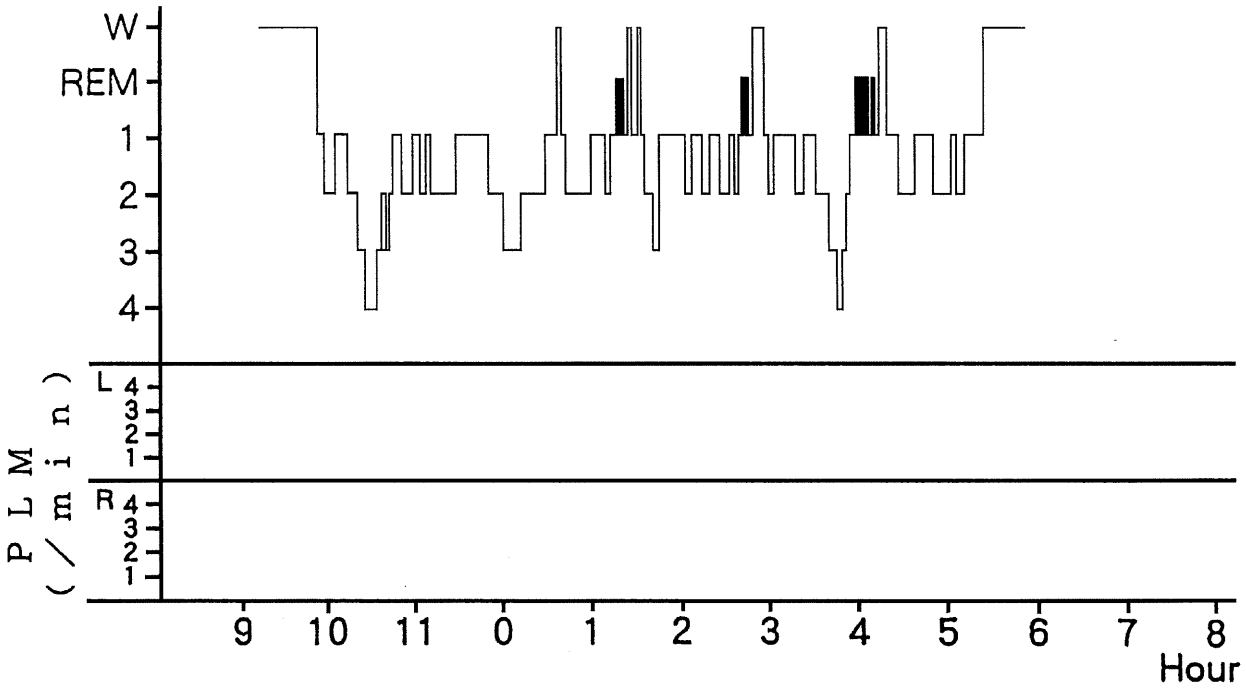

Fig. 2 (c). Sleep pattern and numbers of PLM per minute (Non-RLS Control Case 3)
No PLM are shown in this figure.

number of PLM per hour during sleep decreased in both legs while under medication. Frequent awakenings were recorded both before and during treatment with relatively scarce stage 3 and 4 sleep.

Total Number of PLM

All patients with RLS showed PLM on polysomnograms both before and during clonazepam treatment. We compared the total number of PLM bilaterally before and during medication. Cases with a decrease in numbers of PLM are shown by solid lines and those with an increase

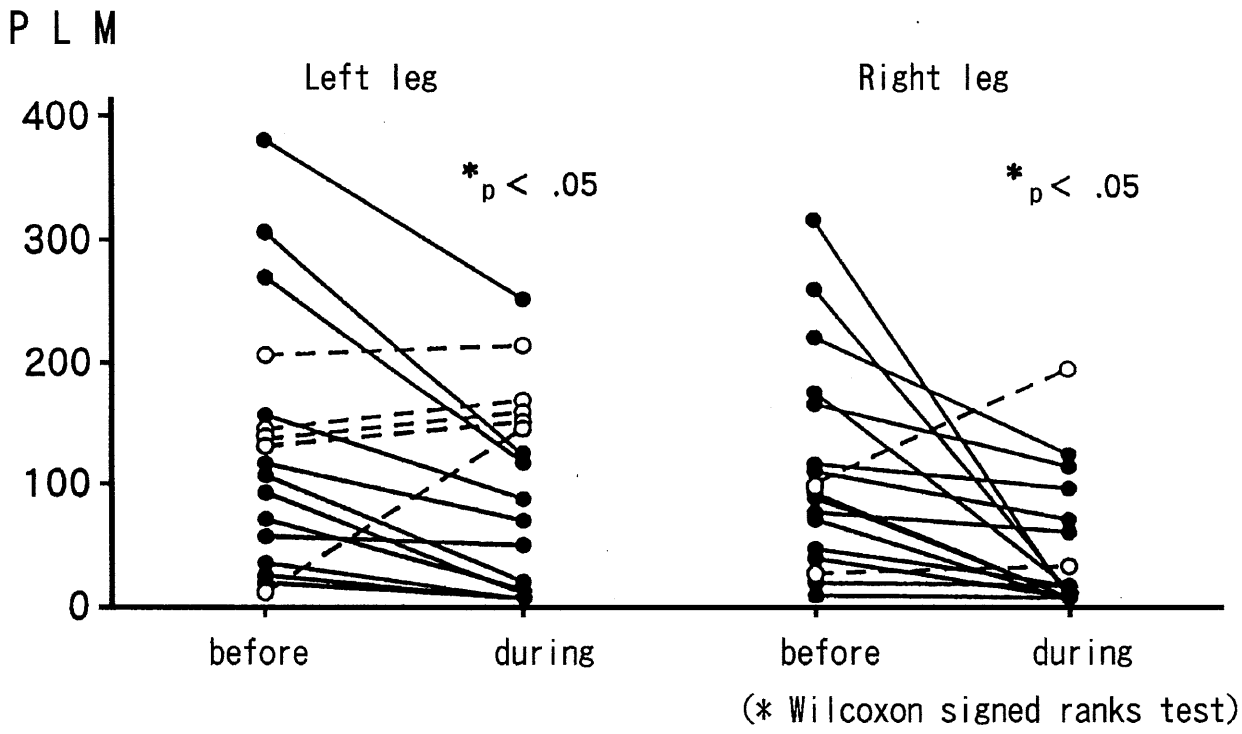

Fig. 3. Total numbers of PLM in RLS patients before and during treatment
Cases with a decreased number of PLM are shown by solid lines, and cases with an increased number of PLM are shown by broken lines.

Table 3. PLM of NIA patients

Case	left right	total number of PLM		number of PLM per hour		mean interval of PLM(sec)	
		before	during	before	during	before	during
1	left	143	27	81	5	32.1	47.5
	right	132	20	76	4	35.0	48.1
2	left	62	9	8.5	1	32.4	45.2
	right	133	26	18.3	4	27.8	43.8
3	left	17	0	1.7	0	49.1	(–)
	right	40	2	4.0	0.2	46.5	60.3
4	left	0	0	0	0	(–)	(–)
	right	0	0	0	0	(–)	(–)

in numbers of PLM by broken lines (Fig. 3). Clonazepam decreased significantly the total number of PLM bilaterally ($p<.05$).

Two control subjects without RLS exhibited PLM. The sleep recording of a control subject (non-RLS Control 3) was shown in Fig. 2 (c). He had a generally stable sleep with less frequent awakenings and more frequent stage 3 and 4 sleep than RLS patients.

Remarkable changes in PLM with clonazepam treatment were observed in three out of 4 NIA patients (1–3) in both their legs (Table 3). Clonazepam decreased their total number of PLM bilaterally. Case 4, the mildest one according to the Clinical Assessment for Akathisia[40], did not show any PLM before or during treatment. No non-NIA controls showed any PLM.

Number of PLM per hour

The number of PLM per hour significantly decreased on each side during clonazepam treatment in patients with RLS (left, $p<.05$; right, $p<.01$) (Fig. 4). The number of PLM per hour decreased bilaterally in NIA patients on each side during clonazepam treatment (Case 1–3 in Table 3).

Inter-movement Intervals

The inter-movement intervals were prolonged in 7 RLS patients, and shortened in 4 RLS patients by clonazepam treatment (Fig. 5). Seven patients with PLM less than 10 were excluded. The mean inter-movement intervals in all 3 NIA cases were prolonged by treatment (Table 3).

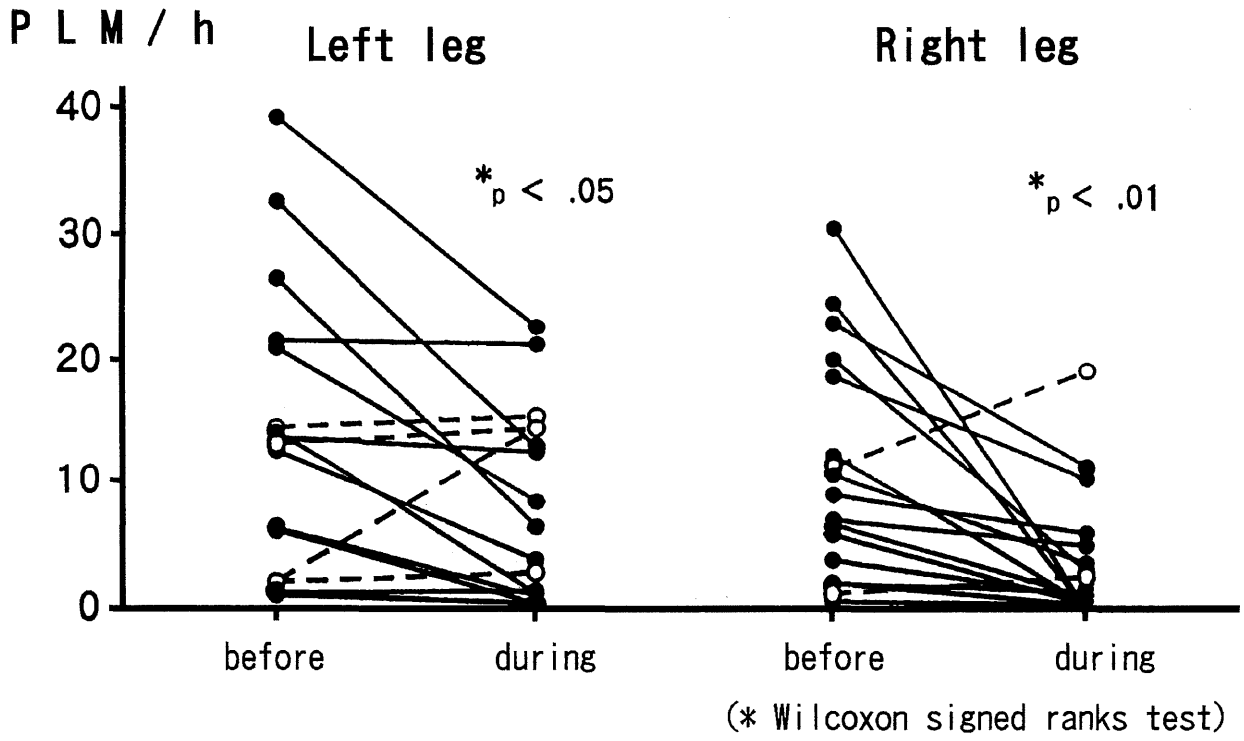

Fig. 4. Total numbers of PLM per hour in RLS patients before and during treatment
The frequency represents numbers of PLM in an hour. The solid and broken lines are explained in Fig. 4.

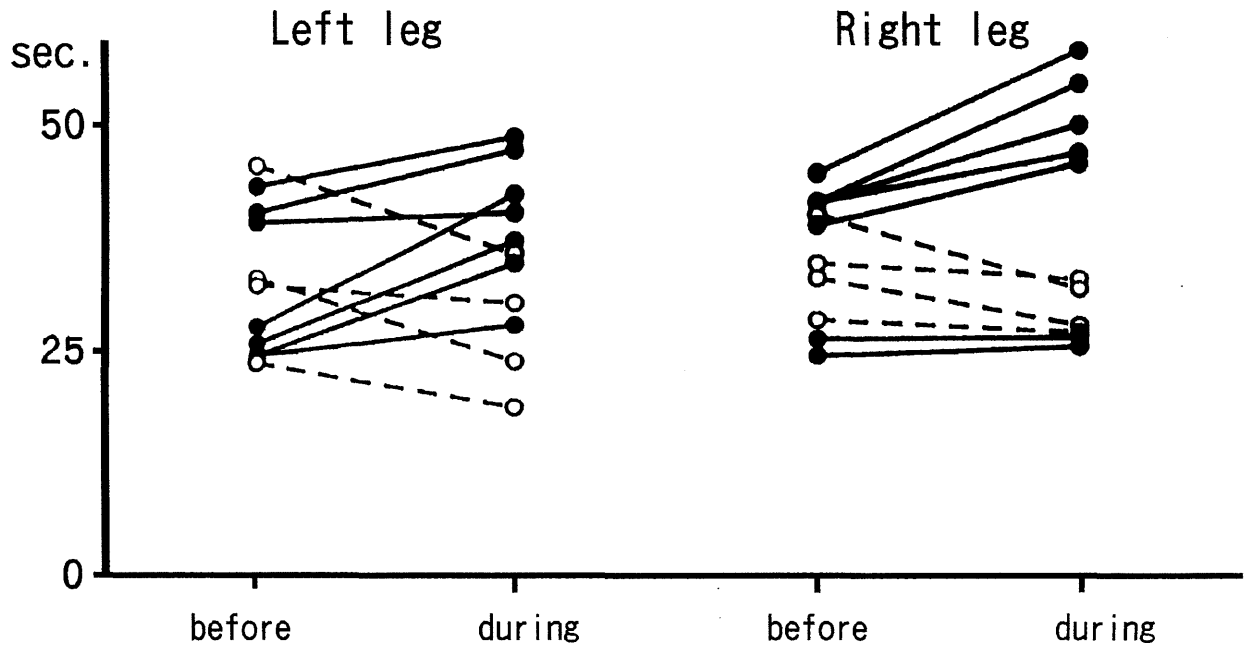

Fig. 5. Intervals between movements of PLM in RLS patients before and during treatment
Increased and decreased intervals before and during treatment are expressed by solid and broken lines, respectively.

DISCUSSION

Drugs such as vasodilators[10], analgesics[10], sedatives[10], hypnotics[10], iron[11] and anticonvulsants including clonazepam[5,26,36] have been reported to be of value in treating RLS. We examined the effect of clonazepam on RLS using 15 patients in our previous study[19].

Antiparkinsonian drugs such as biperiden or trihexyphenidyl have been recommended for treating NIA, though drugs such as propranolol[21] and clonazepam[17] have been reported to be effective. We first reported the usefulness of clo-

nazepam in 21 patients with NIA[16]. Sandyk reported a successful treatment of a NIA patient using baclofen and clonazepam in 1985[34].

In this study, clonazepam ameliorated symptoms of RLS and NIA in all patients except for one with RLS. Clonazepam is known to increase the waking threshold and muscle relaxation, making sleep stage 2 longer, and shortening sleep stages 3, 4 and REM[30]. Although symptoms of RLS and NIA in most of our patients were improved by clonazepam, the basic mechanism of RLS and NIA is still not fully clarified. We have reported that patients with RLS and NIA had significantly lower serum iron concentrations than controls[18], together with the effectiveness of iron treatment in NIA patients[20].

Except for one subject, all the RLS cases showed PLM in the present study. Few investigations have been performed on PLM in NIA. Lipinski et al. have reported that eight of nine patients with NIA exhibited 10 to 40 sec bursts of increased muscle tone before sleep onset on all-night polysomnography[22], and we also detected PLM in a patient with NIA on an all-night polysomnogram[29].

Mitchell first described PLMD as a specific sleep disorder[25]. He noted a similarity to "sleep jerks" on falling asleep and also suggested a possible relationship to "foot fidgets." Symonds considered it epileptic myoclonus, using the name "nocturnal myoclonus"[14,35], but Lugaresi et al recorded polysomnograms and found no epileptic activity on EEGs[23]. Since the pattern and length of the movements differed from those of true myoclonus[24], the term PMS (periodic movements in sleep) had been used[7,30]. Recently, PMS have been termed PLMD by the International Classification of Sleep Disorders (ICSD; 1990). PLM has been found in various sleep-wake disorders[6,7]. In the present study, 2 of 10 non-RLS control subjects exhibited PLM, but were unaware of them and did not complain of insomnia. Coleman et al. have reported that 53% of healthy elderly individuals have PLM by polysomnography[8].

A number of drugs such as clonazepam[31], baclofen[12], maprotiline, septiptillin and opiates[15] have been advocated for the treatment of PLMD. Montplaisir et al. have reported that PMS (PLM) may result from reduced dopaminergic activity in the CNS, possibly resulting from the decreased sensitivity of postsynaptic dopamine receptors[27,28]. They found that L-DOPA was an effective drug for PMS (PLM). A previous study reported higher levels of free dopamine and homovanillic acid in the CSF of a patient with PMS (PLM)[27]. Decreased serotonin activity was found to be involved in non-periodic myoclonus in humans[37] but 5-hydroxytryptophan not found effective in treating PMS (PLM)[13]. Clonazepam reduces serotonin utilization[32], and affects dopaminergic neurotransmission[40].

In short, we found that clonazepam significantly decreased PLM and resulted in electrophysiological improvement for both RLS and NIA.

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REFERENCES

1. **American Psychiatric Association.** 1987. Diagnostic and Statistical Manual of Mental Disorders (3rd ed. revised). American Psychiatric Association, Washington, DC.
2. **American Sleep Disorders Association.** 1990. Periodic limb movement disorder, p. 65–68. In Diagnostic Classification Steering Committee, Thorby M.J., Chairman, International Classification of Sleep Disorders, Diagnostic and Coding Manual. Allen Press, Lawrence.
3. **Association of Sleep Disorders Centers.** 1979. Diagnostic classification of sleep and arousal disorders. Sleep **2:** 17–121.
4. **Barnes, T.R.E. and Braude, W.M.** 1985. Akathisia variants and tardive dyskinesia. Arch. Gen. Psy. **42:** 874–878.
5. **Boghen, D.** 1980. Successful treatment of restless legs with clonazepam. Ann. Neurol. **8:** 341.
6. **Coleman, R.M., Pollack, C.P. and Weitzman, E.D.** 1978. Periodic nocturnal myoclonus occurs in a wide variety of sleep-wake disorders. Trans. Am. Neurol. Assoc. **103:** 230–235.
7. **Coleman, R.M., Pollak, C.P. and Weitzman, E.D.** 1980. Periodic movements in sleep (nocturnal myoclonus): Relation to sleep disorders. Ann. Neurol. **8:** 416–421.
8. **Coleman, R.M., Miles, L.E., Guilleminault, C., Zarcone, V.P., Jr., Van-den-Hoed, J. and Dement, W.C.** 1981. Sleep-wake disorders in the elderly; a polysomnographic analysis. J. Am. Geriat. Soc. **29:** 289–296.
9. **Coleman, R.M.** 1982. Periodic movements in sleep (nocturnal myoclonus) and restless legs syndrome, p. 265–295. *In* C. Guilleminault (ed.), Sleeping and Waking Disorders. Addison-Wesley, Menlo Park.
10. **Ekbom, K.A.** 1960. Restless legs. Neurology **10:** 868–873.
11. **Ekbom, K.A.** 1970. Restless legs, p. 311–320. *In* P.J. Vinken and G.W. Bruyn (eds.), Handbook of Clinical Neurology. New Holland, Amsterdam.
12. **Guilleminault, C., Raynal, D., Takahashi, S., Carskadon, M. and Dement, W.C.** 1967. Evaluation of short-term and long-term treatment of the narcolepsy syndrome with chlomipramine hydrochloride. Acta Neurol. Scand. **54:** 71–78.
13. **Guilleminault, C., Montplaisir, J. and Dement, W.C.** 1974. Nocturnal myoclonus and 5-HTP. Abstracts of the Fourth Annual Meeting of the Society for Neuroscience, 28.
14. **Guilleminault, C., Raynal, D., Weitzman, E.D. and Dement, W.C.** 1975. Sleep-related periodic myoclonus in patients complaining of insomnia. Trans. Am. Neurol. Assoc. **100:** 19–21.
15. **Hening, W.A., Walters, A.S. and Kavey, N.** 1986. Dyskinesias while awake in restless legs syndrome; treatment with opioids. Neurology (Minneap.) **36:**

1363–1366.
16. **Horiguchi, J.** 1985. Clinical effects of clonazepam treatment for oculogyric crisis and akathisia induced by neuroleptics (in Japanese). J. Pharmaceut. Med. Sci. **14:** 1465–1470.
17. **Horiguchi, J., Nishimatsu, O. and Inami, Y.** 1989. Successful treatment with clonazepam for neuroleptic-induced akathisia. Acta Psychiat. Scand. **80:** 106–107.
18. **Horiguchi, J.** 1991. Low serum iron in patients with neuroleptic-induced akathisia and dystonia under antipsychotic drug treatment. Acta Psychiat. Scand. **84:** 301–303.
19. **Horiguchi, J., Inami, Y., Sasaki, A., Nishimatsu, O. and Sukegawa, T.** 1992. Periodic leg movements in sleep with restless legs syndrome: Effect of clonazepam treatment. Folia Psychiat. Neurol. Jap. **46:** 727–732.
20. **Horiguchi, J., Hosoda, Y., Watanabe, S., Sukegawa, T., Sasaki, A. and Akita, K.** 1995. Iron therapy of patients with neuroleptic-induced akathisia. Jap. J. Psychiat. Treat. (in Japanese) **10:** 1070–1074.
21. **Lipinski, J.F., Zubenko, G.S., Barreira, P. and Cohen, B.M.** 1983. Propranolol in the treatment of neuroleptic-induced akathisia. Lancet **i:** 685–686.
22. **Lipinski, J.F., Hudson, J.I., Cunningham, S.L., Aizley, H.G., Keck, P.E., Jr., Mallya, G., Aranow, R.B. and Lukas, S.E.** 1991. Polysomnographic characteristics of neuroleptic-induced akathisia. Clin. Neuropharmacol. **14:** 413–419.
23. **Lugaresi, E., Coccagna, G., Berti-Ceroni, G. and Ambrosetto, C.** 1968. Restless legs syndrome and nocturnal myoclonus, p. 285–294. *In* W. Gastaut (ed.), The Abnormalities of Sleep in Man. Aulo Gaggi, Bologna.
24. **Marsden, C.D., Hallett, M. and Fahn, S.** 1982. The nosology and pathophysiology of myoclonus, p. 196–248. *In* C.D. Marsden and S. Fahn (eds.), Movement Disorders. Butterworths, London.
25. **Mitchell, S.W.** 1980. Some disorders of sleep. Am. J. Med. Sci. **100:** 109–127.
26. **Montagna, P. and Sassoli de Bianchi, L.** 1984. Clonazepam and vibration in restless legs syndrome. Acta Neurol. Scand. **69:** 428–430.
27. **Montplaisir, J., Godbout, R., Boghen, M.D., Dechamplain, J., Young, S.N. and Lapierre, G.** 1985. Familial restless legs with periodic movements in sleep: Electrophysiologic, biochemical, and pharmacologic study. Neurology (NY) **35:** 130–134.
28. **Montplaisir, J., Godbout, R., Poirier, G. and Bedard, M.A.** 1986. Restless legs syndrome and periodic movements in sleep: Physiopathology and treatment with L-Dopa. Clin. Neuropharmacol. **9:** 456–463.
29. **Nishimatsu, O., Horiguchi, J., Inami, Y., Sasaki, A. and Kondo, K.** 1992. Nocturnal myoclonus observed in a patient with neuroleptic-induced akathisia. Folia Psychiat. Neurol. Jap. **46:** 121–126.
30. **Ohanna, N., Peled, R., Rubin, A.H.E., Zonev, J. and Lavie, P.** 1985. Periodic leg movements in sleep: Effect of clonazepam treatment. Neurology **35:** 408–411.
31. **Oshtory, M. and Vijayan, N.** 1980. Clonazepam treatment due to sleep myoclonus. Arch. Neurol. **37:** 119–120.
32. **Pratt, J., Jenner, P., Reynolds, E.H. and Marsden, C.D.** 1979. Clonazepam induced serotonergic activity in the mouse brain. Neuropharmacol. **18:** 791–799.
33. **Rechtschaffen, A. and Kales, A.** 1968. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. UCLA Brain Information Service/Brain Research Institute, Los Angeles.
34. **Sandyk, R.** 1985. Successful treatment of neuroleptic-induced akathisia with baclofen and clonazepam. Eur. Neurol. **24:** 286–288.
35. **Symonds, C.P.** 1953. Nocturnal myoclonus. J. Neurol. Neurosurg. Psychiat. **16:** 71.
36. **Telstad, W., Larsen, S. and Lillevold, P.E.** 1984. Treatment of the restless legs syndrome with CBZ; A double blind study. Brit. Med. J. **288:** 444–446.
37. **Van Woert, M.** 1980. New treatment for myoclonus patients. J.A.M.A. **243:** 1705–1706.
38. **Walters, A.S., Hening, W.A., Kavey, N., Chokroverty, S. and Gidro-Frank, S.** 1988. Double-blind randomized crossover trial of bromocriptine and placebo in restless legs syndrome. Ann. Neurol. **24:** 455–458.
39. **Walters, A.S., Hening, W., Rubinstein, M. and Chokroverty, S.** 1991. A clinical polysomnographic comparison of neuroleptic-induced akathisia and the idiopathic restless legs syndrome. Sleep **14:** 339–345.
40. **Weiner, W.J., Goetz, C., Nausieda, P.A. and Klawans, H.L.** 1977. Clonazepam and dopamine-related stereotyped behavior. Life Sci. **21:** 901–906.
41. **Yagi, K.** 1974. Symptomatology of drug-induced akathisia with special reference to the so-called psychoanaleptic effect of antipsychotic drugs (Neuroleptics). Psychiat. Neurol. Jap. **76:** 757–779.