Excessive Fragmentary Myoclonus: Time of Night and Sleep Stage Distributions

Otavio Lins, Michelle Castonguay, Wayne Dunham, Sonya Nevsimalova and Roger Broughton

ABSTRACT: Excessive fragmentary myoclonus during sleep consists of high amounts of brief twitch-like movements occurring asynchronously and asymmetrically in different body areas and has been reported to occur in association with a number of sleep disorders. It was analyzed using a new technique of quantification, the fragmentary myoclonus index (FMI). The FMI exhibited high rates in all stages of sleep but with a somewhat lower frequency in slow wave sleep explaining, as well, a significantly lower rate in the first hour after sleep onset compared to later hours. There was no evidence for greater sleep fragmentation or lighter sleep compared to a matched patient group in whom it had not been noted.

RÉSUMÉ: Myoclonie fragmentaire excessive: horaire nocturne et stades du sommeil. La myoclonie fragmentaire excessive pendant le sommeil consiste en un nombre considérable de mouvements fasciculaires se produisant de façon asynchrone et symétrique dans différentes régions du corps. Ce phénomène a été rapporté en association avec un grand nombre de troubles du sommeil. Nous l'avons analysé au moyen d'une nouvelle technique de quantification, l'indice de myoclonie fragmentaire (IMF). L'IMF était élevé dans tous les stades du sommeil, avec une tendance vers des fréquences moins élevées pendant le sommeil à ondes lentes, ce qui explique également des fréquences significativement plus basses dans la première heure après l'endormissement par rapport aux heures suivantes. Il n'existait pas d'évidence de fragmentation du sommeil ou de sommeil plus léger comparé à un groupe de patients appariés, chez qui ce phénomène n'avait pas été noté.

Can. J. Neurol. Sci. 1993; 20: 142-146

Physiological fragmentary myoclonus occurring in normal human subjects was first described by De Lisi[1] as consisting of brief, fine, twitch-like movements involving various body areas in asynchronous and asymmetric fashion and observable at sleep onset and at times during sleep. Using surface EMG electrodes, normal fragmentary myoclonus has been recorded as muscle potentials of 50-200 μV in amplitude and less than 150 msec in duration most prominent in the distal limbs and facial areas and predominating during REM sleep and at sleep onset.[2,3]

Fragmentary myoclonus (FM) must be distinguished from the normal phenomenon of so-called sleep starts or hypnic jerks, which also occur at sleep onset, but consist of bilaterally synchronous gross body movements.[4,5] It also differs from several pathological forms of sleep-related myoclonus. Epileptic myoclonus can occur during sleep and is associated with a EEG discharge.[6] Periodic limb movement disorder[7,8] is easily distinguished by the more sustained nature and pseudorhythmic repetition of the jerks.

Excessively intense and frequent FM has been reported to occur in association with a variety of clinical diagnoses, almost always in males and in combination with high amounts of sleep fragmentation.[9] It has also been reported in patients in whom excessive daytime sleepiness (EDS) was the sole complaint and who showed no other significant abnormality in the polysomnogram.[9,10] In some sleep apnea patients, the FM rate has been found to rise during periods of decreased oxygen saturation.[9,11] Excessive FM is mainly found in males.[9]

In none of the above studies of patients showing high amounts of FM has its frequency across sleep stages or time of night been carefully quantified. The present study develops a technique to quantify FM and provides such a statistical analysis. The data are compared, as well, to those of a control patient group in order to test the suggestion[9] that sleep fragmentation may be causal.

Methods and Materials

The FM group consisted of 11 male patients (mean age 53.4 years, s.d. 10.1, range 34-72) in whom excessive amounts of fragmentary myoclonus had been noted in the report by the clinical polysomnographer. The patients had been referred to the Ottawa General Hospital Sleep Disorders Clinic to investigate a number of symptoms or suggested diagnoses including EDS and snoring with suspected sleep apnea (n = 5), observed sleep apnea without EDS (n = 2), and EDS alone (n = 4) (Table 1). A sex and age matched (mean age 53.8, s.d. 8.5, range 37-68)

From the Ottawa General Hospital and University of Ottawa, Ottawa
Received June 29, 1992. Accepted in final form January 11, 1993
Reprint requests to: Dr. Roger Broughton, Division of Neurology, Ottawa General Hospital, Ottawa, Ontario, Canada K1H 8L6

Table 1. Clinical and polysomnographic (PSG) data of myoclonic patients

Patient	Age (yrs)	Object of PSG	PSG findings: PMS (%)	PSG findings: Apnea/hipop. (/hour)	PSG findings: O_2 sat. (%)	Clinical interpretation
1	34	EDS, snoring	13	0	n/a	Marked FM, moderate PMS
2	44	EDS, snoring	0	2 (obstr)	85-100	Marked FM
3	47	EDS	0	1 (centr)	n/a	Marked FM, bradycardia
4	50	EDS	0	1 (centr)	n/a	Non-specific
5	52	EDS, snoring	0	58 (obstr)	n/a	Obstructive sleep apnea
6	52	Sleep apnea	0	1 (obstr)	82-97	Marked FM
7	57	EDS	56	2 (obstr)	n/a	Marked FM and PMS
8	57	EDS	76	1 (centr)	81-98	Marked PMS
9	59	Sleep apnea	0	13 (centr)	n/a	Central sleep apnea
10	63	EDS, snoring	0	10 (obstr)	n/a	Non-specific
11	72	EDS, apnea	71	0	86-96	Marked FM and PMS

FM: fragmentary myoclonus
PMS: periodic movements of sleep
EDS: excessive daytime sleepiness
n/a: data not available

group of patients not noted to display excessive FM or other significant polysomnographic abnormalities was chosen for the control group. The majority (n = 8) of this second group of patients had a history of snoring, three of whom also complained of EDS, and three were referred for EDS alone. The project protocol had prior approval of the local human ethics committee.

The recording montage used in all subjects studied consisted of five EEG channels (1 frontopolar, 2 central, 2 occipital, all referred to the contralateral mastoid), ECG (lead II), right and left EOG, submental EMG, right and left anterior tibialis EMG (surface electrodes), nasal and oral airflow (thermocouple), thoracic and abdominal movement (Respitrace) and, in some cases only, percent oxygen saturation (Ohmeda Biox 3700). The myoclonic potentials were analyzed using the bilateral anterior tibialis EMG channels which were calibrated at 5μV/mm, with low and high frequency filters set at 5 and 70 Hz, respectively. An example of typical fragmentary myoclonus during sleep is shown in Figure 1. All recordings were sleep staged using 30 sec epoques by the criteria of Rechtschaffen and Kales.[12] Apneas were scored in the standardized manner of Guilleminault.[13] Presence of periodic limb movements (PLM) followed the criteria of Coleman et al.[14] and were quantified as a percent of total sleep time.

To quantify the phenomenon, a fragmentary myoclonus index (FMI) was defined. First, each 30 sec scoring epoch was divided into ten 3 sec mini-epochs. The number of mini-epochs with one or more FM potentials exceeding 50μV was then counted for each 30 sec epoch, the number therefore ranging from 0 to 10. The FMI was the calculated mean of individual epoch counts. These were averaged across subjects by sleep stage and by hour of night. Since some patients had little or no stage 4, stages 3 and 4 were collapsed together as slow wave sleep (SWS).

The use of an index was chosen for several reasons. First, most of the recordings had a very large number of potentials. The counting of the absolute number of potentials on paper recording would be extremely time consuming. No automated technique existed. Second, this approach helps to distinguish the phenomenon from other types of potentials such as physiological twitching in REM and stage 1 sleep. This quantification method tends to "dilute" potentials occurring in bursts (as REM and stage 1 twitching) while relatively preserving those which occur scattered across the epoch (as fragmentary myoclonus). This is particularly important when quantifying FM during REM and stage 1 sleep, as the identification of isolated potentials as part of one or other pattern can be difficult. Third, the use of an index is already in widespread use for quantifying periodic movements of sleep.

The FMIs by sleep stage and by hour of night were compared within and between groups by two-way analysis of variance. Regression analyses were employed to study possible differences in FMI as a function of age. The Student t-test and Mann-Whitney U test examined for differences in sleep parameters between the groups.

Results

Sleep Stage Distribution

FMI scores were, as expected, significantly higher in the FM group compared to the control group: and this was true for all sleep stages. In the FM group a significant difference ($p < 0.05$) by ANOVA was found as a function of sleep stage. Post-hoc Tukey tests showed that FMI was greater in REM than in SWS (Table 2, Figure 2). No similar stage differences were found in the control group.

Time of Night Distribution

FMI scores were also significantly higher in the FM group than in the controls for all hours of the night. In the FM group, the first hour of the night contained a significantly lower FMI than all remaining hours (Figure 3). The FMI rose sharply after the initial low in hour 1 to remain unchanged across the rest of the night. In the control group, by comparison, the FMI was not significantly different across hours after sleep onset.

https://doi.org/10.1017/S0317167100047715 Published online by Cambridge University Press

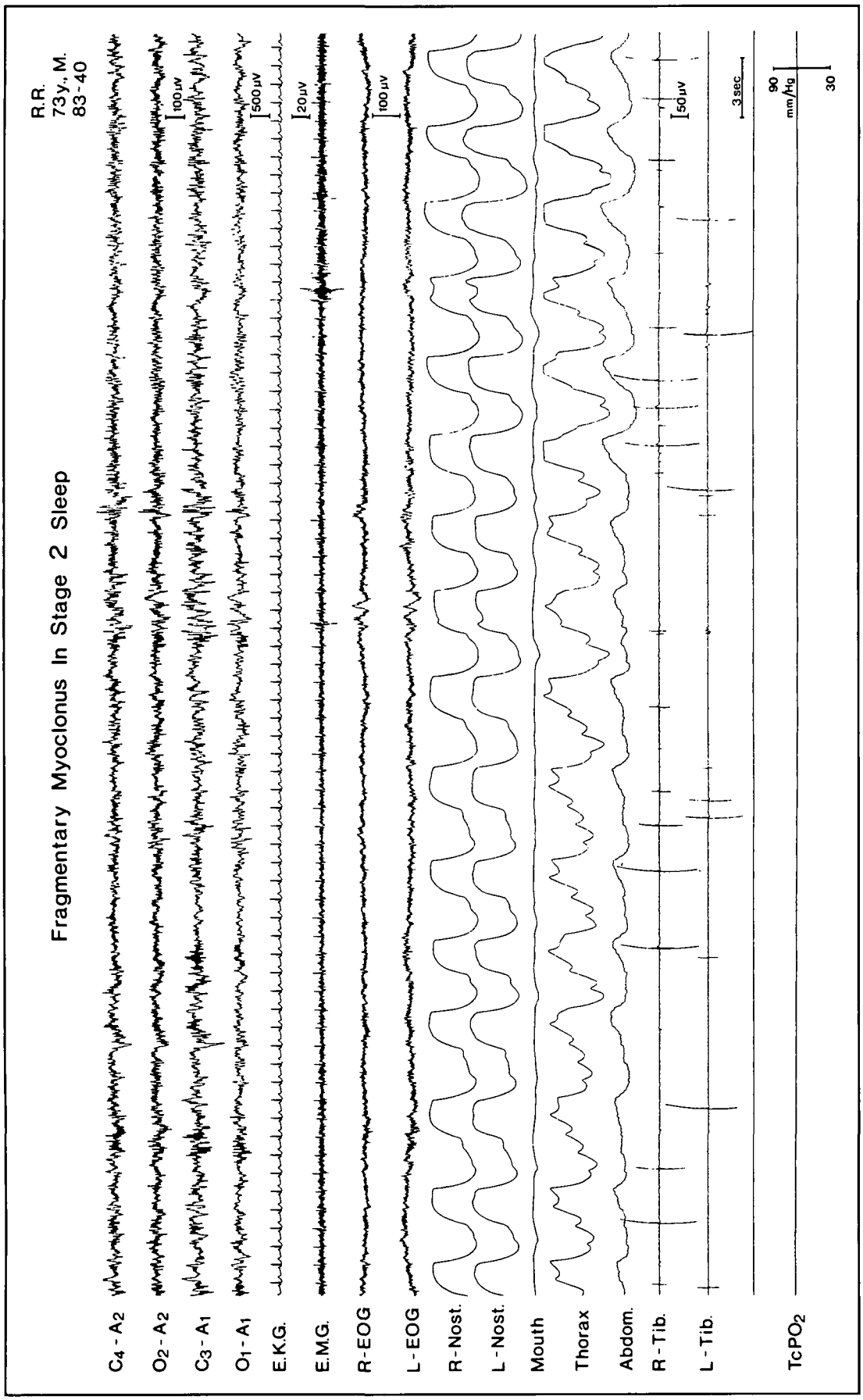

Figure 1 — Fragmentary myoclonus during stage 2 sleep in a 73-year-old patient. The polysomnogram was done to investigate possible sleep apnea in a snorer with daytime sleepiness. FM is recorded as brief high amplitude potentials in the right and left anterior tibialis leads. No apnea was present.

https://doi.org/10.1017/S0317167100047715 Published online by Cambridge University Press

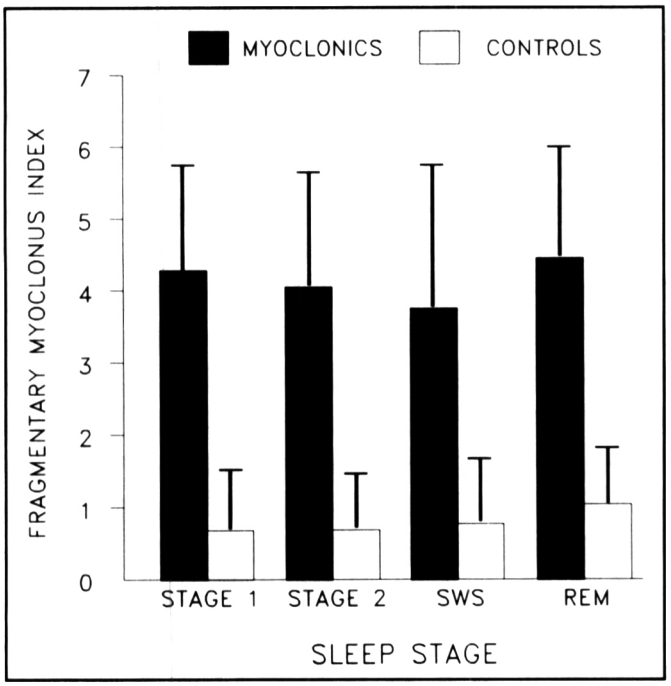

Figure 2 — The fragmentary myoclonus index (means and SDs) in 11 male patients exhibiting high amounts compared to matched patient controls in whom the phenomenon had not been noted by the clinical polysomnographer. There was a significant group difference for all sleep stages and, within the high FMI group, there was significantly more myoclonus in REM sleep than in SWS.

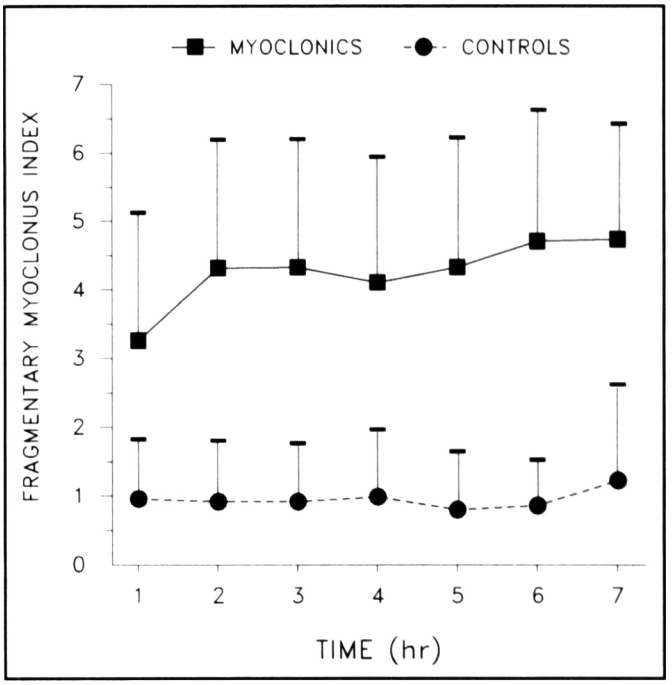

Figure 3 — The fragmentary myoclonus index (means and SDs) as a function of hour of night after sleep onset in high FM patients compared to matched control patients. There was a significance between group difference for all hours of the night. Within the high FM group, there was significantly less myoclonus in the first compared to all later hours.

Since REM sleep rarely occurs in the first hour of sleep, it was thought that perhaps the significantly higher FMI in REM sleep found by the stage analysis might be responsible for the lower level in the first hour of the FM group. The within-group time of night analysis was therefore repeated with all REM epochs removed from the data (Figure 3). Again, the first hour exhibited a significantly lower FMI. Since the FMI in the myoclonics had also been found to be lower in SWS, the analysis was again repeated with SWS epoch data removed. This resulted in a flattening of the original curve and the first hour of the night was no longer significantly different from subsequent hours.

Age Effects

Age did not correlate significantly with the FMI in either group or in collapsed data from both groups.

Sleep Structure Between Groups

There were no significant differences in measures of sleep structure between the FM group and the matched patient controls. Major variables are summarized in Table 2. Others include total sleep time without stage 1, sleep efficiency without stage 1, latency to stage 3, number of REM periods, mean REM length, mean REM cycle and total number of stage shifts.

Table 2. Sleep parameters in myoclonics and controls

Sleep parameter	Myoclonics	Controls
Total sleep time + st. 1 (min.)	336 ± 42	311 ± 42
Sleep efficiency + st. 1 (%)	88 ± 8	80 ± 23
Stage 1 latency (min.)	3 ± 3	3 ± 2
Stage 2 latency (min.)	24 ± 23	24 ± 17
REM latency (min.)	95 ± 46	111 ± 54
Wake after sleep onset (%)	11 ± 6	14 ± 7
Stage 1 (%)	18 ± 7	15 ± 7
Stage 2 (%)	49 ± 10	45 ± 5
SWS (%)	8 ± 7	9 ± 7
REM (%)	13 ± 4	17 ± 6
REM efficiency (%)	72 ± 25	85 ± 13
Awakenings > 1 min. (n^0)	8 ± 4	8 ± 4
Stage shifts / hour (n^0)	107 ± 20	21 ± 6

Discussion

This study, to our knowledge, is the first to provide a quantitative index of excessive fragmentary myoclonus in patients and to analyze its modification as a function of sleep stages and time of night. We found a trend for decreasing amounts of excessive FM within sleep as one goes across stages REM, 1, 2, and SWS, with the only significant difference being between REM and SWS. With removal of SWS, it was noted that the decreased amount of FM in the first hour of the time of night was attributable to a suppressive effect within SWS. The physiological mechanism for this suppression remains uncertain.

Another clinical and polysomnographic finding, periodic limb movement disorder, which is found at times in both patients and normal subjects, has been found to increase with age.[14] For FM no similar increase with age was found within either group or with the two groups combined. However, as this

https://doi.org/10.1017/S0317167100047715 Published online by Cambridge University Press

study used a relatively small sample per age group, the finding must be considered preliminary and confirmed with a greater number of subjects per age group and more evenly distributed across age groups.

An earlier proposed[9] possible relationship between excessive FM and sleep fragmentation was not clarified by this study. The two patient groups did not differ in measures of sleep fragmentation or in any of the other sleep parameters studied. Although FM may also be observed during periods of nocturnal wakefulness, accurate data collection proved too difficult, due to obscuring by the increase in background muscle tone and by movement artifacts; therefore, waking data were not used in the analyses. The possibility that fragmentary myoclonus during nocturnal awakenings might keep patients awake longer was not supported by this study, as the patient groups did not exhibit any differences in percent of wakefulness after sleep onset. The similar amount of SWS between the groups gives support to a previous study which suggested that fragmentary myoclonus does not lead to any degree of sustained lightening of sleep.[9]

As only symptomatic patients are referred to our sleep laboratory the control group was a patient group and not a "true" normal group. As the aim of the paper was to the study the evolution of fragmentary myoclonus across the night and as a function of sleep stages, and not to define limits of normality, such a control group seemed to us to be adequate.

Because our control group was a patient group it showed a somewhat different pattern of FM from that of normal subjects, as reported by Dagnino et al.,[3] in whom highest levels occur in stage 1 drowsiness and REM sleep. Our controls did not show any significant stage effects, although highest absolute levels were reached in REM sleep. The difference might be due to one of quantification methodology (a derived index versus an absolute count), to the relatively small group sizes in both studies or, we believe most likely, because our patient controls, being symptomatic, were not true normals and had a pattern more closely similar to the high FM group. We believe that the lack of any significant association with sleep stage in the control group was probably a floor effect relating to the overall low amounts.

Further studies are indicated which would compare high and low FMI patients with a larger sample of asymptomatic normal controls and include measures of daytime somnolence. The latter would help define the clinical significance of this sleep abnormality, which is a proposed nosological entity in the new classification of sleep disorders.[15]

Acknowledgements

The project was supported by a grant (to R.B.) of the Medical Research Council of Canada. Dr. Lins was supported by a training fellowship of the Conselho Nacional de Desenvolvimento Cientifico e Tecnologico (CNPq), Brazil. Dr. Nevsimalova was on leave from, and supported by, the Department of Neurology, Charles University, Czechoslovakia.

References

1. De Lisi L. Su di fenomeno motorio costante del sonno normale: le myioclonie ipniche fisiologiche. Rev Path Nerv Ment 1932; 39: 481-496.
2. Loeb C, Massazza G, Sacco G, Arnone A. Etude polygraphique des 'myoclonies hypniques' chez l'homme. Rev Neurol 1964; 10: 358-368.
3. Dagnino N, Loeb C, Massazza G, Sacco G. Hypnic physiological myoclonias in man: an EEG-EMG study in normals and neurological patients. Europ Neurol 1969; 2: 47-58.
4. Oswald I. Sudden body jerks on falling asleep. Brain 1959; 832: 93-103.
5. Gastaut H, Broughton R. A clinical and polygraphic study of episodic phenonema during sleep. Rec Adv Biol Psychiat 1965; 8: 111-136.
6. Roger J, Gastaut H, Toga M, et al. Epilepsie myoclonie progressive avec corps de Lafora: étude clinique polygraphique et anatomique d'un cas. Rev Neurol 1967; 12: 50-61.
7. Coleman RM, Pollak CP, Weitzman ED. Periodic movements in sleep (nocturnal myoclonus): relation to sleep-wake disorders. Ann Neurol 1980; 8: 416-421.
8. Lugaresi E, Cirignotta F, Coccagna G, Montagna P. Nocturnal myoclonus and restless legs syndrome. *In*: Fahn S et al., eds. Adv Neurol. New York: Raven 1986; 295-306.
9. Broughton R, Tolentino M, Krelina M. Excessive fragmentary myoclonus in NREM sleep: a report of 38 cases. Electroencephalogr Clin Neurophysiol 1985; 61: 123-133.
10. Broughton R, Tolentino M. Fragmentary pathological myoclonus in NREM sleep. Electroencephalogr Clin Neurophysiol 1984; 57: 303-309.
11. Brösig B, Meier-Ewert K. Fragmentary myoclonus frequency correlates with tissue oxygenation. Presented at 8th Europ Congr Sleep Res, 2 Sept. 1986, Szeged, Hungary.
12. Rechtschaffen A, Kales A, eds. A Manual of Standardized Terminology and Scoring Systems for Sleep Stages of Human Subject (Institute of Health Publication No. 2041). US Government Printing Office, Washington, DC, 1968.
13. Guilleminault C, ed. Sleep and waking disorders: indications and techniques. Menlo Park, CA: Addison-Wesley.
14. Coleman RM, Bliwise DL, Sajben N, et al. Epidemiology of periodic movements in sleep. *In*: Guilleminault C, Luagresi E, eds. Sleep-wake Disorders: Natural History, Epidemiology, and Long Term Evolution. New York: Raven Press 1983; 217-229.
15. ICDS - International Classification of Sleep Disorders: Diagnostic and Coding Manual. Diagnostic classification steering committee, Thorpy MJ, ed. Rochester, Min., American Sleep Disorders Association, 1990.