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Circadian Temperature and Activity Rhythms in Unmedicated Narcoleptic Patients

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MAYER, G., F. HELLMANN, E. LEONHARD AND K. MEIER-EWERT. *Circadian temperature and activity rhythms in unmedicated narcoleptic patients.* PHARMACOL BIOCHEM BEHAV **58**(2) 395–402, 1997.—Fifteen unmedicated narcoleptic patients with and without sleep-onset REM period (SOREMP) were compared with 16 unmedicated, age-and-sex-matched control subjects with respect to polygraphic, core body temperature and motor activity recordings. Whereas narcoleptic patients with SOREMPs had significantly more quiet wakefulness during sleep, those without SOREMPs had significantly more quiet wakefulness during daytime than the other groups. Compared with that of controls, temperature of both narcoleptic groups showed (a) less rise of temperature curve in the morning, (b) dampening of temperature amplitude, (c) phase advance of acrophase, and (d) advance of temperature minimum after sleep onset. Maximal temperature decline occurred earlier in patients with SOREMPs during naps and sleep than in the other groups. We could confirm parallels between temperature and motor activity with controls and found no change in the oscillator of narcoleptic patients. Advanced temperature minima and first REMPs relative to sleep onset and maximal temperature decline occurring nearer to sleep onset indicate a defect in the temperature-locked triggering of REM in narcoleptic patients with SOREMP and a circadian rhythm disorder. © 1997 Elsevier Science Inc.

Narcolepsy Core body temperature Actimetry Circadian rhythm disorders

NARCOLEPTIC features such as daytime sleepiness and the sleep-onset REM period (SOREMP) have been a challenge for sleep researchers in the last two decades to investigate; these researchers are interested in whether narcolepsy represents a circadian rhythm disorder. Baldy-Moulinier et al. (1) found a circadian rhythmicity in narcoleptic patients with maximal amounts of REM sleep between 3 and 7 a.m. and minimal amounts between 3 and 7 p.m. that was similar to those of healthy subjects. They found a progressive temperature decrease from 10 p.m. to 2 a.m., constant low temperature between 2 and 4 a.m. and progressive increase from 4 to 8 a.m. In one of their study protocols in which narcoleptic patients were recorded while lying in the bed for 24 h with the lights on, they found more SOREMPs in narcoleptic patients than in patients who were allowed to move around freely, a finding confirmed by Volk et al. (15). An increase of SOREMPs between 12 and 2 p.m. and a clear reduction in SOREMPs from 6 p.m. on were assigned to temperature maxima by Billiard et al. (2). In 1983, Mosko et al. (9) investigated narcolepsy for an underlying circadian rhythm disorder. They studied nine patients with SOREMPs and three patients without SOREMPs under entrained conditions and compared their data to those of nine healthy subjects. SOREMP was polygraphically defined as occurrence of stage REM within 20 min of initial sleep onset. Significant differences were only found when data were normalized for 24-h midline estimatory statistics of rhythm (mesor) and expressed with respect to the hour of sleep onset. In patients with SOREMPs, they found an advanced temperature minimum 1 h after sleep onset compared with 4–5 h after sleep onset in healthy controls. Their narcoleptic patients revealed higher nocturnal T mesor (98.4 ± 0.1°F vs. 98.0 ± 0.1°F), which was related to the sleep disturbance observed in these patients.

In a recent study, Pollak and Wagner (11) could not confirm differences in temperature levels, period, amplitudes and phases of the circadian temperature rhythms in six patients studied under free-running conditions in an isolation unit as compared with healthy controls. In narcoleptic patients, they observed smaller increases of temperature following main sleep periods and decreases of temperature in involuntary naps. Campbell and Broughton (5) investigated changes of core body temperature in relation to the decision to go to sleep in young healthy subjects to clarify the temporal relationship between the nightly decline in body temperature and the timing of nocturnal sleep. Their finding of maximum rate of temperature decline before decision to retire seems to rule out that temperature declines are caused by behaviour.

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After considering this information, we asked the following questions: Do narcoleptic patients

1. show different circadian temperature rhythms, e.g., a phase advance in patients with SOREMPs, as compared with healthy controls?
2. have different ultradian distribution of naps with and without SOREMPs?
3. have temperature-dependent ultradian nap positions?
4. have either temperature declines prior to naps and sleep as compared with controls?

SUBJECTS

Narcolepsy was defined on the basis of excessive daytime sleepiness, with sleep latencies of less than 10 min in the multiple sleep latency test MSLT and cataplexy plus at least two SOREMPs (<10 min) in either polysomnography or MSLT (7). Subjects included in the investigation were patients referred to our clinic and control patients recruited from advertisements. Individuals younger than 18 years or older than 50 years, suffering from acute or chronic diseases or mental illness or taking sleep-enhancing substances, alcohol or drugs were excluded from the study.

We studied 15 unmedicated narcoleptic patients (seven women, mean age = 32 years; nine men, mean age = 33.25 years) and 16 unmedicated age- and sex-matched healthy control subjects (eight women, mean age = 31 years; eight men, mean age = 32.5 years).

All investigated narcoleptic patients and control subjects gave written consent for participation in this study. Three healthy subjects were excluded from data analysis because of missing data.

METHODS

All subjects were continuously monitored for 36 h (from 6 p.m. to 9 a.m.) by using a Medilog 9200 (Oxford Medical Limited, Abingdon, England). The equipment recorded two-channel electrooculogram, four-channel electroencephalogram (EEG) [C4/M1, C3/M4, O2/P4, O1/P3 and one-channel electrocardiogram and electromyogram (EMG) of the submental region]. Subjects were monitored simultaneously with an actimeter and a rectal temperature probe (Fa. Zak, Simbach/Inn, Germany); sampling rates of one data point were recorded every 3 min. Subjects were also required to fill out two standardized sleep questionnaires (SFA and SFB) (8) concerning sleep habits of the last 2 weeks (SFB) and the night prior to the study (SFA). They also had to fill out a specifically designed sleep–wake diary to record sleep time, frequency of hallucinations, sleep paralysis, voluntary and involuntary naps and the amount of caffeine-containing beverages such as coffee, cola and tea.

Recordings for 20 subjects were performed at home on weekdays, and 10 subjects were monitored on the ward because they lived too far away from the clinic to report for battery change and electrode checks. All subjects were not working during the time of the study but were asked to keep a structured daily routine with three meals a day with an equilibrium of carbohydrates, fat and protein. Subjects were requested to keep their normal nocturnal total sleep time during this recording. Physical exercise was not limited, and actimetric, sleep diary and temperature recordings were compared. The comparison led to the exclusion of one control subject, whose temperature rose almost 2°C when bicycling vigorously.

Data Analysis

The sleep–wake determination of the Medilog recordings were performed visually in 32-s epochs according to the standard criteria of Rechtschaffen and Kales.

Classification of wakefulness was performed according to a modification of the criteria of Simon et al. (14). Criteria were defined as

TABLE 1

SLEEP PARAMETERS OF NARCOLEPTIC PATIENTS WITH AND WITHOUT SLEEP ONSET REM AND HEALTHY CONTROLS (MEAN ± SE) GAINED BY 36 H RECORDING WITH THE MEDILOG RECORDER

Sleep Parameters (min)†	Narcoleptic Patients Without SOREMP	Narcoleptic Patients With SOREMP	Healthy Controls	p n − SO vs. n + SO‡	p n − SO vs. con§	p n + SO vs. con¶
Sleep lat. obj. 1	21.89 ± 1.19	22.57 ± 1.23	23.47 ± 1.10	NS	NS	NS
Sleep lat. sub. 1	21.80 ± 0.95	22.33 ± 1.90	22.95 ± 0.64	NS	NS	NS
Sleep lat. obj. 2	22.72 ± 0.72	23.23 ± 1.08	23.30 ± 0.75	NS	NS	NS
Sleep lat. sub. 2	22.51 ± 0.72	22.86 ± 1.21	22.70 ± 1.08	NS	NS	NS
Total sleep time 1	522.00 ± 25.60	495.00 ± 36.92	455.50 ± 30.49	NS	NS	NS
Total sleep time 2	468.33 ± 21.31	479.00 ± 37.92	463.25 ± 29.33	NS	NS	NS
NREM 1 + 2 1	247.00 ± 25.85	271.00 ± 17.45	242.25 ± 26.87	NS	NS	NS
NREM 1 + 2 2	237.67 ± 27.94	277.00 ± 16.15	253.75 ± 34.84	NS	NS	NS
NREM 3 + 4 1	97.67 ± 18.28	63.00 ± 19.44	109.64 ± 17.12	NS	NS	NS
NREM 3 + 4 2	85.33 ± 13.58	77.40 ± 21.76	116.18 ± 17.72	NS	NS	NS
REM 1	103.13 ± 17.80	127.00 ± 19.73	85.50 ± 12.42	NS	NS	NS
REM 2	91.50 ± 19.40	124.20 ± 22.34	87.50 ± 15.15	NS	NS	NS
REM latency 1	108.38 ± 13.58	28.00 ± 14.69	105.75 ± 17.83	0.014*	NS	0.012*
REM latency 2	129.38 ± 25.14	50.40 ± 26.02	97.75 ± 25.43	0.063	NS	NS

†1 = night 1; 2 = night 2; sleep lat. obj. = objectively recorded time to fall asleep (by Medilog); sleep lat. sub. = subjectively recorded time to fall asleep (by sleep log). Data are given in minutes and minutes (as a percentage).

‡p n − SO vs. n + SO: p of narcoleptic patients without versus patients with SOREM.

§p n − SO vs. con: p of narcoleptic patients without SOREM versus healthy controls.

¶p n + SO vs. con: p of narcoleptic patients with SOREM versus healthy controls.

*$p < 0.05$, two-tailed t-test.

TABLE 2

WAKE STAGES DURING NOCTURNAL WAKE TIMES AND NOCTURNAL MOTOR ACTIVITY IN NARCOLEPTIC PATIENTS WITH AND WITHOUT SOREM AND IN CONTROL SUBJECTS (MEAN ± SE)

	Narcoleptic Patients Without SOREMP	Narcoleptic Patients With SOREMP	Controls	n − SO vs. n + SO	n − SO vs. con	n + SO vs. con
Actimetry 1 (% of nocturnal activity)†	6.68 ± 2.1	11.67 ± 5.38	8.49 ± 3.08	NS	NS	NS
Actimetry 2 (% of nocturnal activity)†	6.12 ± 2.49	13.72 ± 4.51	9.93 ± 3.64	NS	NS	NS
Quiet wake 1 (min)	72.38 ± 35.83	19.5 ± 8.15	20.63 ± 6.32	NS	NS	NS
Quiet wake 2 (min)	27.42 ± 11.92	32.0 ± 13.89	6.86 ± 1.82	NS	NS	0.027*
Active wake 1 (min)	27.43 ± 6.85	35.5 ± 9.66	21.43 ± 7.9	NS	NS	NS
Active wake 2 (min)	47.5 ± 15.56	36.0 ± 12.12	19.71 ± 8.97	NS	NS	NS

†1 = night 1; 2 = night 2.
*$p < 0.05$, two-tailed t-test.

1. active wakefulness: >20% muscle artefacts, >20% of EMG amplitudes >25–50 μV, rapid eye movements; and
2. quiet wakefulness: <20% artefacts in EEG, >50% undisturbed, fast low amplitude graphoelements, EMG amplitudes <25 μV.

Missing data in the Medilog recording was corrected by actimetric data (restricted to sleep and wake only) and vice versa. Missing data of less than 15 min of temperature data were normalized between the two last recorded data points. Temperature analysis was performed by smoothing and cosinor fitting. The recordings were synchronised to temperature minima for comparison. Smoothed fitting replaced measured data points by values extracted from linear interpolation of data every 15 min.

To investigate whether a constant relationship exists between temperature change and transition from wakefulness to sleep during nocturnal sleep or during daytime naps or from sleep to wakefulness, the mean difference of five adjacent temperature measurements of 3-min epochs were collected, and a moving average was constructed. The time of maximal temperature declines in the transitions from onset of quiet wakefulness (which always preceded nocturnal sleep or daytime naps) to sleep onset and nap onset was calculated. A similar calculation of the maximal temperature rise after awaking from nocturnal sleep and daytime naps was performed.

Cumulative scores of several questions indicating sleep quality, sleep recovery and sleep disposition were extracted from SFA and SFB. The sleep diaries were used to control nocturnal sleep time and daytime naps of Medilog recordings and to evaluate frequency of occurrence of narcoleptic symptoms.

Statistics

Statistical analyses used one- and two-tailed t-tests for comparison of pairs of groups and analysis of variance for comparison of more than two groups. We performed the Tukey test for comparison of subjective sleep data for the three groups on an α level of 0.05. All tests were performed with the SPSS program.

RESULTS

Subjects were divided into three groups based on the analysis of the Medilog recordings:

1. narcoleptic patients with excessive daytime sleepiness and cataplexy without SOREMPs ($n = 9$);
2. narcoleptic patients with excessive daytime sleepiness and cataplexy with SOREMPs during nocturnal ($n = 5$ during nights 1 and 2) and daytime sleep ($n = 2$, also having SOREMPs during nights 1 and 2) episodes;
3. control subjects ($n = 11$).

TABLE 3

DAYTIME WAKE STAGES AND DAYTIME SLEEP EPISODES OF NARCOLEPTIC PATIENTS WITH AND WITHOUT SOREM AND OF HEALTHY CONTROLS†

Parameters	Narcoleptic Patients Without SOREMP	Narcoleptic Patients With SOREMP	Healthy Controls	*p* n − SO vs. n + SO	*p* n − SO vs. con	*p* n − SO vs. con
Actimetric activity	33.06 ± 3.51	31.36 ± 4.75	42.95 ± 3.95	NS	0.088	0.095
Daylength	962.00 ± 15.79	982.00 ± 37.29	959.00 ± 31.27	NS	NS	NS
NREM 1 + 2	67.50 ± 17.27	76.00 ± 19.03	79.50 ± 39.66 (4)	NS	NS	NS
NREM 3 + 4	32.40 ± 8.61 (5)	13.50 ± 10.50 (2)	37.50 ± 7.50 (2)	NS	NS	NS
REM	25.50 ± 16.50 (2)	78.75 ± 25.82 (4)	24.00 ± 0.00 (1)	NS	NS	NS
Quiet wakefulness	131.67 ± 29.83	117.00 ± 50.66	59.50 ± 13.81	NS	0.027*	NS
Active wakefulness	746.66 ± 40.02	732.00 ± 43.84	864.25 ± 42.45	NS	0.065	0.069

†Number of subjects are given within parentheses. Four controls are napping. All data are given in minutes and seconds (as a percentage).
*$p < 0.05$, two-tailed t-test.

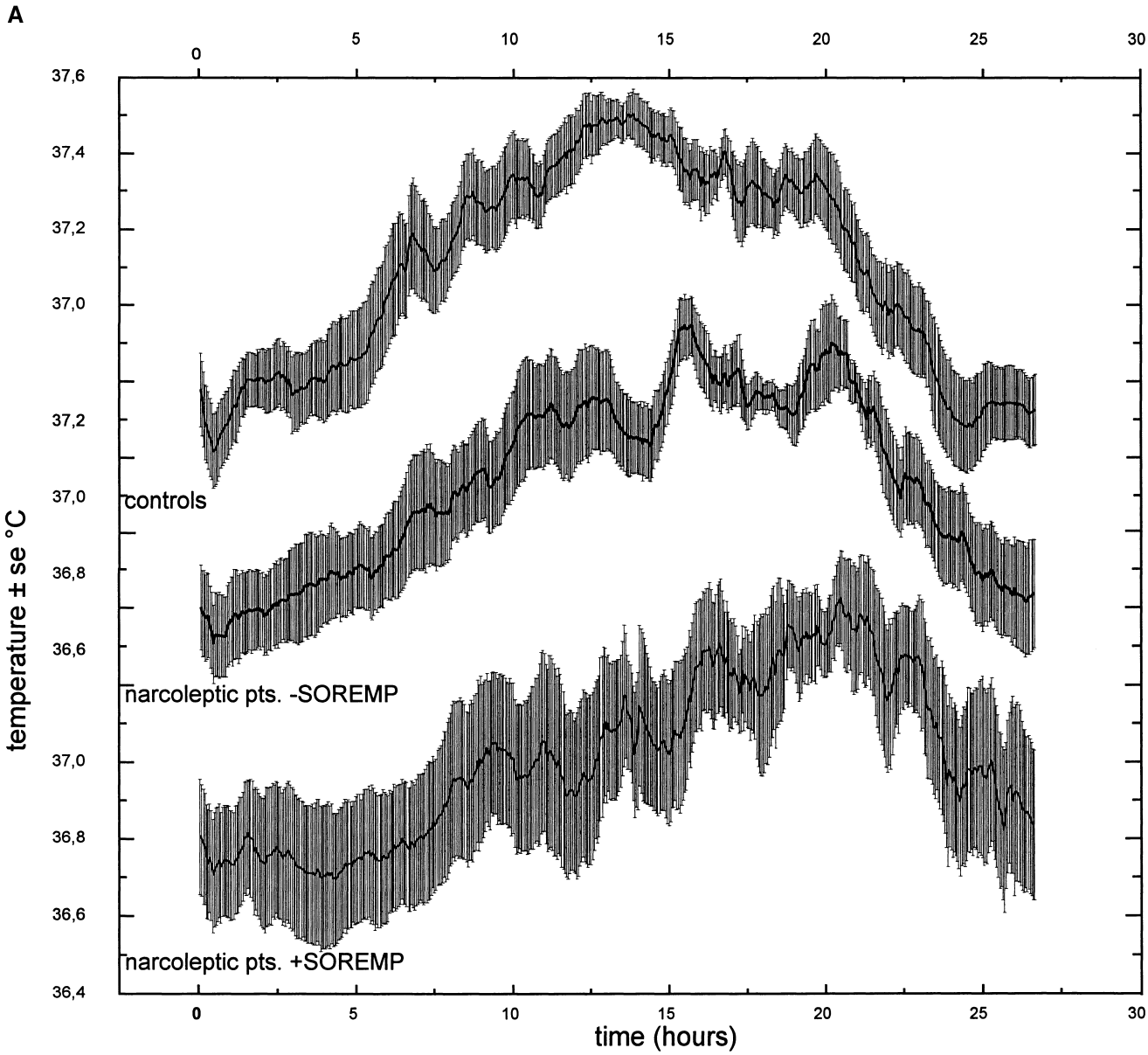

FIG. 1. A: Means and standard errors of 36-h temperature curves of narcoleptic patients with and without SOREMP and of controls synchronised to temperature minima.

SOREMPs in subjects monitored on the ward and at home were distributed equally.

Nocturnal Findings

Table 1 shows subjective and objective times for falling asleep and distribution of sleep stages during nights 1 and 2, which did not differ between narcoleptic patients and controls, except for REM latencies. Table 2 shows actimetric results for both nights and distribution of wake stages. Although mean nocturnal motor activity did not differ between narcoleptic patients and controls, the distribution of wake stages during awakening showed significantly longer stages of quiet wakefulness in narcoleptic patients with SOREMPs than in controls during night 2. Duration of nocturnal wakening corresponded well between Medilog data and reports of sleep–wake diaries (range −8–12 min).

Daytime Findings

The narcoleptic group with SOREMPs was comprised of only the two patients who displayed SOREMPs during daytime naps. Daytime actimetric data (Table 3) showed a tendency towards lower daytime motor activity in narcoleptic patients than in controls. Distribution of wake stages throughout daytime showed longer periods of quiet wakefulness for narcoleptic patients, but only narcoleptic patients without SOREMPs showed significant differences as compared with controls. Ac-

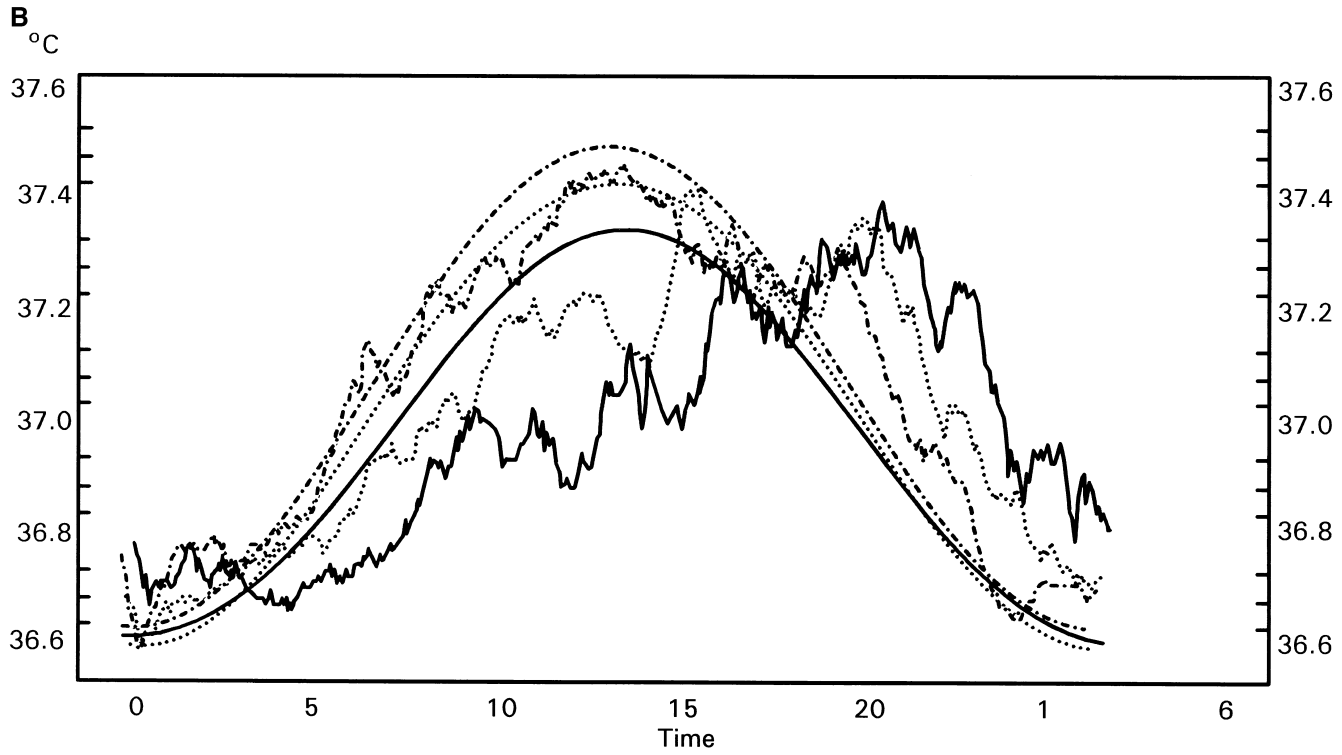

FIG. 1. B: Means of 36-h temperature curves of narcoleptic patients with and without SOREMP and of controls synchronised to temperature minima (cosinor fitting and 3-min interval recording). Solid line indicates temperature mean of narcoleptic patients with SOREMP. Dotted line indicates temperature mean of narcoleptic patients without SOREMP. Dashed line indicates temperature mean of controls.

tive wakefulness was also reduced as compared with controls, barely missing significance for both narcoleptic groups. Distribution of sleep stages in naps was not different between narcoleptic patients and controls.

Rectal Temperature

Figure 1A shows the curves for temperature means and standard errors; Figure 1B shows the temperature curves of cosinor fitting and the temperature means of the three groups recorded every 3 min. In all groups, data were synchronised to temperature minima. The curves show that temperature is dampened for narcoleptic patients in both curves, with lowest amplitudes in narcoleptic patients with SOREMP. The findings are nonsignificant (Table 4) for cosinor fitting.

Figure 1 displays less temperature rise and steepness in both narcoleptic groups as compared with controls; their temperature decline began earlier. Calculation of steepness of temperature decline and rise (°C/min) did not elicit significant differences between narcoleptic patients and controls. Figure 1B also shows that acrophase in controls corresponds well with acrophase of cosinor fitting, although it is delayed in both narcoleptic groups. When not synchronised to temperature minima, acrophase in narcoleptic patients occurred earlier than acrophase in controls (Table 4). In addition, position of temperature minima relative to that of midnight was significantly advanced in both narcoleptic groups during night 1 but nonsignificant during night 2 (Table 5), although the time for falling asleep did not differ significantly (Table 1). Interval between sleep onset and temperature minima of the temperature

TABLE 4

ANALYSIS OF VARIANCE OF CONTINUOUSLY MEASURED RECTAL TEMPERATURE (36 H) TRANSFORMED BY COSINOR ANALYSIS FOR NARCOLEPTIC PATIENTS WITH AND WITHOUT SLEEP ONSET REM AND FOR HEALTHY CONTROLS

Temperature (°C)	Narcoleptic Patients Without SOREMP	Narcoleptic Patients With SOREMP	Healthy Controls	p*	F
Temperature maximum	37.36	37.21	37.32	NS	0.4
Temperature minimum	36.97	36.86	36.86	NS	0.6
Temperature mesor	37.17	37.04	37.08	NS	0.6
Time from sleep onset to temperature minimum (h)	0.39	0.25	0.4	NS	0.6

*$p < 0.05$.

TABLE 5

VISUAL ANALYSIS OF CONTINUOUSLY MEASURED RECTAL TEMPERATURE (36 H) AND ITS RELATION TO THE SLEEP–WAKE CYCLE IN NARCOLEPTIC PATIENTS WITH AND WITHOUT SOREMP AND IN HEALTHY CONTROLS (MEAN ± SE)

Parameters†	Narcoleptic Patients Without SOREMP	Narcoleptic Patients With SOREMP	Healthy Controls	p n − SO vs. n + SO	p n − SO vs. con	p n + SO vs. con
d el temp 1 min	89.33 ± 48.63	54.50 ± 29.51	137.25 ± 36.41	NS	NS	NS
d el temp 2 min	103.67 ± 55.25	25.50 ± 17.69	159.25 ± 42.58	NS	NS	0.011*
d el REM temp 1 min	−9.38 ± 52.07	26.50 ± 19.23	31.50 ± 43.29	NS	NS	NS
d el REM temp 2 min	−2.63 ± 58.19	−22.20 ± 37.66	61.50 ± 40.42	NS	NS	NS
acrophase h of day	14.52 ± 0.61	14.43 ± 0.97	15.82 ± 0.37	NS	0.072*	NS
temp min 1 > < 24 h	−0.54 ± 0.85	−0.54 ± 0.69	1.93 ± 0.63	NS	0.031*	0.034*
temp min 2 > < 24 h	0.66 ± 0.91	−0.56 ± 0.55	1.72 ± 0.76	NS	NS	0.065*

†d el temp 1 and 2 = time between sleep onset and temperature minimum on nights 1 and 2; d el REM temp 1 and 2 = time between begin of first REM period and temperature minimum on nights 1 and 2; acrophase = time of day (minutes in %); temp min 1 and 2 > < 24 h = temperature minima on nights 1 and 2 given in hours and minutes (% of hour) before and after 24 h.

*$p < 0.05$, two-tailed t-test.

curves collected at 3-min intervals were advanced in narcoleptic patients, a finding significant ($p < 0.011$) only for narcoleptic patients with SOREMP when compared with controls.

The time span between falling asleep and temperature minimum was significantly longer ($p < 0.007$) during naps with SOREMP (56.3 ± 12.2 min) than during naps without SOREMP (21.1 ± 5.9 min). Because there were only two naps in the control group, comparison between groups was not possible. In narcoleptic patients with SOREMP, maximal temperature changes in naps were significantly ($p < 0.044$) shorter prior to nap onset (2.0 ± 3.5 min) than in narcoleptic patients without SOREMP (16.6 ± 5.9 min). Interaction of maximum temperature decline with first REMP occurred significantly ($p < 0.000$) earlier in narcoleptic patients with SOREMP (3.3 ± 3.7 min) than in those without SOREMP (44.5 ± 4.9 min). We could not find smaller temperature decreases during involuntary naps. Comparison of time elapsing between quiet wakefulness and calculated mean maximum temperature decline and between sleep onset and mean maximum temperature decline in narcoleptic patients with SOREMP showed significantly shorter time spans for quiet wakefulness before onset of naps (−2.2 ± 2.7 vs. 28.6 ± 12.8 min, $p < 0.28$) and longer time spans for quiet wakefulness to maximum temperature decline for night 1 (−75.0 ± 29.3 vs. 3.8 ± 17.4 min, $p < 0.067$); during night 2, the time span for the latter was nonsignificantly shorter after quiet wakefulness (−41.1 ± 44.53 vs. −40.2 ± 16.9 min, $p <$ NS). Temperature declines also occurred constantly during quiet wakefulness if there was no consecutive sleep. Maximum temperature declines in narcoleptic patients with SOREMP during nocturnal sleep of nights 1 and 2 were significantly closer to the first REM period than in narcoleptic patients without SOREMP (63.4 ± 33.7 vs. 145.8 ± 47.9 min for night 1, NS; 142.8 ± 58.8 vs. 147.0 ± 46.74 min for night 2, NS). Length of quiet wakefulness prior to sleep onset did not differ between the two narcoleptic groups.

Maximum rise of temperature during naps was located at a mean of several minutes prior to awakening (narcoleptic patients with SOREMP: 5.3 ± 14.6 min, those without SOREMP: 16.2 ± 24.9 min). During night sleep, maximum rise of temperature occurred at a mean of several minutes before or immediately after awakening. During night 2, maximum rise in temperature in narcoleptic patients without SOREMP was significantly ($p < 0.04$) closer (1.1 ± 10.1 min) to awakening than that of controls (36.6 ± 14 min).

24-h Distribution of Sleep

Nocturnal sleep and naps in narcoleptic patients had an ultradian multimodal distribution, with one major nocturnal and three major daytime peaks (Fig. 2). Naps with SOREM clustered around 5–7:30 a.m., 8:30–11:30 a.m., 1:30–4 p.m. and 8:30–10 p.m.

Correspondence between temperature and daytime naps of one narcoleptic patient with SOREMP is shown in Figure 3, which shows that naps and sleep are always preceded by quiet wakefulness.

Questionnaires

SFA and SFB showed no differences between narcoleptic patients and controls.

Sleep-Wake Diary

The mean number of unintended naps in the narcoleptic patients with SOREMPs (2.4 ± 0.75) was significantly higher (0.2 ± 0.2) than that in controls (Tukey test, $F = 0.005$) and not significantly higher than in those without SOREMPs (0.86 ± 0.40); the desire for naps in the latter was not significantly greater. Naps reported in the SFA and SFB questionnaires showed similar results.

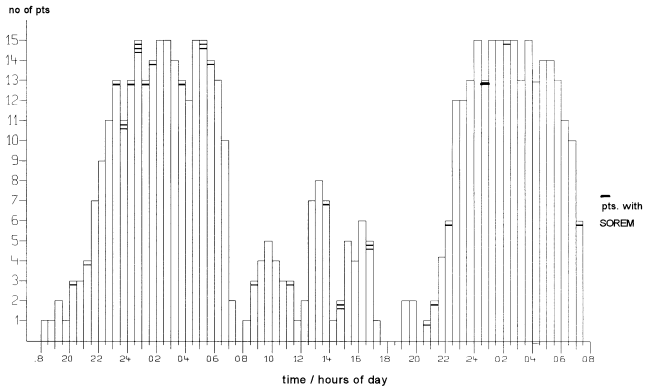

FIG. 2. Distribution of sleep of narcoleptic patients (pts.) with and without SOREMP over 36 h.

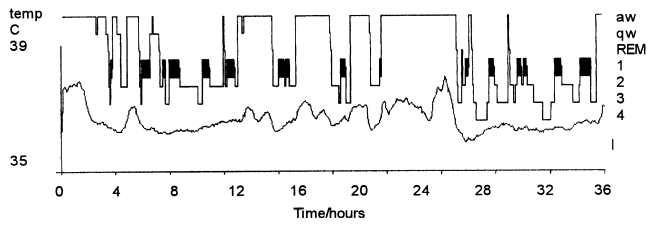

FIG. 3. The 36-h temperature rhythm of a narcoleptic woman with SOREMP. Sleep stages: aw = active wakefulness, qw = quiet wakefulness, REM, 1–4 = NREM 1–4.

Only narcoleptic patients without SOREMPs had cataplexies, with an average index of 1.71/36 h, hypnagogic hallucinations (0.86/36 h) and sleep paralysis (0.71/36 h).

DISCUSSION

Mosko et al. (9) were the first to postulate the disturbed 24-h temperature rhythm in narcoleptic patients. Their findings could not be reproduced by Pollak and Wagner (11), who, in contrast to Mosko et al. (9), studied their subjects under free-running conditions. In our subjects, recorded under entrained conditions, we found no phase advance of rectal temperature minima and acrophase in the cosinor fittings. However, we were able to demonstrate these in the temperature recordings at 3-min intervals. Like Campbell and Broughton (5), we think that smoothing techniques such as the cosinor filter out small temperature fluctuations that are important for studying relations between temperature and naps, as we did. Another important finding is that temperature minima occur earlier in both narcoleptic groups than in controls, although time for falling asleep does not differ between the groups.

Concerning temperature amplitude, we could not confirm Mosko et al.'s (9) findings of higher temperature mesor for narcoleptic patients with SOREMP. Mosko et al. attributed this finding to higher nocturnal motor activity in these patients, which we could not confirm. In contrast to Pollak and Wagner's results (11) we demonstrated that low temperature amplitudes in narcoleptic patients correspond with lower motor activity as opposed to controls, even during wake times at night.

We found dampening of temperature amplitudes with slow rise in the morning in narcoleptic patients. Our findings address Pollak and Wagner's (11) question about whether slow temperature rise is related to lower heat generation due to less motor activity, which they did not record. Compared with controls, both groups of narcoleptic patients had less motor activity during daytime, almost reaching the level of significance, and significantly more quiet wakefulness in the group without SOREMP. Moreover, we were able to show that temperature declines are preceded by quiet wakefulness, a wake stage of low motor activity. Pollak and Wagner (11) concluded that temperature decreases could be due to a combination of decreased heat production caused by little motor activity and by increased thermal conductance associated with inactivity or sleep. To follow this question more closely, we used Campbell and Broughton's (5) paradigm of maximum temperature decline as an indicator of sleep onset. We found maximum decrease of temperature always prior to sleep onset. This finding allows us to demonstrate a close relation between temperature declines and sleepiness, which can be modulated in amplitude but not in temporal distribution by motor activity. This close relation exists for controls and for narcoleptic patients and is in full accordance with the findings of Baldy-Moulinier et al. (1). Shahal et al. (13) named the temperature decrease a "preparatory step" towards sleep. For nocturnal sleep of narcoleptic patients, we found no advance of maximum temperature decline prior to sleep onset as compared with controls. However, maximal temperature decline in naps with SOREMP was earlier than in the other groups, and interaction with the first REMP was significantly shorter in the group with SOREMPs than in the group without SOREMPs. The temperature advance agrees with Mullington and Broughton's (10) finding of advanced naps in narcoleptic patients. The advanced rhythm may also be represented by a significantly closer temporal relationship between maximal temperature decline and first REM period in narcoleptic patients with SOREMP, whose maximal temperature decline begins earlier than in controls and narcoleptic patients without SOREMP. Assuming that temperature regulation could be under the control of sleep, the advance could be an indicator for SOREMPs.

Are temperature anomalies sequelae of patients' behaviour? Although there are no significant differences between the subjective reports on falling asleep and objectively recorded time in falling asleep, narcoleptic patients report falling asleep earlier than do controls. If we assume the subjective time to be the time to go to bed, sleep latencies are long in controls in both nights and shortest in narcoleptic patients with SOREMPs. Earlier bed time in narcoleptic patients may explain advances of temperature minima relative to midnight but not to earlier minima after sleep onset. Short sleep latencies and much shorter time spans from sleep onset until temperature minima may confirm Campbell and Broughton's findings that sleep rules behaviour and not vice versa. This finding is also consistent with that of healthy subjects with internally synchronised rhythms under free-running conditions, whose voluntary sleep time is closer to temperature nadir than under entrained condition (6). The important finding that temperature minima are advanced in narcoleptic patients with SOREMPs and that maximal temperature decline occurs nearer to sleep onset and to REMPs may indicate a defect in temperature-locked REM triggering in narcoleptic subjects.

The distribution of naps and sleep was multimodal. By extrapolating the daytime troughs, the curve closely resembles the bimodal distribution of free-running healthy subjects who are free to nap, as found in Campbell and Zulley's (4) study. Naps with SOREMP clustered during certain daytime periods, but ultradian rhythms could not be confirmed due to the small number of naps with SOREMP, a result we anticipated according to Baldy-Moulinier et al.'s (1) and to Broughton et al.'s (3) experience of a lower frequency of SOREMPs in ambulatory recordings and the masking effects.

Quiet wakefulness, which is higher in narcoleptic patients than in controls, is related to lower core body temperature and temperature decline. This finding could imply a state of higher tendency towards sleepiness or higher proneness towards sleep. Thus, we can add our result of a constant phase relationship between the circadian temperature and motor activity rhythm to that of Refinetti and Menaker (12).

CONCLUSION

In narcoleptic patients studied under entrained conditions, dampened temperature curves, advance of temperature nadir, shorter interval between sleep onset and temperature minima

and a quasi-ultradian distribution of naps are very similar to those of free-running narcoleptic and healthy subjects, thus supporting the hypothesis of an underlying disturbance of circadian rhythms in narcolepsy. One oscillator seems to rule motor activity and temperature in narcoleptic patients and healthy subjects. Only narcoleptic patients with SOREMPs have a closer temporal relation between temperature decline and the first REM period, indicating a defect in temperature-related REM triggering. Future research has to address the relation of maximal temperature decline and REMPs in a larger population to elicit ultradian rhythms. This relation could be extended to motor activity, which should be analyzed in a way similar to the temperature prior to and near sleep onset and offset.

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