Yamanashi Med. J. 7(2), 57~66, 1992

# Changes in Sleep Spindle and Sleep Slow Wave during the Menstrual Cycle

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**Abstract**: Five healthy adult women, aged from 20 to 28, had 12–15 polysomnographic recordings taken. Sleep stages were scored according to the Rechtschaffen and Kales criteria. Cz-A1 EEG recordings were also analyzed with a spindle and delta wave real-time automatic analyzing system in a 16-bit microcomputer. Sleep stage analysis revealed no significant changes in the ordinary sleep parameters, i.e. percentage of each sleep stage, sleep latency or REM latency when the low and high body temperature phases were compared. On the other hand, the sleep spindle parameters derived from the Personal Spindle Delta-wave Analyzer changed markedly during the menstrual cycle. Spindle frequency was slower at about 14 days before the first menstruation day and increased after that and it was faster at just before the first menstruation day. The pattern of spindle density change was similar to that of frequency. Amplitude and duration did not tend to change during the menstrual cycle nor did the parameters of the slow wave. No prior reports have mentioned the relationship between the menstrual cycle and sleep spindle. From these results, it can be hypothesized that the frequency of the sleep spindle reflects sleep propensity and that it is a very important sleep parameter.

**Key words**: Sleep, Sleep Spindle, Sleep slow wave, Automatic analysis, Menstrual cycle

## INTRODUCTION

It is well known that the sleep condition of a healthy woman changes during the menstrual cycle. But details of a woman's sleep condition are still unknown. We studied woman's subjective evaluations of their sleep feeling using a sleep questionnaire and found that subjective sleep feelings change regularly during the menstrual cycle[1]. Generally speaking, sleep feeling in the high temperature phase, that is two weeks before the menstrual period, is worse than that in the low temperature phase. On the other hand earlier studies by many other researchers using polysomnography (PSG) have not yet had fruitful results. We can now analyze the electroencephalography (EEG) of PSG more easily than hitherto by means of a personal computer. In this study, analyzing the EEG of PSG with a new sleep EEG analyzing system, changes in the sleep spindle and sleep slow wave during the menstrual cycle were examined.

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Received February 26, 1992
Accepted April 8, 1992

## SUBJECTS AND METHODS

### *Subjects*

The subjects were five females who had been included in our former study of subjective sleep change during the menstrual cycle[1]. The subjects were one 20-year-old (subject MT), two 22-year-old (subjects MI and HN), one 25-year-old (subject MO) and one 28-year-old (subject YK). All of them were healthy, their menstrual cycles were regular and had not been pregnant or taken oral contraceptives.

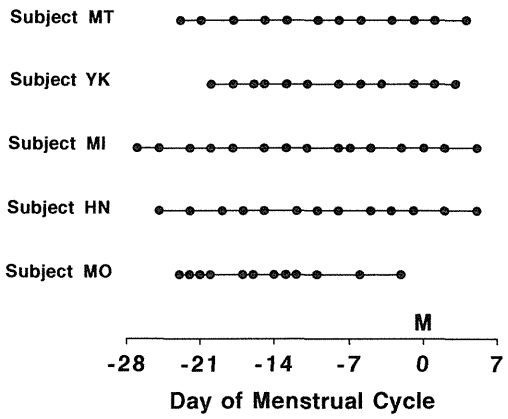


Fig. 1. Schedule of this study
In a period of 35 days from the 28th day before menstruation to the 7th day after menstruation, polysomnographic recordings for each subject were done 12–15 times. Each dot indicates one polysomnographic recording. The first day of menstruation is shown as day 0 in the figures and is marked with an M. The days before menstruation are indicated with a minus symbol.

Informed consent was obtained.

*Methods*

Subjects were asked to live ordinary and not to drink alcohol, take drugs or smoke during the study.

1) Polysomnographic study and visual sleep stage scoring

After one adaptation night, sleep studies were performed in quiet single rooms in our sleep laboratory. The electroencephalogram (EEG), electromyogram (EMG), electrooculogram (EOG), electrocardiogram (ECG) and the respiratogram were monitored at the rate of 10 mm/second at least three nights a week during a menstrual cycle. For the EEG, Fpz-A1, Cz-A1 and Oz-A1 leads were used according to the international ten/twenty system. For the EMG, electrodes were placed at a point on the mental muscle; for the EOG, the electrodes were applied to the left and right canthi. The recordings started about 11:00 p.m.-12:00 p.m. according to the ordinary life schedule of the subjects and were terminated compulsorily eight hours after the start. Twelve PSGs for subjects MT, MO and YK, thirteen for subject HN, and fifteen for subject MI were obtained during a menstrual cycle (Fig. 1). PSGs were recorded on paper and magnetic tape simultaneously. Sleep stages were scored by the Rechtschaffen & Kales criteria[2]. From the results for sleep stages, the percentage of each sleep stage, sleep latency and REM sleep latency were calculated.

2) Measurement of Basal Body Temperature (BBT)

BBT was measured every morning during the experimental schedule.

3) Measurement of sex hormone concentration

Once in the low temperature phase and twice in the high temperature phase, the blood concentrations of the luteinizing hormone, follicle stimulating hormone, estradiol and progesterone were measured.

4) Autoanalysis of sleep EEG

Cz-A1 EEGs, which were recorded on magnetic tape, were analyzed with a Personal Spindle Delta Analyzer (PSDA) developed by the Tokyo Metropolitan Institute for Neurosciences[3,4]. By means of this analyzing system, spindle structure, i.e. the density (number per minute), duration (msec), amplitude ($\mu$V) and frequency (Hz) of the sleep spindle, and slow wave structure, i.e. total number, density (number per minute), amplitude ($\mu$V) and frequency (Hz) of the slow wave, can be analyzed. The PSDA consists of a 16-bit personal computer, 12-bit A/D convertor and software digital filter. In this study, the sleep spindle was defined as composed of over six waves with a frequency range of 11 to 16 Hz and amplitude greater than 5 $\mu$V. The sleep slow wave was defined as having a 0.5–1.5 Hz frequency and over 50 $\mu$V amplitude. Following these definitions, the structure of the sleep spindle and slow wave were studied in detail during sleep stage 2, 3 and 4 for the entire night.

In the figures, the first day of the menstrual

period is shown as day 0 and marked with an M. The X axis is shown from 28 days before to 7 days after the first day of the menstrual cycle.

## Results

1) The BBT of all subjects showed a biphasic (low temperature phase and high temperature phase) pattern during the menstrual cycle and the change in sex hormones had a normal pattern parallel to BBT. From these results, these subjects were judged to have healthy menstrual cycles.

2) Changes in sleep parameters which were scored visually (Table 1)

Since the time and date of PSG differed from subject to subject, we selected two PSG parameters each from the low and high temperature phases and compared them by paired t-test. There were no significant changes in the percentages of REM sleep, each NREM sleep and sleep latency and REM sleep latency.

3) Changes in the sleep spindle structure analyzed by means of the autoanalysing system

Average duration (msec), average amplitude ($\mu$V), density (number per minute) and average frequency (Hz) were studied statistically by ANOVA for each subject.

The average duration of the sleep spindle of subjects MO and YK did not change significantly. Though that of subject MI changed ($F=4.11$), we could not find a relationship to the menstrual cycle. Those of subject HN ($F=6.87$) and subject MT ($F=7.45$) changed significantly. There was no common pattern of change in the average duration of the spindle during the menstrual cycle seen among the subjects (Fig. 2a).

The average amplitude of the spindle in subject MO increased transiently at 14 days before menstruation ($F=14.9$). That of HN increased towards menstruation ($F=5.3$). That of MI changed more in the second half of the menstrual cycle than in the first half ($F=10.56$). Those of subjects YK and MT changed significantly, but no change related to the menstrual cycle could be seen. Although the change in the average amplitude for each subject was statistically significant, there was great individual difference among change patterns for these subjects and the change pattern was not necessarily related to the menstrual cycle (Fig. 2b).

Although the density of the spindle differed from subject to subject, the change patterns which were related to the menstrual cycle were relatively similar. They increased from 14 days before menstruation and then decreased immediately before menstruation. The changes were significant ($p<0.005$) in ANOVA, the F values for the subjects being as follows: MO=9.47, HN=8.53, MI=11.57, YK=12.9 and MT=6.6, (Fig. 2c).

The average frequency of the spindle underwent a clear common change in five

Table 1. Changes in sleep parameters in two phases of the menstrual cycle
There were no significant changes in sleep parameters in low temperature and high temperature phases

| | Low Temperature Phase | High Temperature Phases | |
|---|---|---|---|
| Sleep Latency (min) | 27.1 (28.8) | 20.8 (13.5) | NS |
| REM Latency (min) | 86.1 (40.0) | 83.7 (27.5) | NS |
| % Stage REM | 22.3 (2.5) | 21.3 (3.3) | NS |
| % Stage 1 | 4.5 (2.1) | 5.2 (2.2) | NS |
| % Stage 2 | 53.5 (6.4) | 55.9 (6.4) | NS |
| % Stage 3+4 | 19.7 (5.5) | 17.6 (3.8) | NS |

(n=5) Mean (SD) (paired t test)

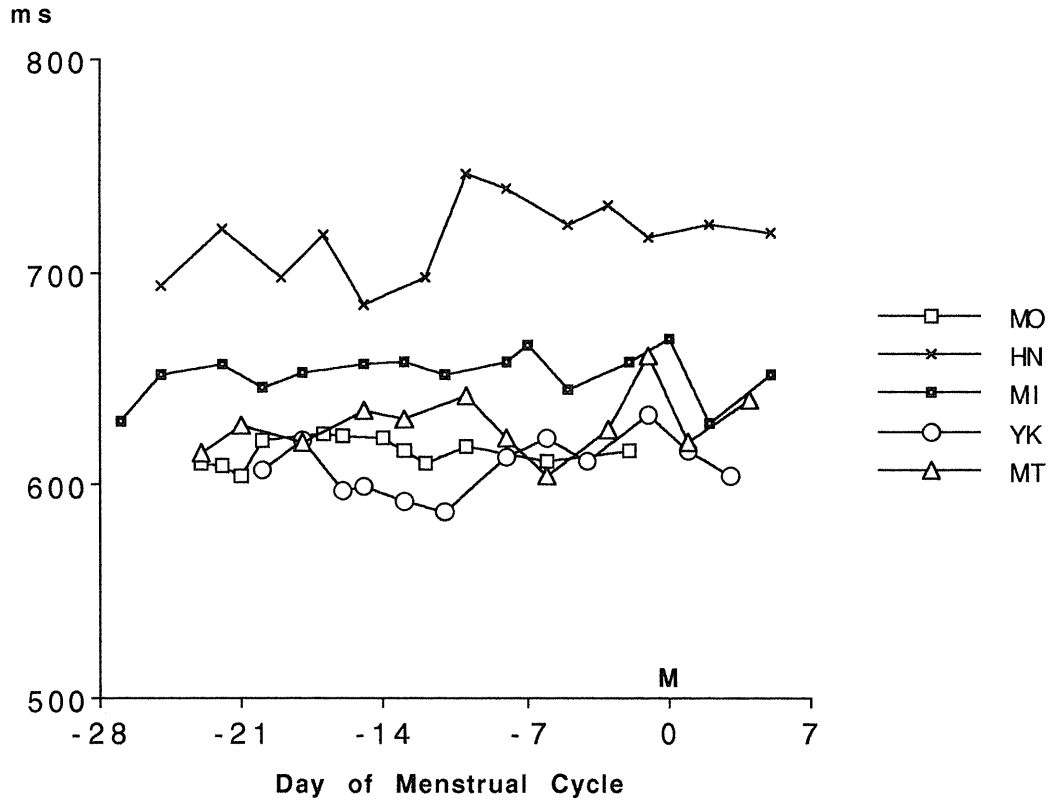


Fig. 2a. Average duration of sleep spindle
There was no common tendency for the pattern to change in these subjects.

subjects. The average frequency was low about 14 days before menstruation, then increased and again decreased about the first day of menstruation. This change was significant ($p<0.005$) in all subjects in ANOVA. Maximum, minimum and F values for spindle frequency in the subjects were MO=13.03, 13.36, 51.2, HN=12.9, 13.11, 53.75, MI=13.09, 13.33, 41.68, YK=12.81, 13.01, 12.32 and MT=12.97, 13.22, 35.92 (Fig. 2d).

4) Changes in the structure of the sleep slow wave analyzed by means of the autoanalysis system.

Changes in the sleep slow wave which are as important for the sleep EEG as the sleep spindle were studied. The sleep slow wave was defined as 0.5–1.5 Hz because waves in this frequency band most adequately reflect the change in the entire sleep slow wave throughout the night (Hamada. Personal commucication).

The structure of the slow wave in this analyzing system is the total number of slow waves, density (number per minute), average amplitude and average frequency.

Figure 3 shows the density. There is no common pattern of change for the five subjects and there is no relationship to the menstrual cycle. No other slow wave parameter is related to the menstrual cycle.

## Discussion

It is widely recognized that in most women the menstrual cycle is accompanied by changes in subjective sleep feelings. We studied women's subjective evaluation of sleep by means of an OSA (Oguri, Shirakawa and

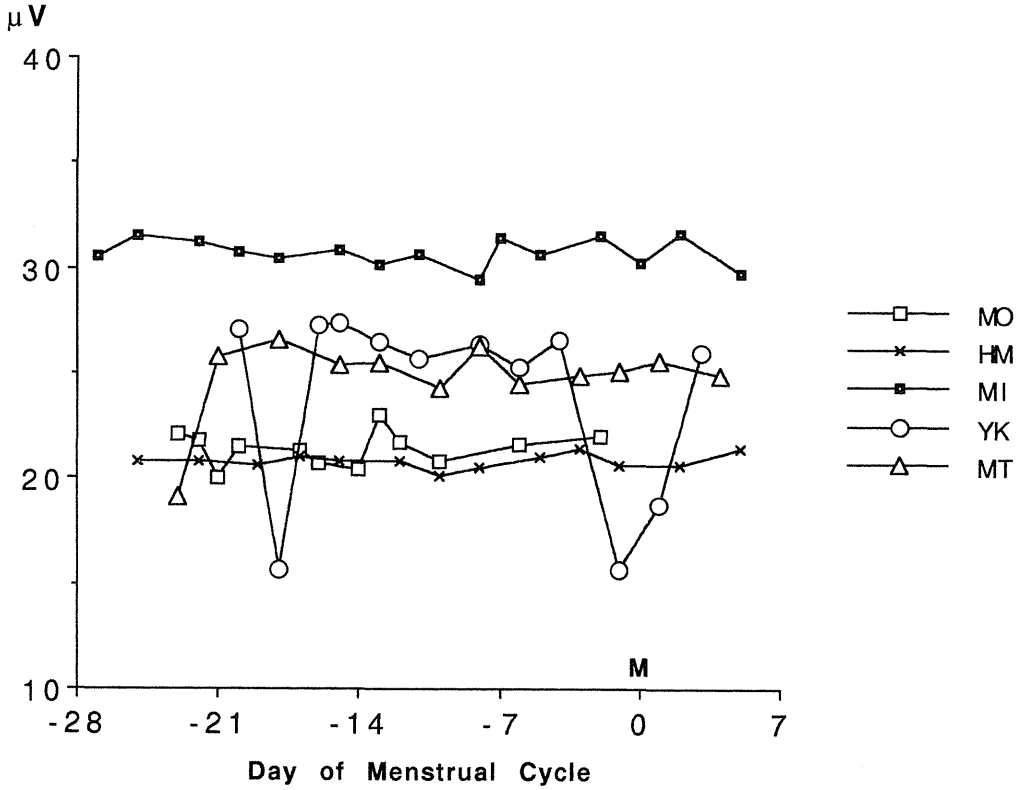


Fig. 2b. Average amplitude of sleep spindle
Although changes in amplitude are statistically significant in three subjects, there were considerable differences among subjects and the pattern of change was not related to the menstrual cycle.

Azumi's) Sleep Inventory[5] and found that the subjective sleep feelings educed by means of the inventory change with the menstrual cycle[1].

A look at the pattern of changes in the five sleep feelings shows that, generally, sleep feelings are worse in the second half (high temperature, luteal phase) than in the first half (low temperature, follicular phase) of the menstrual cycle. Based on the results of earlier studies, we attempted to determine if there were polysomnographic changes during the menstrual cycle. Some results of a pilot study dealing with the same theme have already been reported[6].

(1) Results of visual sleep stage scoring

In the present study, no significant changes in sleep parameters between the low and the high temperature phases were found.

In previous studies by various researchers on the menstrual cycle, sex hormones and sleep, in which polysomnography was employed, the following information was obtained.

Ho reported that in human subjects before the menstrual period, although the amount of slow wave sleep was reduced, other sleep parameters were not appreciably changed[7]. Hartmann reported that the amount of REM sleep increased immediately before the menstrual period[8),9]. Lee compared the follicular and luteal phases and reported that, although the period of REM sleep latency was longer in the follicular phase than in the luteal phase, there was no change in other sleep parameters[10]. Kapen *et al.* also reported little

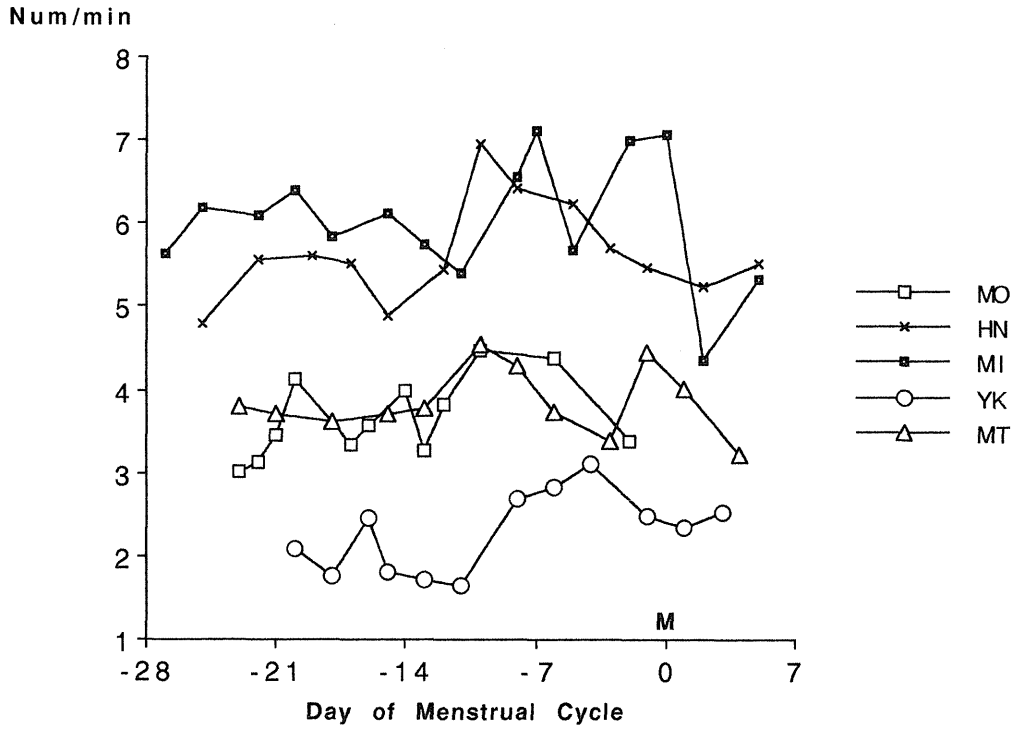


Fig. 2c. Density (number per minute) of sleep spindle
In all subjects, the density increased after about 14th day of the menstrual cycle and began to decrease as the beginning of the menstrual period approached. These change were statistically significant ($p<0.005$) in all subjects.

change in sleep parameters during the menstrual cycle[11]. The results obtained in this study, according to Rechtschaffen and Kales criteria, support Kapen's report. Taking all of these results together, it seems that even if sex hormone or menstrual cycle related changes occur in the sleep structure, such changes are very small.

However, the reason no clear polysomnographic changes during the menstrual cycle have been reported may be that researchers have depended solely on Rechtschaffen and Kales criteria. Although the Rechtschaffen and Kales criteria offer many advantages, they define stages 3 and 4 by making a large 20% and 50% slow wave division. For example, according to those criteria, an epoch which has 20% slow waves and an epoch which has 49% slow waves are both defined as stage 3. This definition is too broad to use in distinguishing sleep changes, especially NREM sleep changes, in detail.

(2) Sleep spindle structure analyzed with autoanalyzer

In this study, by autoanalysis with a personal computer, it was found that the average frequency of the sleep spindle changes with the menstrual cycle. Recently, a lot of fruitful research has been done on changes in the spindle and on the slow wave itself[12)–14)], however, there are few reports referring to spindle frequency. Principe *et al.* reported that the spindle frequency of a child is low and that of an elderly person is high[15]. Using the autoanalyzing method, especially with PSDA, changes in the spindle structure, especially its frequency, corresponding to various body conditions.

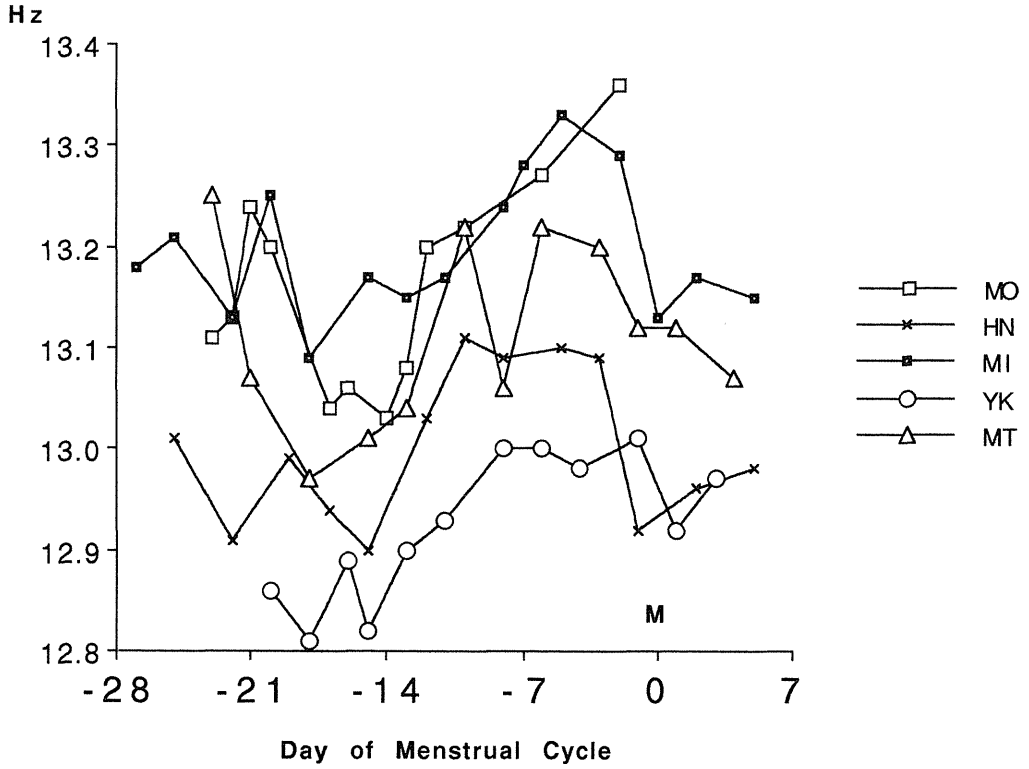


Fig. 2d. Average frequency of sleep spindle
There was a clear pattern of change in the sleep spindle frequency in five subjects. Frequency was low until 14th day of the menstrual cycle. After that, frequency increased and then decreased again about the beginning of menstruation. This change was statistically significant ($p<0.005$) in all subjects.

Usui reported that the average frequency of the spindle in delayed sleep phase syndrome changed when various treatments were tried[16].

It has been reported that, even in a healthy person, spindle frequency changes as conditions change. Shirakawa reported differences in night sleep spindle structure after sleep deprivation and after a daytime nap. According to his report, in nighttime recovery after sleep deprivation, the sleep spindle frequency became lower, and that on a night after a daytime nap became higher[12]. In this present study also, the most characteristic change accompanying the menstrual cycle was the change in the average frequency of the sleep spindle.

From the results of this study and Shirakawa's, it can be found that the spindle frequency becomes low in the low temperature phase as in night sleep after sleep deprivation, and it becomes high in the high temperature phase as in night sleep after a daytime nap. In our study conducted with the sleep inventory, we found that women's sleep condition changes during the menstrual cycle. For example, sleep initiation is better and sleep is more sound at night in the low temperature phase, whereas, sleep initiation is worse and sleep is less sound in the high temperature phase. From the results of our study of subjective sleep feeling and those of the sleep spindle, it may be hypothesized that the sleep spindle frequency is low when sleep propensity is high and the sleep condi-

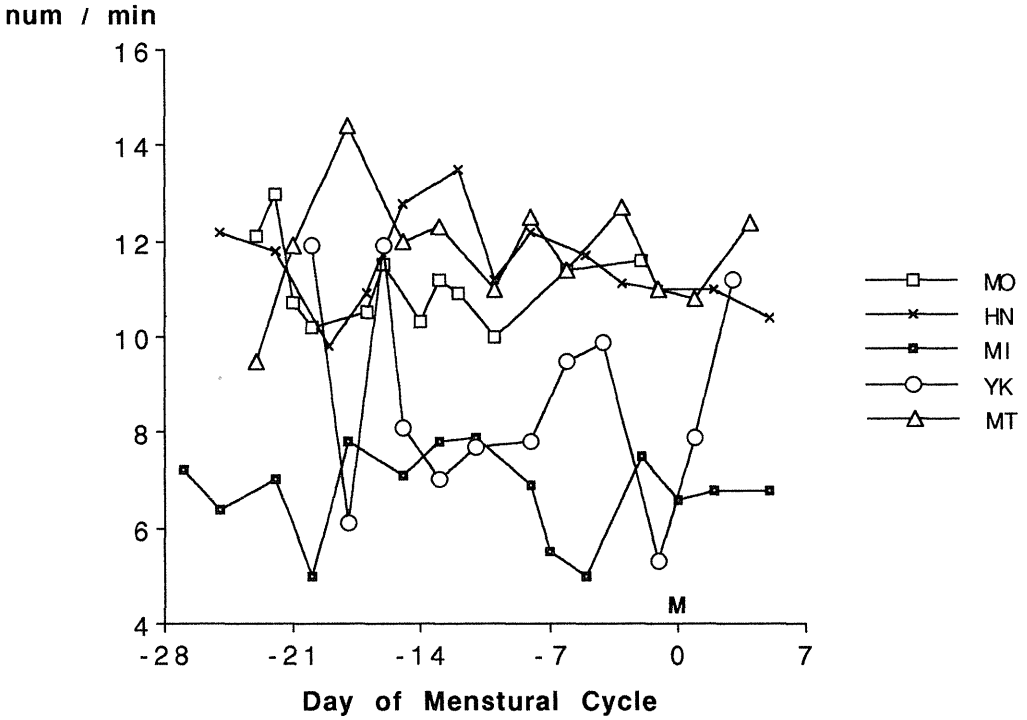


Fig. 3. Density of sleep slow wave
Density (number per minute) of the slow wave which had a 0.5–1.5 Hz frequency and over 50 $\mu$V amplitude are shown in this figure. The sleep slow wave did not change during the menstrual cycle in a manner comparable to the change in the frequency of the sleep spindle.

tion at night is good, but that it is high when sleep propensity is low and the sleep condition at night is bad.

The exact mechanism of the sleep spindle appearance is not yet sufficiently clear, but the thalamic reticular nucleus is reported to form the spindle or to modulate its frequency[17),18)]. To put it the other way around, it should be possible to guess the function of the thalamic reticular nucleus from the sleep spindle frequency.

The exact mechanism of the sleep spindle modulating effect on the central nervous system (CNS) is still unknown, but sex hormones may play a role in this mechanism. Ovarian steroids are known to influence CNS function. Colvin reported that the amount of REM sleep in rats was decreased by estrogen administration[19)]. Ramirez reported that intravenous injections of progesterone exert brief generalized anesthetic effects on EEG and hypothalamic unit firing rates in rats[20)]. Moreover, Nikiforova mentioned that the longterm removal of sex hormone secretion in rats causes a discrepancy between the decrease in behavioral patterns and increased excitability in CNS[21)]. Moreover it is known that nuclear progesterone receptors exist in the hypothalmus and anterior hypophysis[22)]. The spindle frequency change noted in this study may be derived from changes in the amounts of sex hormones associated with the menstrual cycle.

The sleep spindle is a very useful parameter in studying sleep because of the reproducibility of its appearance pattern. The autonomic function is reported to change during the menstrual cycle[23)], but there are no detailed

reports of changes in the sleep EEG during the menstrual cycle. It is very interesting that the sleep spindle structure changes regularly during the menstrual cycle because the spindle might reflect brain function.

(3) Slow wave structure analyzed with the autoanalyzer

The sleep slow wave did not change during the menstrual cycle in a manner comparable to the change in the sleep spindle frequency. Moreover, there are differences among subjects and in the same subject in the study night. From the results of visual scoring, it was not possible to find a regular pattern of change in the slow wave sleep (in stages 3 and 4) during the menstrual cycle. In view of these results, and those of other researchers, it can be concluded that there are no changes in slow wave sleep during the menstrual cycle.

Until recently, sleep research has been based on visual scoring of the sleep stages. But now, by means of a new auto-analyzing system incorporating a personal computer, we can easily do a frequency analysis of the sleep spindle. By this method, it was found objectively that the known changes in subjective sleep feelings accompany the changes in the sleep spindle frequency. It is planned to further study other body phenomena which might be related to changes in the spindle frequency, and to clarify the relationship between subjective sleep feeling and the sleep spindle.

## Acknowledgements

The author is grateful to Prof. Tetsuhiko Kariya for his valuable comments on the manuscript. The author also thanks Associate Prof. Hitoshi Fukuzawa, Dr. Kazuo Azumi and Dr. Shuichiro Shirakawa for advice and encouragement, and Dr. Akira Usui, and Dr. Kouichi Shiraishi for valuable assistance.

This study was supported in part by Grant-in-Aid for Scientific Research No. 63770812 and No. 01770814 from the Ministry of Education of Japan.

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