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Persistence of the Circadian Rhythm of REM Sleep: A Variety of Experimental Manipulations of the Sleep-Wake Cycle

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Summary: Many studies of nocturnal sleep, daytime naps, and phase shifts of sleep time indicate that rapid eye movement (REM) sleep has a circadian rhythm with an acrophase in the early morning, whereas slow wave sleep (SWS) correlates positively with the length of prior wakefulness. We confirmed that REM sleep has a stable circadian variation; large REM sleep amounts occurred in morning naps despite increase of SWS, owing to 1 night of total sleep deprivation. Heart rate and oral temperature both continued to show a circadian rhythm in spite of 1 night of total sleep deprivation. The lowest point of both cycles occurred in the early morning and the highest point in the late afternoon. The amount of REM sleep was largest near the low point of the circadian cycle of oral temperature and heart rate, and smallest at the high point, indicating a phase reversal relationship between the circadian rhythm of REM sleep and the autonomic functions. During 1 week of absolute bed rest under entrained conditions, subjects were most able to sleep near the low point of their oral temperature cycle and least able to sleep near the high point, and the amount of REM sleep was largest near the low point of the oral temperature and smallest at the high point. **Key Words**: Circadian rhythm—REM sleep—Nap—Total sleep deprivation—Morita therapy.

Slow wave sleep (SWS) is most heavily concentrated during the first third of nocturnal sleep, whereas the percent of rapid eye movement (REM) sleep gradually increases throughout the course of nocturnal sleep, reaching a plateau during the last third of the night (Dement and Kleitman, 1957*a,b;* Williams RL et al., 1964, 1966). Furthermore, naps taken early in the morning closely resemble sleep during the last third of the previous nocturnal sleep episode in that there is a large

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percentage of REM sleep and a small percentage of SWS. In contrast, naps taken in the evening resemble sleep occurring during the first part of the nocturnal sleep episode (Maron et al., 1964; Webb and Agnew, 1967; Karacan et al., 1970). Such studies on daytime naps following nocturnal sleep suggest that the percentages of SWS and REM sleep change systematically in sleep occurring at different times of day or night.

To investigate the factors responsible for these systematic changes of SWS and REM sleep ratios, many experimental studies used techniques of sleep deprivation and phase shifting of scheduled sleep times. Both partial and total sleep deprivation result in increased amounts of SWS in the following nocturnal sleep episode (Berger and Oswald, 1962; Williams HL et al., 1964; Webb and Agnew, 1965; Kales et al., 1970). Following a 180° phase shift of the usual nocturnal sleep episode (e.g., sleep taken from 12 noon to 8:00 p.m. instead of from 12 midnight to 8:00 a.m.), SWS remained concentrated within the first third of the sleep episode (Weitzman et al., 1970; Berger et al., 1971; Webb and Agnew, 1971*b*). In contrast, REM sleep was no longer concentrated in the last third of such sleep episodes; rather, the inverted sleep episodes had short REM sleep latencies and increased amounts of REM sleep during the first portion of sleep (Weitzman et al., 1970). Webb and Agnew (1971*a*) reported that there was a positive correlation between the amount of SWS and the length of prior wakefulness, whereas the amount of REM sleep showed a circadian variation without a similar relationship to prior wakefulness. These studies made it clear that the amount of SWS was dependent on the length of prior wakefulness, whereas the amount of REM sleep was related to the time of day.

In order to further examine the circadian variation of REM sleep, and to investigate the phase relationship between the circadian variation of REM sleep and other autonomic functions, we have undertaken two very different kinds of experimental protocols. In the first, the temporal distribution of REM sleep in daytime naps taken after usual nocturnal sleep was compared to that in naps taken at the same time of day following one night of total sleep deprivation. In the second, the temporal distribution of both REM sleep and body temperature were measured during a period of absolute bed rest (the subjects were physicians undergoing Japanese Morita psychotherapy).

METHODS

Part I: Nap Study

Subjects

The subjects for the nap study following sleep deprivation (a) were 5 healthy male university students (ages 20 to 21) who had been instructed to maintain regular sleep habits and to abstain from all drugs, including alcohol. Subjects for the nap study following usual nocturnal sleep (b) were 4 healthy males (ages 21 to 24) who had received similar instructions.

Experimental Protocol (a)—Nap Study Following Sleep Deprivation

The subjects' sleep patterns were recorded polygraphically in separate, soundattenuated rooms. Each was recorded for 3 consecutive base-line nights, approximately 1 month prior to the first nap recording. For the nap recording, each subject was recorded during a morning nap (M), from 0900 to 1200 hr, following one night's total sleep deprivation. The morning nap procedure was repeated 2 more times, each recording separated by at least 1 week. Recordings for afternoon naps (A) (1300 to 1600 hr), and evening naps (E) (1700 to 2000 hr), after a night's sleep deprivation, also were obtained 3 times each at intervals of at least 1 week. Thus each subject had 3 nap conditions recorded 3 times for a total of 9 nap recordings.

Experimental Protocol (b)—Nap Study Following Usual Nocturnal Sleep

Subjects for this study were recorded for morning, afternoon, and evening naps taken at the same times of day as the naps recorded in (a) above.

Part II: Absolute Bed Rest

Subjects

Subjects were 4 medical doctors (ages 24 to 26) who were studied during the course of the absolute bed rest phase of Morita therapy. Morita therapy is a kind of Japanese psychotherapy consisting of 4 different phases, which include absolute bed rest, a light work phase, a moderately hard work phase, and a hard work phase. Under the condition of absolute bed rest, subjects must remain in bed both day and night, except for meals and to use the bathroom. During that week in our study, they remained exposed to a usual light–dark cycle that is entrained to the 24-hour day. During this phase of Morita therapy, they were prohibited to speak to any other person or to engage in any kind of physical exercise. In that sense, they were socially isolated.

Experimental Protocol

Each of the subjects was polygraphically recorded throughout the entire week under this condition, except during mealtimes. Lights were turned off at 2100 hr daily and back on at 0600 hr. Meals were served at 0700 hr, 12 noon, and 1700 hr. Oral temperature was measured at 0600, 0800, 12 noon, 1900, and 2100 hr.

RESULTS

Part I: Nap Study

Sleep Latency, REM Sleep Latency, and Stage Three Sleep Latency

There was no significant difference in sleep latency between morning, afternoon, and evening naps in either the naps following usual nocturnal sleep or in those following sleep deprivation. However, on average, the subjects had a shorter sleep latency in each of the nap conditions after 1 night of total sleep deprivation than in those same conditions after the usual nocturnal sleep (Table 1).

Latency to stage 3 showed a significant difference within the 3 nap conditions in naps following the usual nocturnal sleep ($p < 0.05$), but no significant differences

TABLE 1. *Mean min (±SD) of sleep latency, stage 3 sleep latency, and REM sleep latency*

Sleep measure	Type of nap	Morning nap		Afternoon nap		Evening nap		Significance level[a]
		Mean	SD	Mean	SD	Mean	SD	
Sleep latency	U.N.	10.3	5.23	4.9	0.83	7.2	2.68	NS
	TSD.N.	2.2	1.24	1.3	0.79	2.4	2.19	NS
Stage 3 sleep latency	U.N.	58.7	21.55	26.2	6.52	22.1	6.67	$p < 0.05$
	TSD.N.	18.7	4.55	14.3	2.12	12.9	2.15	NS
REM sleep latency	U.N.	18.6	20.30	44.3	16.51	56.8	4.29	$p < 0.05$
	TSD.N.	21.7	16.61	69.7	32.03	74.2	4.57	$p < 0.01$

[a] Significance level based upon one-way ANOVA of the overall differences among three nap conditions.

U.N., naps after the usual nocturnal sleep; TSD.N., naps after one night total sleep deprivation.

were observed in those nap conditions following total sleep deprivation. Again, the subjects had a shorter latency to stage 3 following total sleep deprivation than did those whose naps followed usual nocturnal sleep.

On the other hand, the differences in REM latency between morning, afternoon, and evening naps were significant whether those naps followed a usual night of sleep or a night of total sleep deprivation ($p < 0.05$ and $p < 0.01$, respectively). For both conditions, there was a shorter REM sleep latency during the morning nap than in the naps taken in either the afternoon or evening.

Amounts of SWS and REM Sleep

The amount of time spent in REM sleep or SWS in the 2 hr following sleep onset at each of the 3 nap times, in both groups, is presented in Table 2. Significant differences in the amount of REM sleep accumulated at those 3 different times of day were found in both groups—that is, after usual nocturnal sleep and after a night of total sleep deprivation ($p < 0.05$ in both cases). The amount of REM sleep in the morning naps following total sleep deprivation was significantly greater than

TABLE 2. *Mean min (±SD) of REM sleep and slow wave sleep during 120 min after sleep onset*

Sleep measure	Type of nap	Morning nap		Afternoon nap		Evening nap		Significance level[a]
		Mean	SD	Mean	SD	Mean	SD	
REM sleep	U.N.	36.3	11.68	30.8	7.08	15.2	4.65	$p < 0.05$
	TSD.N.	25.7	5.66	13.3	7.21	12.8	5.65	$p < 0.05$
Slow wave sleep	U.N.	8.3	3.83	26.1	8.66	30.0	7.89	$p < 0.05$
	TSD.N.	52.9	5.78	61.9	11.72	62.5	7.27	NS

[a] Significance level based on one-way ANOVA of the overall differences among 3 nap conditions. Abbreviations as in Table 1.

the amount in both afternoon and evening naps ($p < 0.01$ for each comparison, using Ryan's statistical method), but the amount in the afternoon naps did not differ significantly from evening naps. Following usual nocturnal sleep, morning and afternoon naps each had a significantly greater amount of REM sleep than evening naps ($p < 0.1$). There was no significant difference between REM sleep in morning and afternoon naps in that group.

Amounts of SWS in the naps following usual nocturnal sleep were significantly smaller in the morning than in both the afternoon and evening ($p < 0.01$ for each condition). There was no significant difference for SWS between the afternoon and evening naps. Following total sleep deprivation, there was no significant difference in the amount of SWS present among the 3 nap conditions. As shown in Table 2, while the amount of REM sleep decreased from morning to evening, despite an increase of total sleep deprivation, the amount of SWS gradually increased (although not significantly) with the amount of prior sleep deprivation.

Number of REM Episodes, Length of First REM/Non-REM Cycle, Length of Interval Between First Two REM Episodes, and Duration of First REM Episode

The number of REM episodes in the 3 nap conditions following total sleep deprivation did not differ significantly from that in naps following usual nocturnal sleep (Student's *t*-test). However, there were significant differences between the 3 nap conditions whether or not these were preceded by usual nocturnal sleep. There were a significantly greater number of REM episodes in the morning naps than there were in afternoon or evening naps following total sleep deprivation ($p < 0.05$). Following a night of usual nocturnal sleep, morning naps had a greater number of REM episodes than both afternoon and evening naps ($p < 0.05$). This is shown in Table 3.

While the length of the first REM/Non-REM (NREM) cycle and the interval

TABLE 3. *Number and duration of REM episodes and cycles during 3 nap conditions*

Sleep measure	Type of nap	Morning nap Mean	Morning nap SD	Afternoon nap Mean	Afternoon nap SD	Evening nap Mean	Evening nap SD	Significance level[a]
Number of REM episodes	U.N.	2.4	0.36	1.9	0.27	1.6	0.36	$p < 0.05$
	TSD.N.	2.5	0.17	1.9	0.49	1.7	0.25	$p < 0.05$
Length of first REM/NREM cycle	U.N.	61.3	10.28	78.9	20.27	73.3	7.01	NS
	TSD.N.	78.7	11.41	76.1	14.52	82.4	9.67	NS
Interval between first 2 successive REM episodes	U.N.	48.2	9.36	58.2	12.01	64.1	4.30	NS
	TSD.N.	66.4	6.39	65.7	10.82	70.3	6.43	NS
Duration of first REM episode	U.N.	13.1	2.29	25.8	9.34	18.8	9.66	NS
	TSD.N.	12.3	7.32	15.7	3.22	14.4	5.01	NS

[a] Significance level based on one-way ANOVA of the overall difference among 3 nap conditions. Abbreviations as in Table 1.

between the first 2 REM episodes showed no significant differences in naps following both total sleep deprivation and the night of usual nocturnal sleep, both lengthened significantly in the morning nap following total sleep deprivation (Student's t-test). However, REM sleep latency and the duration of the first REM episode in the morning nap following total sleep deprivation did not differ significantly from those in the morning nap following usual nocturnal sleep. It was evident that REM sleep was most prominent in morning naps, increases of SWS resulting from total sleep deprivation notwithstanding.

Sleep Onset REM Episodes

Several sleep researchers have reported that REM sleep sometimes appears during nap recordings within 10 min of sleep onset. Carskadon and Dement (1975) refer to this phenomenon as a "sleep onset REM (SOREM)" episode. Using their criterion for SOREMs (i.e., REM latency of less than 10 min), the differences among the 3 nap conditions following usual nocturnal sleep and total sleep deprivation were examined statistically (χ^2 test).

As shown in Table 4, the number of SOREMs in morning naps was significantly greater than during afternoon or evening naps, whether or not the naps followed usual nocturnal sleep or total sleep deprivation ($p < 0.05$ and $p < 0.001$, respectively).

Circadian Rhythm of Heart Rate, Oral Temperature, and REM Sleep

As shown in Fig. 1, heart rate and oral temperature reached their lowest levels in the early morning and highest levels in the afternoon in both experimental protocols of the nap study. In contrast, the circadian rhythm of REM sleep was at its lowest in the evening and reached its highest levels in the early morning. The circadian rhythm of oral temperature and heart rate therefore was out of phase with that of REM sleep.

Part II: Absolute Bed Rest

The total sleep time decreased gradually toward the end of the absolute bed rest phase of Morita therapy. In addition, sleep onset tended to occur near the low point of the oral temperature cycle.

Figure 2 shows the relationship between the temporal distribution of REM sleep and the oral temperature cycle during absolute bed rest. The oral temperature

TABLE 4. *Number of sleep onset REM episodes*

Type of nap	Morning nap	Afternoon nap	Evening nap	Significance level[a]
U.N.	7	4	0	$p < 0.05$
TSD.N.	10	3	1	$p < 0.001$

[a] Significance level based upon χ^2 test.
Abbreviations as in Table 1.

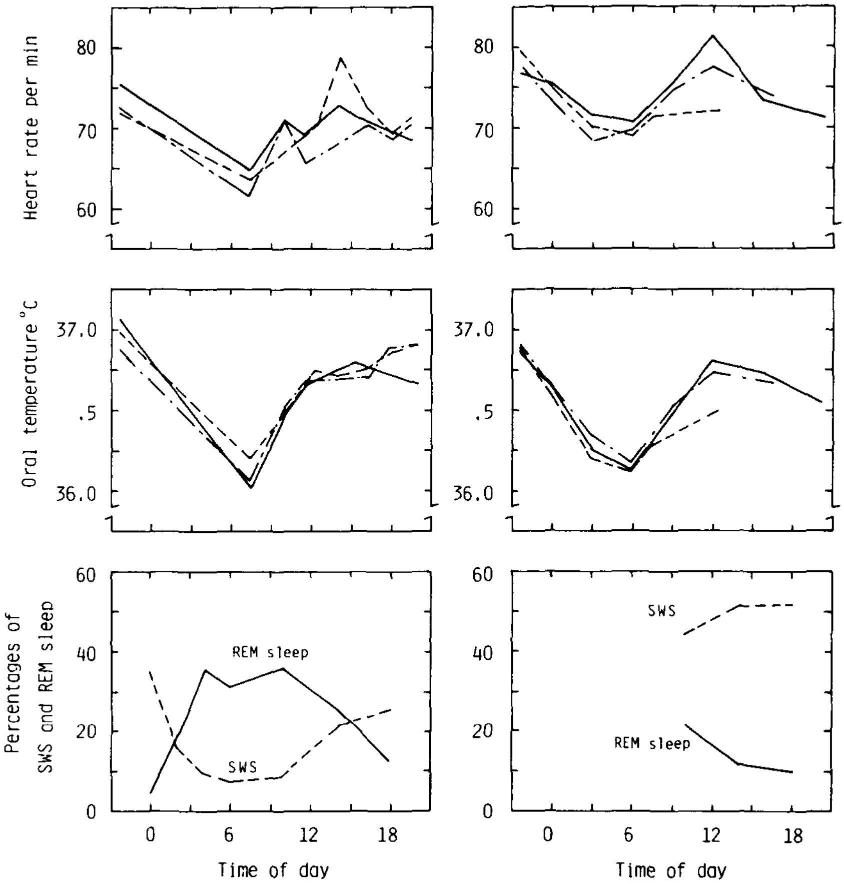

FIG. 1. The reciprocal relationship between the circadian variations of autonomic functions such as heart rate and oral temperature and the timing of REM Sleep. **Left**: results following naps taken after the usual nocturnal sleep; **right**: results following total sleep deprivation. Note that although there was an increase in slow wave sleep following one night of total sleep deprivation, there was a persistence of the circadian variation of REM sleep.

cycle, indicated in the upper panel of Fig. 2, and the hourly percentage of REM sleep, indicated in the lower panel, maintained a consistent phase relationship throughout the study. It is clear that subjects were most able to sleep near the low point of their oral temperature cycles, and least able to sleep near the high point, and that percentages of REM sleep were greatest near the low point and lowest at the high point of oral temperature.

DISCUSSION

Sleep patterns changed systematically in association with the time of day when subjects napped after one night of total sleep deprivation. Marked increases of SWS were observed in the 3 nap conditions following 26, 30, and 34 hr of total sleep deprivation, compared with SWS in the 3 nap conditions after usual noctur-

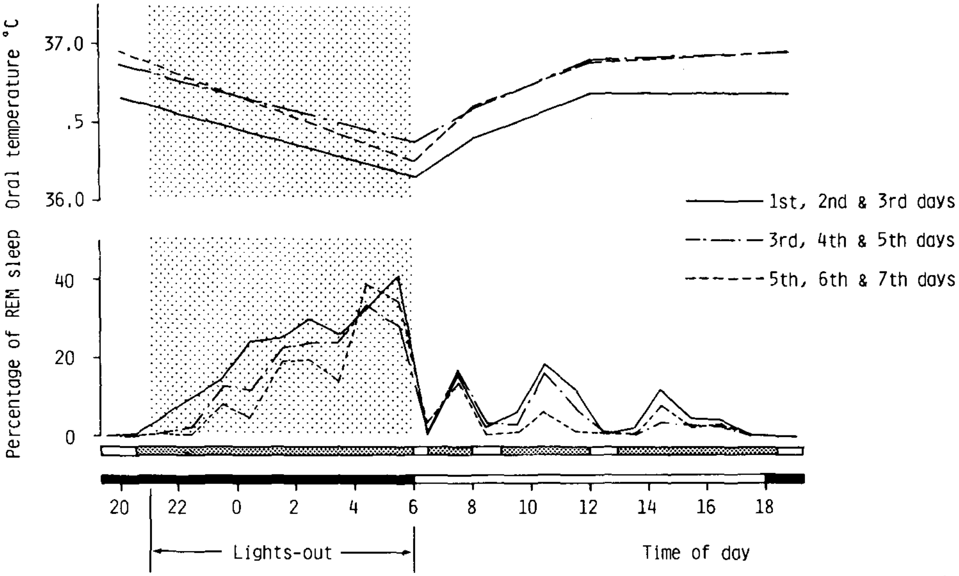

FIG. 2. The circadian variation of REM sleep and oral temperature under the absolute bed rest phase of Morita therapy. **Top**: mean oral temperature curve for the days indicated; **bottom**: variation of the mean hourly percentage of REM sleep in each of the 4 subjects. The lights out episode for the absolute bed rest condition was from 2100 hr to 0600 hr. Stippling within the upper horizontal bar above time axis shows the polygraphic recording time.

nal sleep. Amounts of SWS in afternoon and evening naps after total sleep deprivation were greater than those in morning naps. These findings indicate that the length of prior wakefulness has a determinative effect on SWS. This is consistent with the observation by Webb and Agnew (1965) of increases in stage 4 sleep during restriction of sleep to 3 hr per 24 hr, with 21 hr of intervening wakefulness instead of the usual 16 hr, even when the time of sleep onset was kept constant. Stage 4 has been noted to increase on nights following total sleep deprivation (Berger and Oswald, 1962; Williams HL et al., 1964; Kales et al., 1970). Berger et al. (1971) reported that the increase in stage 4 during daytime sleep after one night of total sleep deprivation did not differ from that observed when recovery sleep occurred at night. This finding indicated that increases of stage 4 were not appreciably influenced by the point in the circadian rhythm in which sleep occurred, but rather by accumulation of certain amounts of prior wakefulness (Webb and Agnew, 1971*b*).

However, in our studies, the amount of REM sleep differed significantly among the 3 nap conditions, each following 1 night of total sleep deprivation. There were larger amounts of REM sleep in the morning naps as compared to both afternoon and evening naps. There was also a slight decrease in the amount of REM sleep in afternoon and evening naps following 1 night of total sleep deprivation, as compared with those naps following a night of usual sleep; this was due to an increase in the amount of SWS. These findings are compatible with previous studies showing large amounts of REM sleep during morning naps and negligible amounts of REM sleep during evening naps (Maron et al., 1964; Webb et al., 1966; Webb and Agnew, 1967; Karacan et al., 1970). Webb and Agnew (1971*a*) also demonstrated the circadian pattern of REM sleep, which was largely independent of the length of prior wakefulness; a greater amount of REM sleep occurred in 4 hr sleep episodes taken at 7:00 a.m. and 3:00 p.m. than in those taken at 11:00 p.m.

The short REM latency in the morning nap after 1 night of total sleep deprivation was similar to that observed during daytime sleep following acute sleep reversal (Weitzman et al., 1970; Berger et al., 1971; Webb et al., 1971). The SOREMs appeared more frequently in the morning naps in spite of extended prior wakefulness, owing to the one night of total sleep deprivation. SOREMs almost never occur in normal nocturnal sleep. Since SOREMs are elicited in man during nocturnal sleep predominantly by extended periods of prior selective REM-sleep deprivation, we believe that the appearance of SOREMs was the result of a greatly increased "REM pressure."

In this experiment, it is clear that in the morning nap the REM pressure at the acrophase of the circadian rhythm of REM sleep is enough to overwhelm the tendency toward increased SWS because of extended prior wakefulness.

The heart rate and oral temperature following sleep deprivation showed a circadian rhythm with the lowest point in the early morning and the highest point in the late afternoon. It is clear that the amount of REM sleep was highest near the low point of the circadian cycle of oral temperature, and that it was lowest at the high point of that cycle. This is consistent with the results of the absolute bed rest Morita therapy study. Both confirm that REM sleep has a circadian rhythm, and that peak REM sleep propensity occurs near the minimum of cycles of autonomic functions such as oral temperature and heart rate. These data also help to explain the previously reported effects of time-zone changes on REM sleep, and the synchrony of REM sleep and heart rate with phase shifting (Endo et al., 1978).

Many studies of nocturnal sleep, daytime naps, and phase shifts of sleep time indicate that REM sleep has a circadian rhythm with an acrophase in the early morning, whereas SWS correlates positively with the length of prior wakefulness. In Part I of this paper, we confirmed that REM sleep has a stable circadian variation; large REM sleep amounts occurred in morning naps despite increases of SWS due to 1 night of total sleep deprivation. Heart rate and oral temperature both continued to show a circadian rhythm in spite of 1 night of total sleep deprivation. The lowest point of both cycles occurred in the early morning and the highest point in the late afternoon. The amount of REM sleep was largest near the low point of the circadian cycle of oral temperature and heart rate, and smallest at the high point, indicating a phase reversal relationship between the circadian rhythm of REM sleep and the autonomic functions.

It has been reported that there is a circadian rhythm of REM sleep under free-running conditions. In Part II, we investigated whether a circadian rhythm of REM sleep persists during 1 week of absolute bed rest, as in that phase of Morita therapy. The results show that subjects were most able to sleep near the low point of their oral temperature cycle and least able to sleep near the high point, and that the amount of REM sleep was largest near the low point of the oral temperature and smallest at the high point.

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