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Distribution of REM Sleep in Entrained 24 Hour and Free-Running Sleep–Wake Cycles

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Summary: One hundred thirty sleep episodes of 6 subjects, living on a natural 24 hr day, were compared with 116 sleep times of the same subjects living isolated from external time cues. The polygraphic sleep recordings were analyzed for the distribution of REM sleep under both conditions. Additionally, the relationship between body temperature and REM sleep was analyzed by comparing sleep episodes in which the temperature minimum occurred early in the sleep episode with those in which there was a late temperature minimum. The results show that there is more REM sleep in the beginning of sleep in sleep episodes of free-running rhythms as compared to sleep episodes of entrained 24 hr rhythms. This higher amount of REM sleep is due to a longer first REM episode and shorter first NREM episodes. The comparison of the sleep episodes that differ in the position of the temperature minimum shows similar differences, i.e., more REM sleep in the beginning of sleep episodes in which the temperature minimum occurs earlier as compared to episodes in which the temperature minimum occurs later. It was hypothesized that the amount of REM sleep depends on the phase relationship between sleep and the circadian temperature cycle. From this point of view, the difference in the distribution of REM sleep in the entrained 24 hr rhythm, on the one hand, and the free-running rhythm, on the other hand, can be explained by the different courses of body temperature during sleep. That only the first REM episode is influenced by circadian parameters may indicate an exceptional role for this REM episode in contrast to the following episodes. **Key Words**: REM sleep—Body temperature—Circadian rhythm.

In human sleep research, the consistency of the internal structure of sleep has been investigated by varying the sleep–wake schedule. The influence of the time of sleep occurrence on the sleep stage structure has been shown by shifting the sleep episode over the 24 hr day (Webb and Agnew, 1967; Kripke et al. 1971; Foret and Lantin, 1972; Knauth and Rutenfranz, 1972; Bryden and Holdstock,

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1973). The same results have come from studies in which the sleep structure was studied in a non-24-hr sleep–wake cycle (Karacan et al., 1970; Moses et al., 1975; Webb and Agnew, 1975; Hume and Mills, 1977; Webb and Agnew, 1977; Webb, 1978). These studies showed a circadian variation of REM sleep with local time. REM sleep was at a maximum in the early morning and at a minimum in the evening. This was correlated with the oral temperature.

Only a few studies have analyzed the sleep of subjects living on a sleep–wake schedule not influenced by external time cues. Polygraphic sleep studies under those conditions have been done by Chouvet et al. (1974), Webb and Agnew (1974), Zulley (1977, 1979), and Czeisler (1978). Some of these studies showed different distributions of REM sleep within the sleep episode during free-running cycles as compared to entrained 24 hr cycles. Studies of Aschoff et al. (1971) showed, on the other hand, that the course of free-running body temperature during bedrest differed from that during entrained 24 hr rhythms. Therefore, the question arises of whether the same differences in the distribution of REM sleep can also be seen in sleep episodes associated with a different course of body temperature, independent of the condition.

This paper compares the structure of REM–NREM sleep in sleep episodes in an entrained 24 hr rhythm with sleep episodes in a free-running rhythm. It had been found that the temperature minimum occurred predominantly either in the beginning (less than 2 hr after sleep onset) or at the end (more than 4 hr after sleep onset) of free-running sleep episodes (Zulley, 1980). In a further step in this investigation, the structure of the REM–NREM cycle was compared in sleep episodes with an early minimum to those with a late minimum.

METHOD

The sleep of 6 subjects (21–28 years old) was recorded in a total of 246 bedrests under two different conditions (Zulley, 1979). In the control conditions, the subjects slept for about a month (14–30 days) at night in a sleep laboratory and followed their normal schedules during the day. In this manner, their sleep–wake cycle was entrained to the natural 24 hr day. In the experimental conditions, the subjects were deprived from all external times cues. They lived for about a month (21–30 days) alone in an underground apartment with no social contact. The experimental conditions, therefore, were the same as in the standard experiments for circadian research by Aschoff and Wever (Wever, 1979). However, in addition, sleep was polygraphically recorded. Under both conditions sleep was recorded continuously with a standard set of electroencephalogram, electro-oculogram, and electromyogram electrodes. In most of the cases, body temperature was also continuously measured by a rectal thermometer. For the experimental condition in the isolation unit, the subjects were trained in the technique of self-application of the electrodes.

The sleep recordings were visually scored, using the criteria of Rechtschaffen and Kales (1968). The first sleep stage 2 was defined as the reference point for sleep onset. The last stage 2 or stage REM was defined as the end of the sleep episode. The sleep was divided into blocks of NREM and REM episodes. Besides the comparison of the two conditions, 24 hr day and isolation, the sleep episodes with different courses of body temperature were compared. Thus, from all the sleep episodes in which temperature recordings were made, those with a clear definite circadian temperature minimum were identified. The circadian temperature minimum was visually scored as the point at which the lowest value of body temperature was recorded in the circadian temperature cycle.

For statistical analysis, the means and standard deviations are given. Significance in the differences was tested by the Student t-test at the 0.1% level (unless otherwise noted). To give additional information about the distribution of the data, the medians are given in Figs. 3–7.

RESULTS

The circadian patterns of the sleep–wake cycle and of body temperature in the experimental condition were generally the same as in the standard experiments without sleep recording with free-running periods (30.23 ± 6.08 hr) longer than 24 hr (Wever, 1979). During the control condition, all the subjects showed a 24 hr period in both the sleep–wake cycle and the temperature cycle (when measured).

Of the 116 bedrest episodes in the free-running rhythm (nonentrained condition), an early circadian temperature minimum was seen in 68 and a late minimum in 14; 34 could not be classified because a clear temperature minimum was not evident. Temperature was recorded in only 17 of the 130 bedrests of the entrained rhythms. Of those 17, 3 had an early minimum and 14 had a late minimum.

The mean sleep duration in the entrained 24 hr rhythm was 7.26 ± 0.86; in the free-running rhythm, 8.83 ± 2.70. This difference is significant. In the free-running rhythm, the sleep episodes with the temperature minimum in the beginning had a mean duration of 7.69 ± 1.30 hr, whereas the sleep episodes with the minimum at the end had a mean of 11.08 ± 2.85 hr. This difference is also significant.

REM Sleep

The absolute amount of REM sleep per sleep episode (Table 1A) showed a significant difference between the sleep episodes in the entrained 24 hr rhythm

TABLE 1. *Amount of REM sleep per sleep episode*

	A. Absolute amount of sleep (min)	B. Relative amount of sleep (%)
Entrained 24 hr rhythm (n = 129)	109.98 ± 24.77	24.12 ± 4.50
Free-running rhythm (n = 108)	133.42 ± 24.77	24.85 ± 4.50
Temperature minimum		
Late (n = 19)	145.92 ± 60.77	23.47 ± 4.55
Early (n = 55)	126.12 ± 27.60	25.98 ± 3.52

Values are means ± SD.

(109.98 ± 24.77 min) and the free-running rhythm (133.42 ± 24.77 min). With regard to the different sleep durations in both conditions (Table IB), there were no significant differences in the relative amounts of REM sleep per sleep episode (entrained 24 hr rhythm, 24.12 ± 4.66%; free-running rhythm, 24.85 ± 4.50%). Because of the smaller number of sleep episodes and the greater variability of these data, the difference in the absolute amount of REM sleep in the sleep episodes with the minimum at the end (145.92 ± 60.77 min) did not differ significantly from the amount of REM sleep in the sleep episodes with the minimum in the beginning (126.12 ± 27.60 min). The difference between the relative amounts of REM sleep in the sleep episodes with different positions of the minimum also did not differ significantly (late minimum, 23.47 ± 4.55%; early minimum, 25.98 ± 3.52%).

For analyzing the distribution of REM sleep within the sleep episode, the relative amounts in each third of the total sleep episode were computed. Figure 1 shows the distribution of REM sleep in the entrained 24 hr and the free-running rhythms. In the entrained rhythm, the increase of the percentage of REM sleep from the first (10.5 ± 8.0%) to the second third (33.0 ± 10.0%) is significant. It is not significant, however, in the free-running rhythm (27.5 ± 10.5 to 30.5 ± 10.0%). Comparing both conditions, the percent of REM sleep in the first third of the sleep episodes in the free-running rhythm is significantly higher than in the entrained rhythm, while in the second third, no significant difference is seen. The final third of the sleep episodes in the free-running rhythm (30.5 ± 10.0%) differs significantly from the sleep episodes in the entrained rhythm (35.5 ± 11.0%). So in the free-running rhythm the distribution over the sleep episode is relatively constant, whereas in the entrained rhythm the percentage of REM sleep increases throughout the sleep episode.

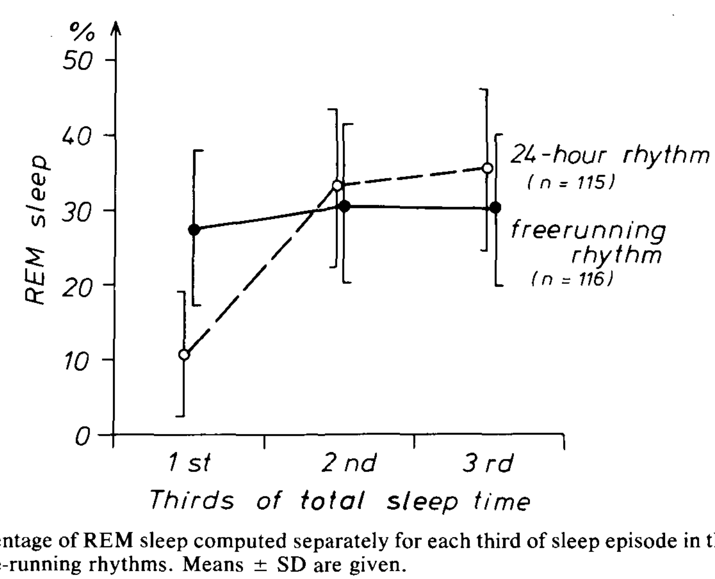

FIG. 1. Percentage of REM sleep computed separately for each third of sleep episode in the entrained 24 hr and free-running rhythms. Means ± SD are given.

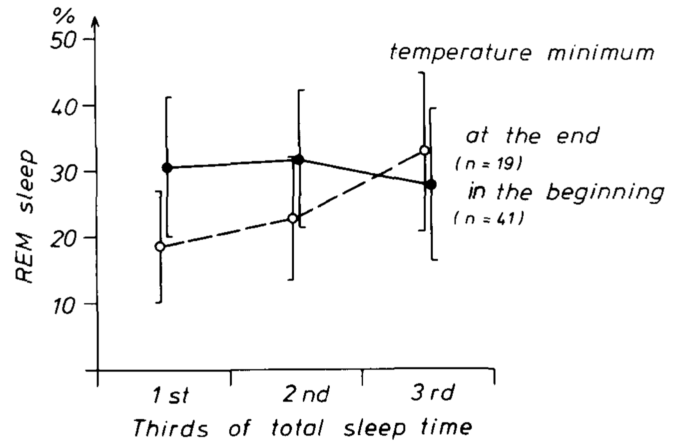

FIG. 2. Percentage of REM sleep computed separately for each third of the sleep episode in sleep with early or late temperature minima. Means ± SD.

Figure 2 shows the same distribution of the percentage of REM sleep in the sleep episodes with different temperature positions. In sleep with a late minimum, the difference from the first (18.57 ± 8.50%) to the second third (22.75 ± 9.28%) is not significant. The increase from the second to the final third (32.77 ± 12.23%), however, is significant ($p < 0.01$). In the sleep episodes with an early minimum, the difference between the first (30.51 ± 10.34%) and the second third (31.84 ± 10.52%) is not significant; neither is the difference between the second and the final third (27.95 ± 11.51%). Comparing the sleep episodes with the different positions of the temperature minimum, only the first third is significantly different from each other, i.e., the percentage of REM sleep increases throughout the sleep episodes with a late temperature minimum, whereas the relative amount of REM sleep is more or less constant throughout sleep episodes with an early temperature minimum.

For analyzing the changes in REM sleep in the beginning of sleep, the absolute amount of REM sleep in the first 3 hr of the sleep episode was determined (Fig. 3). The mean value (49.34 ± 15.73 min) in the sleep episodes of the free-running rhythm was significantly higher than in the entrained rhythm (32.63 ± 11.97 min). The sleep episodes with an early minimum had significantly more REM sleep in the first 3 hr (51.29 ± 14.46 min) than did the sleep episodes with a late minimum (30.69 ± 15.01 min). These differences, which are shown in terms of the relative amounts of REM sleep, were also seen in the absolute values. A further analysis of the distribution of REM sleep involves the comparison of the duration of the REM and NREM episodes. Figure 4 shows the duration of REM episodes in both the entrained and free-running rhythms.

During the sleep in the entrained rhythm, the first REM episode was significantly shorter (15.18 ± 12.67 min) than the second REM episode (29.82 ± 13.64 min), while the following successive REM episodes were not significantly different. In the free-running rhythm, the difference between the duration of the first REM episode (31.42 ± 18.45 min) and that of the second REM episode (28.73 ±

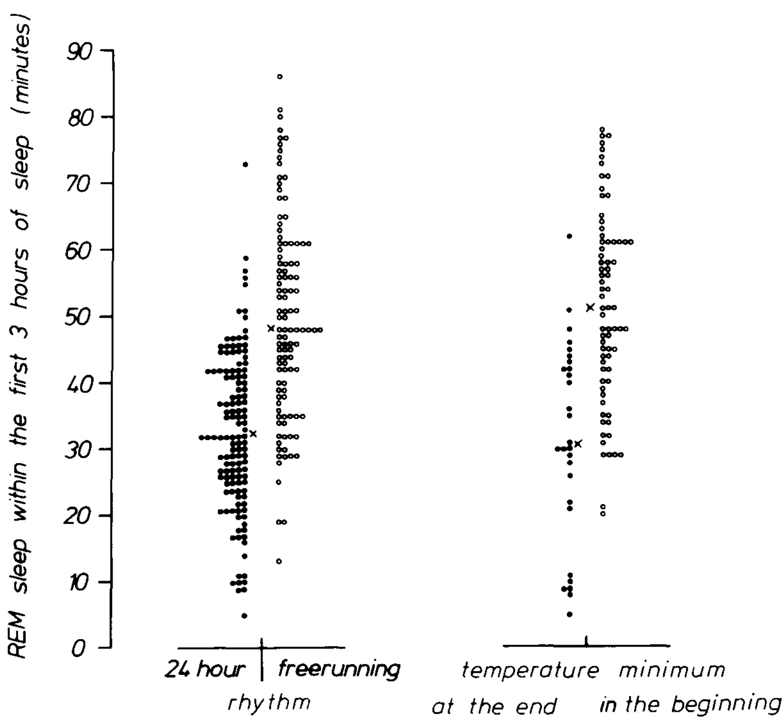

FIG. 3. Absolute amount of REM sleep in the first 3 hr of the sleep episode. The sleep episodes in the entrained 24 hr rhythm are compared with those in the free-running rhythm, and sleep episodes with a late minimum are compared with those with an early minimum. ×, median of each group.

13.64 min) was not significant, which also holds true for the following successive REM episodes. In comparing the two conditions, however, only the first REM episode was significantly different, being of longer duration in the free-running rhythm. The sleep episodes with a late temperature minimum showed no significant differences in the duration of successive REM episodes, which were the same in the sleep episodes with an early minimum (Fig. 5). A comparison between these two groups showed a significantly longer first REM episode (36.42 ± 18.42 min) in the sleep episodes with an early minimum than in the sleep episodes with a late minimum (16.00 ± 8.68 min).

NREM Sleep

The duration of the first NREM episode (68.75 ± 19.96 min) in the entrained sleep episodes (Fig. 6) was significantly shorter than that of the second NREM episode (87.25 ± 16.39 min), and the third NREM episode duration (74.88 ± 16.74 min) was significantly longer than the fourth NREM episode duration (62.55 ± 14.27 min). During sleep in the free-running rhythm, the first NREM episode duration (55.36 ± 18.59 min) was significantly shorter than that of the second NREM episode (70.89 ± 17.76 min). The following successive NREM episodes, however, showed no significant differences in duration. Comparing the durations

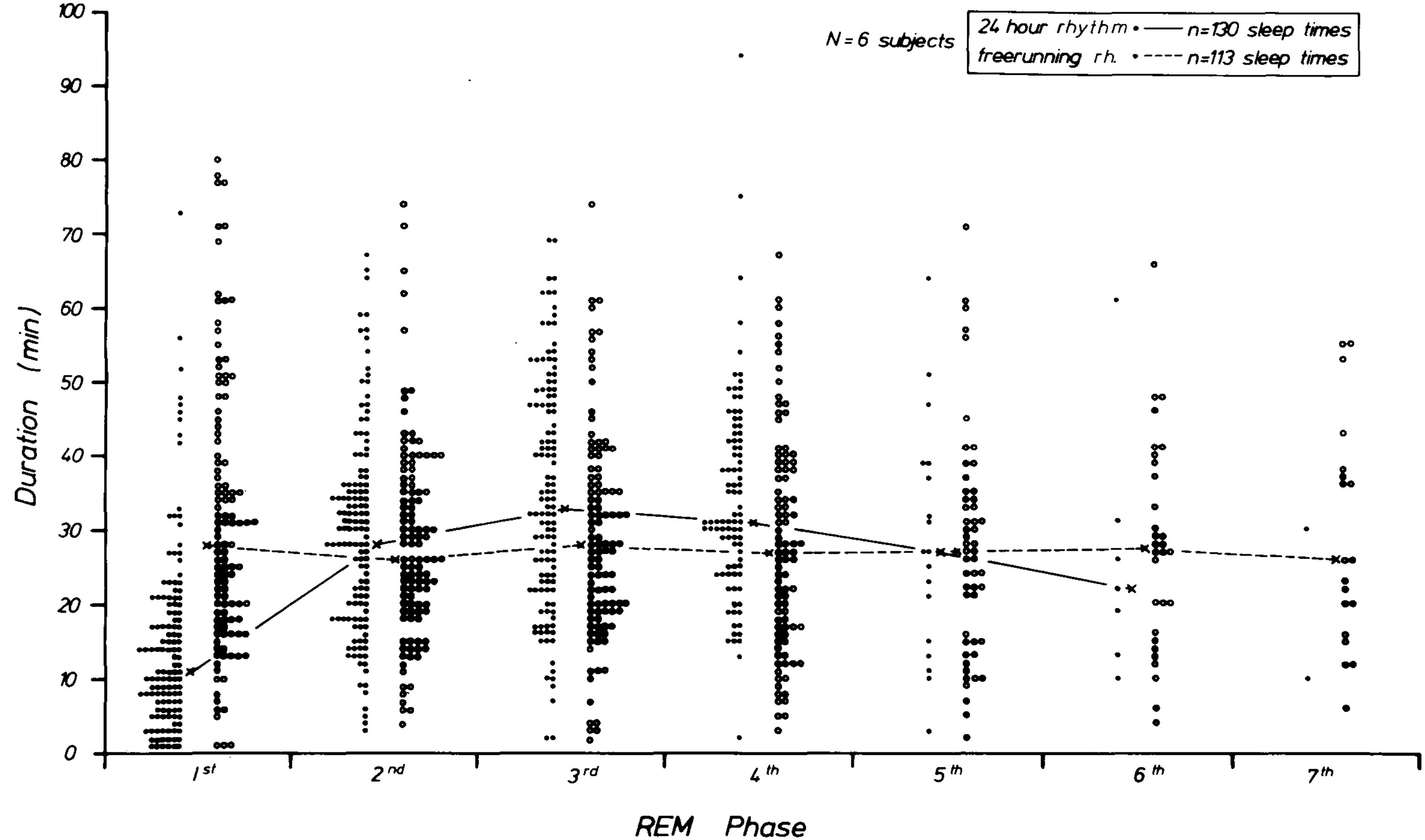

FIG. 4. Distributions of the durations of successive REM episodes in sleep episodes in the entrained 24 hr rhythm and free-running rhythms. ×, median of each group.

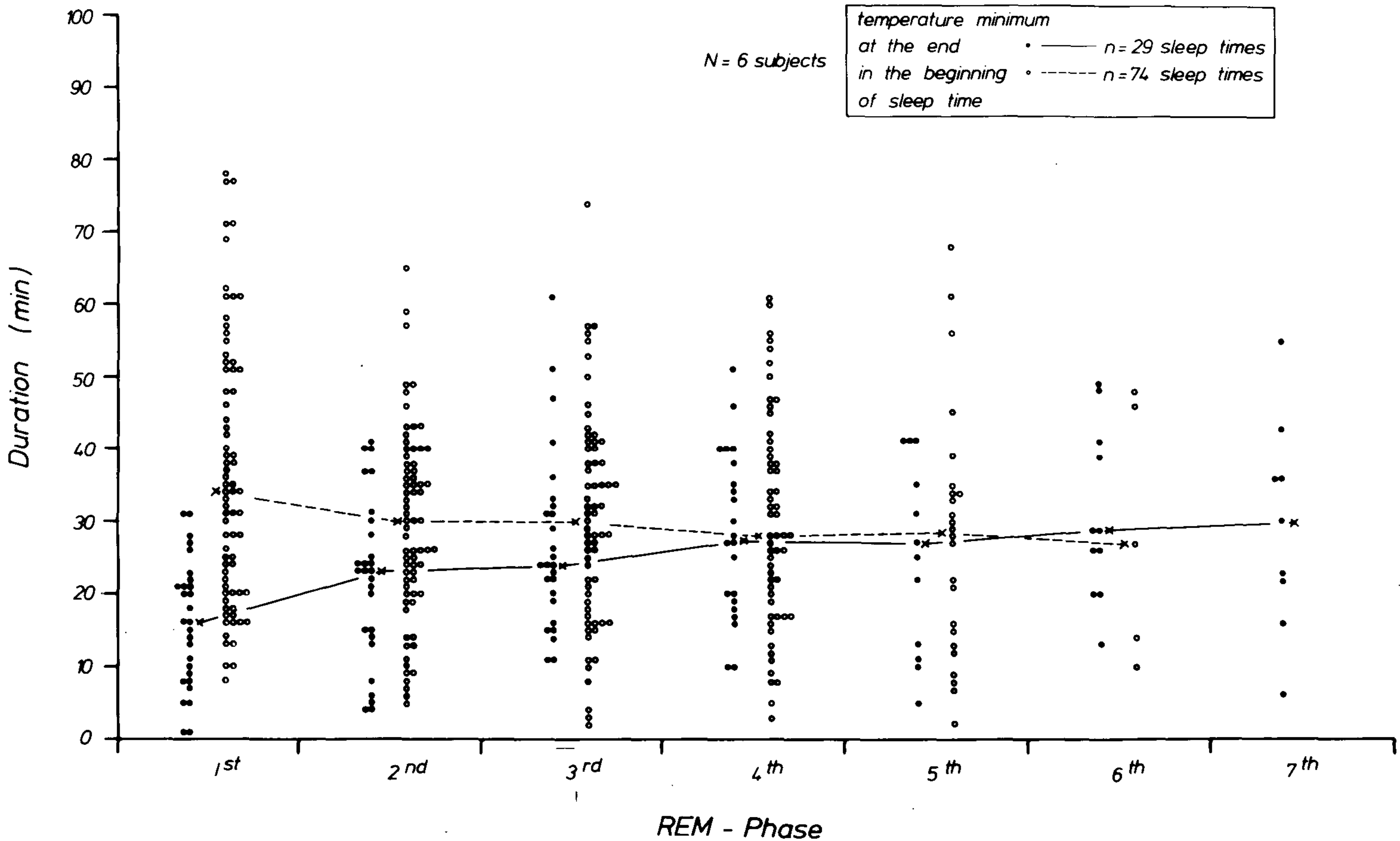

FIG. 5. Distributions of the durations of successive REM episodes in sleep episodes with early or late temperature minima. ×, median of each group.

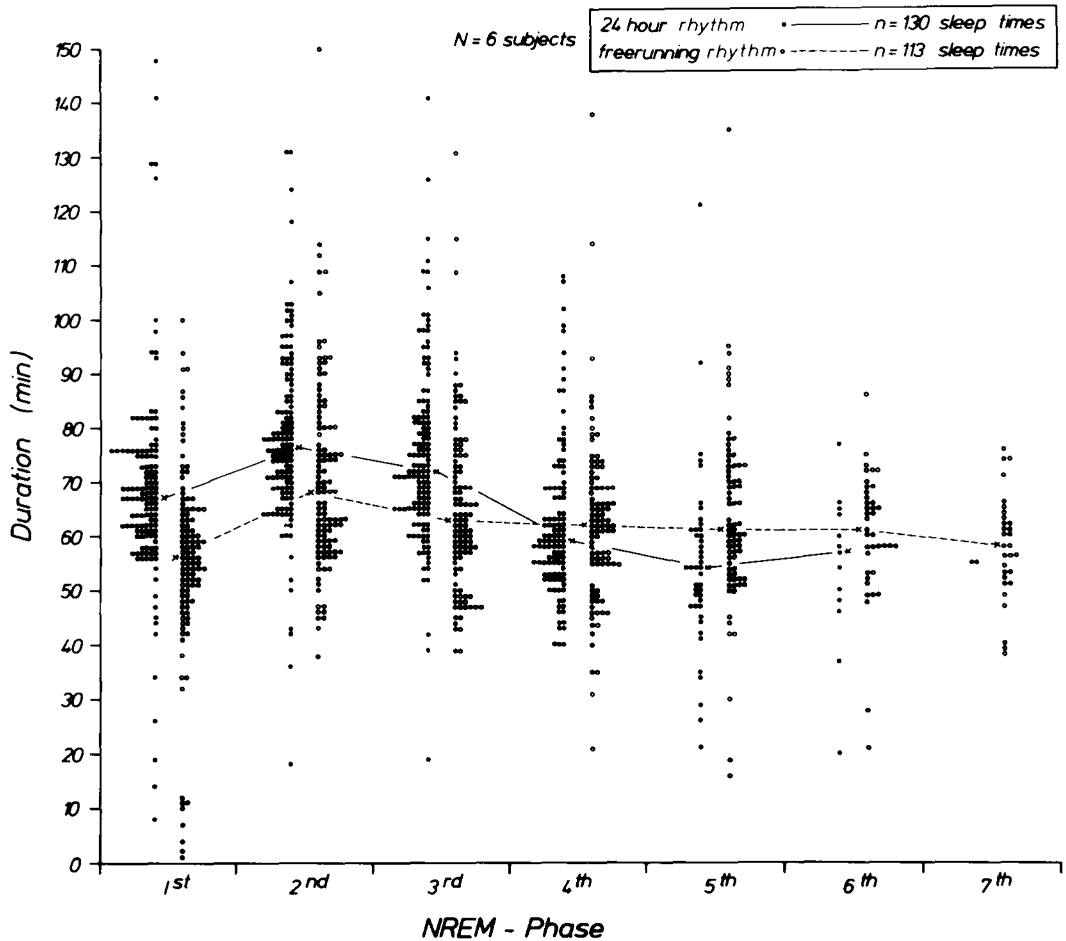

FIG. 6. Distributions of the durations of successive NREM episodes in sleep episodes in the entrained 24 hr and free-running rhythms. ×, median of each group.

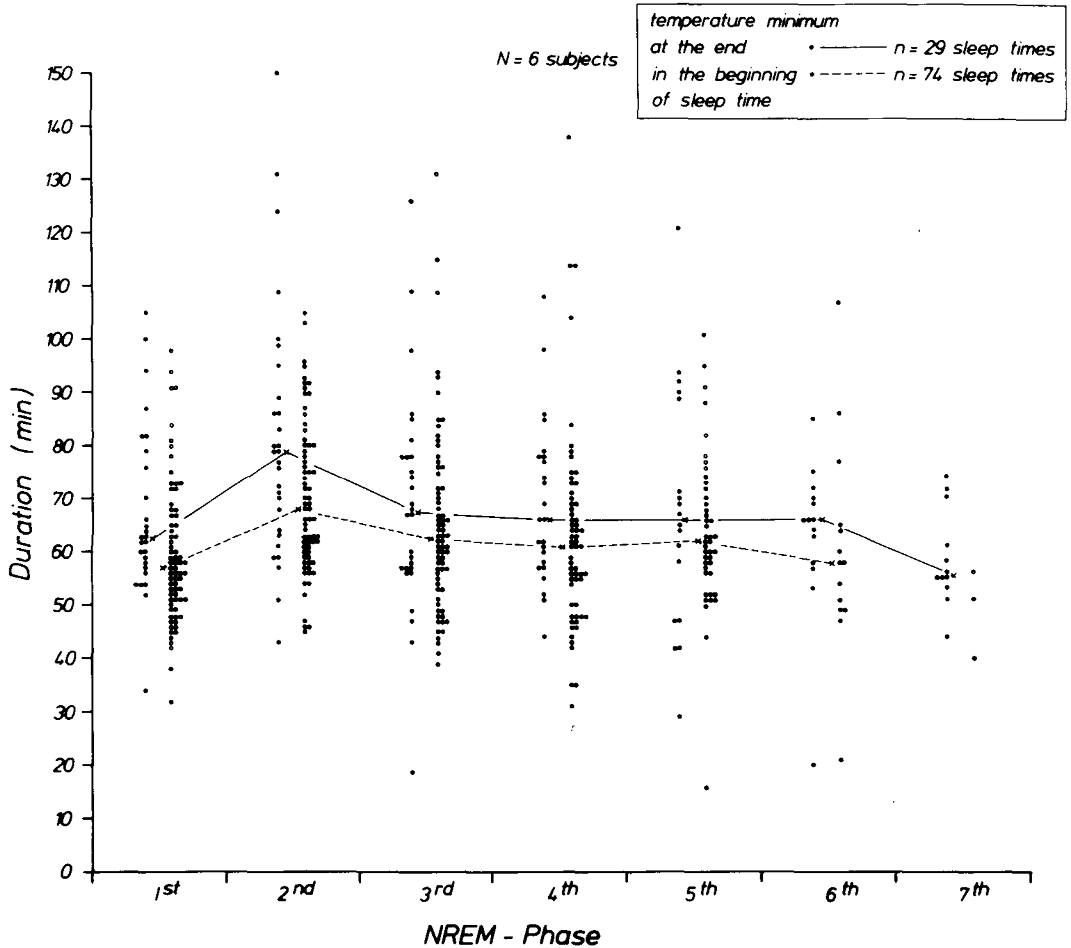

FIG. 7. Distributions of the durations of successive NREM episodes in sleep episodes with early or late temperature minima. ×, median of each group.

of the NREM episodes in the two conditions, each of the first three NREM episodes in the entrained rhythm was significantly longer than in the sleep episodes in the free-running rhythm. There were no significant differences in the duration of the successive NREM episodes due to the position of the temperature minimum of the sleep episode (Fig. 7). However, comparing the duration of the first NREM episode in the sleep episodes with a late minimum (67.52 ± 16.55 min) with that in sleep with an early minimum (59.60 ± 13.32 min) did show a significant difference ($p < 0.05$). The duration of the second NREM episode in sleep with a late minimum (81.95 ± 24.47 min) was significantly longer than the NREM episodes in sleep with a late minimum.

Summarizing the results, the sleep episodes in the free-running rhythm had more REM sleep in the beginning than in the entrained 24 hr rhythm. The sleep episodes with an early temperature minimum also had more REM sleep in the beginning than the sleep episodes with a late minimum.

DISCUSSION

Comparison between sleep in the entrained 24 hr and free-running rhythms shows differences in the distribution of REM sleep. With the same relative percentage of REM sleep, the entrained rhythm shows a progressive increase in REM sleep throughout the sleep episode, whereas in the free-running rhythm, the percentage of REM sleep is constant throughout the sleep episode. This difference results in a lower relative amount of REM sleep in the first third of the sleep episodes in the entrained rhythm than in the free-running rhythm. To separate this difference from the different sleep durations between both conditions, the absolute amounts of REM sleep during the first 3 hr of the sleep were compared. It was found that more REM sleep occurred in the beginning of sleep in the free-running rhythm than in the entrained rhythm.

The higher amount of REM sleep was due to a longer first REM episode and shorter NREM episodes in the beginning of sleep in free-running rhythms. The sleep in the free-running rhythm showed the successive REM episodes with the same distribution. In sleep in the entrained rhythm, however, the short first REM episode deviated from the distribution of the following REM episodes. It was shown in an earlier paper (Zulley, 1979) dealing with single-case studies of 5 of the 6 subjects included in the present study that these results were consistent among all the subjects. A shortening of the first NREM episode was also found by Chouvet et al. (1974) in some of their subjects in a free-running rhythm. Czeisler (1978) found a shortening of the first NREM episode and a higher amount of REM sleep in the first 3 hr of sleep in a free-running rhythm compared to an entrained 24 hr rhythm.

Because of the different courses of body temperature during the sleep in the two conditions, with the minimum mostly at the end of the sleep episode in an entrained 24 hr rhythm and the minimum mostly in the beginning in a free-running rhythm (Aschoff et al., 1971), it seems possible that the difference in the distribution of REM sleep is due to different courses of body temperature. This hypothesis is supported by studies of Moses et al. (1975), who found a correlation between the amount of REM sleep and the circadian temperature cycle. The same result was found in one of the subjects included in this study (Zulley, 1979). In the free-running rhythm, this subject showed various positions of the temperature minimum during sleep (internal desynchronization), with preferred positions of the minimum either in the beginning or at the end of the sleep episode. In sleep episodes with an early minimum, the amount of REM sleep in the beginning of the sleep was higher than in sleep episodes with a late minimum.

Is it possible then that a relationship between the position of the temperature minimum and REM sleep, which was found in the free-running condition in one subject, is independent of conditions for all the subjects? In order to answer this question, the sleep episodes of the present experiment were separated into a group with an early minimum and a group with a late minimum, the two positions predominantly found during sleep (Zulley, 1980). Different distributions of REM sleep were found in these two groups. In the sleep episodes with the early minimum, both the relative and absolute amounts of REM sleep in the beginning of sleep were higher, whereas the first REM episode was longer and the first NREM episodes shorter than in sleep episodes with a late minimum.

Thus, the hypothesis that the amount of REM sleep is related to the course of body temperature is supported by this study. It shows, in fact, more REM sleep in the beginning of the sleep, coinciding with the temperature minimum, than at the end. This result is in agreement with the study of Czeisler (1978), who found a higher REM sleep tendency at the time of the circadian temperature minimum. From this point of view, the difference in the REM sleep distribution found between sleep times in an entrained 24 hr and a free-running rhythm was due to the different positions of the temperature minimum in these conditions. This also holds true for other studies in which sleep was shifted over the 24 hr day (Webb and Agnew, 1967; Foret and Lantin, 1972; Bryden and Holdstock, 1973). These authors found a maximum in the amount of REM sleep in the beginning of the sleep in sleep episodes that began in the early morning, the time of the temperature minimum in the entrained 24 hr rhythm.

As shown in this study, the first REM episode differs from the following episodes in some conditions. While the distribution of the successive REM episodes within the sleep episode of the free-running rhythm and in the sleep times with the early minimum is generally the same, the distribution of the short first REM episode in the sleep episodes in the entrained rhythm and in the sleep episodes with the late minimum differs from the distribution of the following REM episodes. Aside from its duration, the first REM episode in the sleep in 24 hr entrained rhythms also differs in its content from later REM episodes. For example, the first REM episode has fewer eye movements than later REM episodes (Benoit et al., 1974; Caille and Bassano, 1975). The onset of the first REM episode can be predicted by the time at sleep onset, in contrast to the later REM episodes (Schulz et. al., 1975). Therefore, if the first REM episode differs from those which follow, in particular, if a suppressing effect of the body temperature shortens the first REM episode, further studies should be done in which the relationship between body temperature and REM sleep is analyzed.

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DISCUSSION

Dr. Kripke asked whether the bimodal curve in sleep duration implied something about two stable points of coordination between the oscillators. Dr. Zulley replied that those two positions were found only in desynchronized subjects—the first point found 1 hr before the minimum is normally found in synchronized subjects, whereas the second one (found 6–7 hr before the minimum) is found in the 24 hr rhythm of entrained subjects. No theoretical implications were drawn from this observation.