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Temperature and Endocrine Activity during Sleep in Man

Activation of Cortisol and Thyroid-Stimulating Hormone, Inhibition of Human Growth Hormone Secretion by Raised or Decreased Ambient and Body Temperatures

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SUMMARY. 1. Polygraphic night sleep recordings in eight healthy male volunteers with simultaneous measurement of rectal temperature, plasma growth hormone (HGH), cortisol, and TSH concentrations were performed during normal, raised, and lowered ambient and body temperature.
2. There was a statistically significant increase in plasma cortisol and TSH levels during cold nights with a smaller rise during high temperatures.
3. Growth hormone levels, measured as the mean highest plasma concentration in the first two NREM-REM sleep cycles, were slightly lower during hot and cold nights than corresponding baseline values. It is suggested that there may be an inverse relation between ACTH and HGH secretion by the anterior pituitary gland.
4. During the nights of high ambient temperature, decreased total duration of sleep and particularly low values of paradoxical sleep were observed. Night sleep in low ambient temperature with a significant decrease of body temperature is not different from baseline conditions.
5. The results suggest that a pronounced increase in stress hormone secretion may occur without changes in polygraphic EEG criteria.

KEY WORDS: Night Sleep - Body Temperature - Cortisol, TSH, HGH-Hormones - Plasma Levels - Man.

ZUSAMMENFASSUNG. 1. Bei 8 jungen männlichen Versuchspersonen wurden polygraphische Nachtschlafregistrierungen mit Messungen der Rektaltemperatur bei normaler, erhöhter und erniedrigter Umgebungs- und Körpertemperatur durchgeführt. Bestimmungen der Plasma-, Wachstumshormon-, Cortisol- und Thyreotropinsekretion wurden während des Schlafes durchgeführt.
2. Sowohl in Nächten mit erniedrigter als auch erhöhter Umgebungs- und Körpertemperatur fand sich eine vermehrte Sekretion von Cortisol und TSH, die in der Kälte am deutlichsten war im Vergleich mit Indifferenztemperaturen.

3. Die Maxima der Plasma Wachstumshormonkonzentrationen waren im thermisch belasteten Schlaf während der ersten beiden Zyklen leicht vermindert im Gegensatz zu Cortisol. Danach ist eine reziproke Beziehung zwischen ACTH und Wachstumshormonsekretion aus dem Hypophysenvorderlappen möglich.
4. Die Gesamtschlafzeit und der Anteil an paradoxem Schlaf ist bei erhöhter Umgebungs- und Körpertemperatur deutlich vermindert, während der Schlaf in der Kälte normal ist.
5. Die vermehrte Sekretion von Cortisol und Thyreotropin zeigt, daß eine erhöhte Freisetzung von "Streßhormonen" ohne Änderung im polygraphischen Schlafablauf vorkommen kann.

SCHLÜSSELWÖRTER: Nachtschlaf - Körpertemperatur - Cortisol, TSH, HGH-Hormone - Plasmakonzentration - Mensch.

INTRODUCTION

The phasic secretion of human growth hormone (HGH) is associated with slow-wave sleep stages 3 and 4 during the first two cycles of night sleep in man (Takahashi et al., 1968). HGH peak values may be diminished by drugs such as tricyclic antidepressants (Takahashi et al., 1968) and increased by melatonin (Cramer et al., 1975) and after physical exercise during daytime (Adamson et al., 1974). Other factors influencing the sleep-linked HGH secretion are the time of sleep onset and the rhythmicity of sleep with appearance of a second growth hormone peak in broken night sleep (Beck et al., 1975). In restless sleep, e. g., after withdrawal of tranquilizers (Ogunremi et al., 1973), increased plasma cortisol levels have been described as a rebound phenomenon after subnormal levels on medication nights. The exposure to cold and hot environments (Schmidt-Kessen & Kendel, 1972) which was performed in this experiment in healthy volunteers, is considered as a thermic stress inflicted during sleep. Therefore, simultaneous changes of cortisol, TSH, and HGH secretion above baseline values are expected.

SUBJECTS AND METHODS

Eight healthy, nonobese, male volunteers, mean age 25. 4 $\pm$ 1. 9 years and mean body weight 72. 5 $\pm$ 7. 2 kg slept, without bed covers and clothed only in cotton slips, in a climatic chamber from 2300 until 0700 h at constant ambient temperatures of 27. 5° $\pm$ 0. 5°, 31° $\pm$ 0. 4°, or 36° $\pm$ 0. 6° C. The relative humidity was kept between 44 and 55%. The ambient temperature of 31° $\pm$ 0. 4° C was taken as a baseline environment as determined in a previous study (Schmidt-Kessen & Kendel, 1973).

Night sleep was recorded polygraphically by means of a 16-channel EEG machine including four EEG recordings (O_1Cz, O_2Cz, P_3Cz, P_4Cz), recording of horizontal eye movements, and electromyogram of submental muscle. Recording was performed continuously from 23:00 until at 07:00 h in the morning. Recording of rectal temperature was performed by means of a subminiature platinum resistance element. Blood was sampled during the experimental

nights by means of an indwelling intravenous catheter. Each subject adapted to the indwelling venous catheter for one night. The experimental nights were nonconsecutive in randomized order. Samples for the assay of HGH were taken at 30-min intervals from 2300 until 0230 and at 60-min intervals from 0300 until 0700 h. Cortisol samples were taken at 2300, 2400, 0200, and at 30-min intervals from 0300 until 0700 h (13 samples); blood samples for cortisol and for TSH samples were taken at 2300, 0000, 0200 and at 30-min intervals from 0300 until 0700 h. The plasma concentration of these hormones was measured by radioimmunoassay.

Scoring of night-sleep EEG recordings was performed according to the criteria of Rechtschaffen & Kales (1968). Sleep onset was defined as the first stage 2 sleep at the beginning of the night which had to last for 3 min at least. The plasma hormone concentrations were compared for the different nights in relation to clock time. In addition, HGH peak values were compared within the first 2 NREM-REM sleep cycles. The area under the curve was measured for each hormone planimetrically and the data of experimental nights were compared to baseline conditions.

A t-test for paired observations was used for statistical evaluation of EEG and endocrinological data. The hypothesis tested was that increased amounts of HGH, TSH, and cortisol would be found in nights of "stress application," e. g., exposure to coldness and heat, when compared to nights with normal ambient temperature.

RESULTS

I. EEG Data

1. General Characteristics of Sleep

Sleep onset latency, REM sleep latency, and the number of completed NREM-REM sleep cycles were not significantly different in hot and cold nights when compared to baseline conditions. The mean values of total amount of sleep (stages 0 and 1 excluded) were 214 ± 77 min in 36° C and 291 ± 83 min in 28° C nights compared to 295 ± 108 min in baseline nights (31° C), the difference between hot and baseline nights being statistically significant ($t = 1.90$, $P < 0.05$). There was no difference in stage 2 sleep when the three conditions were compared.

2. Slow-Wave Sleep (EEG Stages 3 and 4)

The total duration of sleep stages 3 and 4 were 130 ± 29 and 140 ± 41 min for baseline, 36° and 28° C nights, respectively. The difference of total duration of EEG stages 3 and 4, and of the amount of slow-wave sleep in the first and second NREM-REM sleep cycles, was not significantly different in the three conditions. The latency of stages 3 and 4 after sleep onset was remarkably longer for hot nights with 27 ± 31.1 min, compared to 8.6 ± 5.3 min for baseline nights ($t = 1.90$, $P < 0.05$).

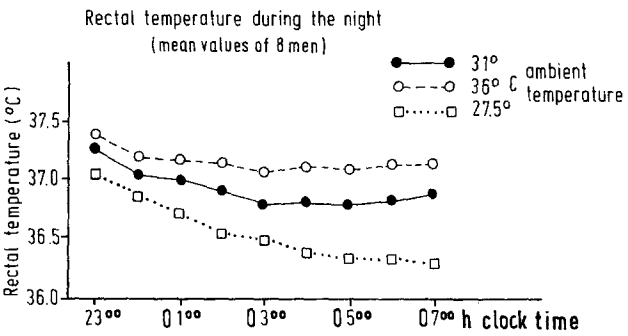

Fig. 1. Rectal temperature curves during night sleep (mean values in ^{o}C), showing significant increase during high and decrease during low ambient temperatures respectively in comparison to baseline conditions

3. REM-Sleep

The total amount of paradoxical sleep was low in all nights with 49 ± 28, 21 ± 16, and 51 ± 18 min in cold, hot, and baseline nights, respectively. The difference between baseline conditions and 36° C was statistically significant ($t = 2.26$, $P < 0.05$).

II. Rectal Temperature (Fig. 1, Table 1)

The single data (mean values and standard deviations) are shown in Table 1. A statistical comparison between "cold" and baseline nights showed statistically significant differences at 0100 ($t = 3.05$, $P < 0.025$), 0300 ($t = 3.60$, $P < 0.05$), 0500 ($t = 4.72$, $P < 0.025$) and 0700 h ($t = 4.77$ $P < 0.025$). Body temperature during "cold" nights was lowest at 0500 and 700 h.

The comparison of "hot" and baseline nights revealed less striking temperature differences, as can be seen in Figure 1. In 36° C nights the body temperature was significantly higher at 0300 ($t = 2.17$, $P < 0.025$), 0500 ($t = 1.95$, $P < 0.05$), and 0700 h ($t = 1.82$, $P < 0.05$).

III. Endocrinologic Findings

1. HGH Plasma Concentration (See Fig. 2, Table 2)

a) Peak Values. The mean highest concentrations during whole-night sleep and the first two NREM-REM sleep cycles were not significantly different, when a comparison is made between 27.5° C, 36° C, and baseline nights. However, the peak values of 5.06 ng/ml plasma in cold and 6.31 ± 5.58 ng/ml plasma in hot nights seem considerably smaller than the corresponding value of 9.10 ± 8.31 ng/ml plasma under baseline conditions. Peak values occurred mainly during slow-wave sleep stages 3 and 4.

Table 1. Comparison of rectal temperature, r.t., C^{o}, mean values of 8 subjects in relation to clock time, during different ambient temperatures

Clock time	Ambient temperature 27.5° C	Comparison 27.5/31° C t	P<	Baseline condition 31° C	Comparison 31/36° C t	P<	Ambient temperature 36°C
	r.t.			r.t.			r.t.
2300	37.03 ± 0.20	1.40	N.S.	37.25 ± 0.38	0.79	N.S.	37.36 ± 0.30
2400	36.86 ± 0.23			37.06 ± 0.26			37.18 ± 0.31
0100	36.71 ± 0.19	3.05	0.025	36.98 ± 0.25	1.43	N.S.	37.16 ± 0.34
0200	36.53 ± 0.23			36.90 ± 0.28			37.13 ± 0.32
0300	36.48 ± 0.15	3.60	0.005	36.80 ± 0.29	2.17	0.025	37.05 ± 0.37
0400	36.38 ± 0.19			36.85 ± 0.33			37.11 ± 0.32
0500	36.36 ± 0.21	4.72	0.0025	36.83 ± 0.31	1.95	0.05	37.09 ± 0.38
0600	36.33 ± 0.23			36.86 ± 0.28			37.13 ± 0.39
0700	36.31 ± 0.24	4.77	0.0025	36.88 ± 0.32	1.82	0.05	37.12 ± 0.35

N.S. = not significant

Table 2. Comparison of mean HGH plasma concentration (ng/ml) in relation to clock time during different ambient temperatures: 8 subjects

Clock time	Ambient temperature 27.5° C	Comparison 27.5/31° C t	P	Ambient temperature 31° C	Comparison 31/36° C t	P	Ambient temperature 36° C
	HGH			HGH			HGH
2300	0.68 ± 0.5	0.94	N.S.	0.99 ± 1.28	1.99	N.S.	1.33 ± 1.68
2330	0.71 ± 0.81	1.58	N.S.	1.15 ± 1.03	0.04	N.S.	1.14 ± 0.93
2400	1.64 ± 1.96	1.14	N.S.	0.95 ± 0.62	1.13	N.S.	2.52 ± 1.13
0030	4.80 ± 5.57	0.57	N.S.	6.10 ± 4.40	1.15	N.S.	3.11 ± 3.25
0100	6.13 ± 5.58	1.34	N.S.	9.10 ± 8.31	1.65	N.S.	4.71 ± 3.84
0130	4.90 ± 4.76	0.11	N.S.	5.13 ± 7.93	0.15	N.S.	4.78 ± 2.92
0200	3.59 ± 3.05	0.07	N.S.	3.76 ± 7.21	0.39	N.S.	5.06 ± 3.01
0230	2.15 ± 1.59	0.13	N.S.	2.31 ± 3.20	0.10	N.S.	2.59 ± 2.65
0300	1.67 ± 1.82	0.20	N.S.	1.92 ± 2.76	0.25	N.S.	2.28 ± 3.14
0330	0.77 ± 0.59	1.38	N.S.	1.90 ± 2.68	0.82	N.S.	1.09 ± 0.92
0400	0.88 ± 0.99	1.01	N.S.	2.09 ± 3.05	0.94	N.S.	0.95 ± 0.76
0500	1.13 ± 1.22	0.16	N.S.	1.04 ± 0.80	1.38	N.S.	0.65 ± 0.22
0600	1.07 ± 0.88	1.57	N.S.	0.57 ± 0.17	1.41	N.S.	1.78 ± 2.27
0700	0.60 ± 0.34	1.17	N.S.	1.21 ± 1.31	0.37	N.S.	1.16 ± 0.06

N.S. = not significant

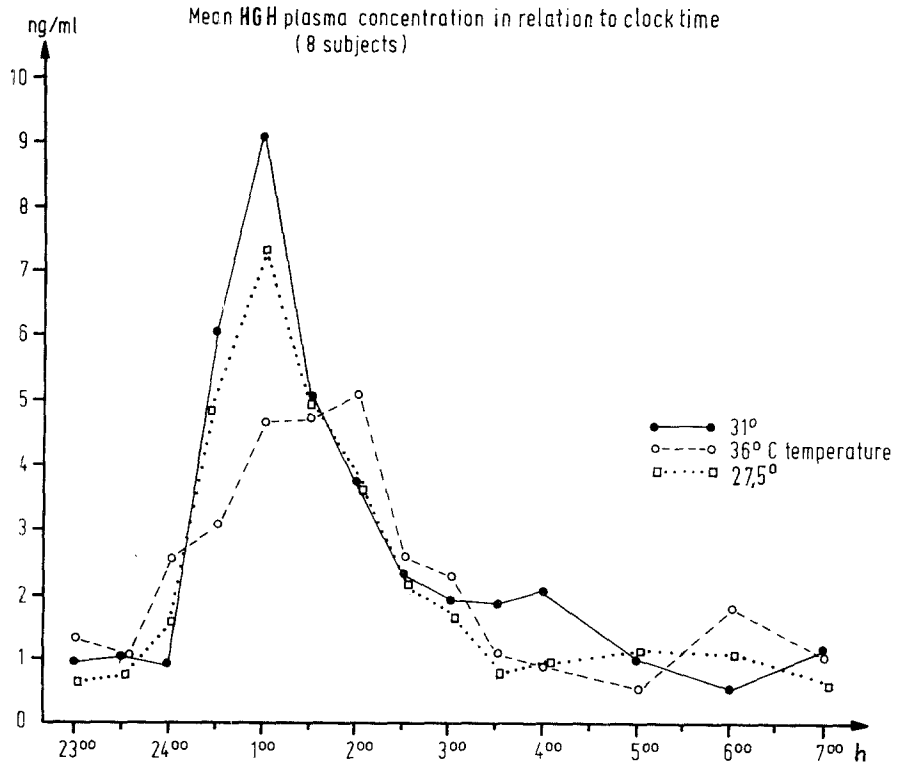

Fig. 2. Mean HGH plasma concentration (ng/ml plasma) in relation to clock time during sleep in various ambient temperatures in eight healthy subjects. Maximal concentrations are slightly lower in experimental nights and the peak is delayed in high ambient temperature

b) The differences of the area under the curve (from 2300 until 0700, integrated HGH response) were not statistically significant.

2. Plasma Cortisol (See Table 3, Fig. 3)

In all conditions the circadian increase of cortisol plasma concentrations from the beginning of the night toward morning could be observed (Weitzmann et al., 1966). The differences in plasma concentrations comparing cold with baseline nights were statistically significant at all corresponding clock times, the level of significance being $P < 0.025$ ($t = 2.52$) at 2300, $P < 0.005$ from 0300 until 0630 and $P < 0.005$ ($t = 3.57$) at 0700 h.

The comparison of cortisol plasma concentrations of baseline and "hot" nights revealed smaller differences, but the same trend of increased plasma concentrations was found. The mean highest cortisol concentrations

Table 3. Comparison of mean plasma cortisol concentrations (ng/ml) in relation to clock time (8 subjects) during different ambient temperatures

Clock time	Ambient temperature 27.5° C	Comparison 27.5/31° C t	P	Baseline condition 31° C	Comparison 31/36° C t	P	Ambient temperature 36° C
	Cortisol			Cortisol			Cortisol
2300	90.75 ± 15.86	2.53	< 0.025	87.87 ± 17.26	0.87	N.S.	88.62 ± 16.27
0100	99.75 ± 16.67	7.14	< 0.0005	89.50 ± 16.87	3.42	< 0.05	92.00 ± 16.47
0300	106.25 ± 17.00	5.98	< 0.0005	96.00 ± 15.00	4.33	< 0.0025	96.87 ± 15.58
0330	113.75 ± 19.83	8.60	< 0.0005	97.88 ± 17.50	2.00	< 0.05	101.87 ± 17.32
0400	117.62 ± 20.22	6.88	< 0.0005	102.25 ± 18.20	1.05	N.S.	105.00 ± 16.40
0430	121.57 ± 20.65	7.36	< 0.0005	103.43 ± 18.15	1.68	< 0.05	111.12 ± 16.83
0500	131.43 ± 24.25	8.89	< 0.0005	111.25 ± 19.68	3.63	< 0.0025	119.62 ± 17.11
0530	134.00 ± 23.45	7.89	< 0.0005	113.71 ± 21.16	3.74	< 0.0025	124.37 ± 18.09
0600	140.87 ± 20.70	1.18	< 0.0005	118.86 ± 22.12	3.43	< 0.05	127.37 ± 17.61
0630	141.62 ± 19.78	8.36	< 0.0005	124.25 ± 20.45	1.06	< 0.05	129.37 ± 18.91
0700	136.75 ± 25.68	3.57	< 0.005	124.50 ± 20.71	1.73	< 0.05	129.25 ± 21.26

N.S. = not significant

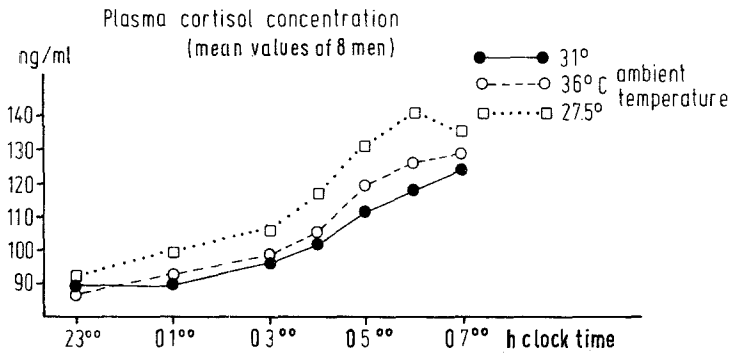

Fig. 3. Mean plasma cortisol concentrations (ng/ml plasma) during night sleep in different ambient temperatures. Pronounced increase above baseline values occurs particularly in low ambient temperatures

were found earlier in time during hot and cold nights than under baseline conditions. The area under the curve was significantly increased in nights with temperature stress.

3. Plasma TSH (Table 4, Fig. 4)

Plasma TSH levels were significantly higher at 0500 ($t = 2.1$, $P < 0.05$), 0600 ($t = 1.76$, $P < 0.05$), 0630 ($t = 2.03$, $P < 0.05$) and 0700 h ($t = 2.62$,

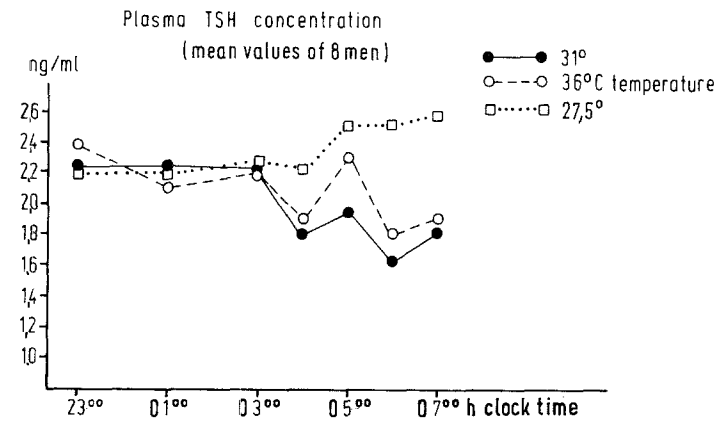

Fig. 4. Plasma TSH concentrations (ng/ml plasma), same experimental procedure as in previous Figures 2 and 3. Significant increase were observed above baseline values during the second part of the night, particularly in 27. 5° C ambient temperature

Table 4. Comparison of mean TSH plasma concentrations (ng/ml) in relation to clock time (8 subjects) during different ambient temperatures

Clock time	Ambient temperature 27° C	Comparison 27.5/31° C t	P	Baseline condition 31° C	Comparison 31/36° C t	P	Ambient temperature 36° C
	TSH			TSH			TSH
2300	2.23 ± 0.065	0.43	N.S.	2.27 ± 0.108	0.22	N.S.	2.39 ± 0.067
0100	2.20 ± 0.075	0.14	N.S.	2.26 ± 0.094	0.30	N.S.	2.15 ± 0.059
0300	2.14 ± 0.081	0.97	N.S.	2.23 ± 0.058	0.09	N.S.	2.04 ± 0.043
0330	2.16 ± 0.083	0.97	N.S.	1.91 ± 0.067	0.78	N.S.	2.06 ± 0.039
0400	2.16 ± 0.061	1.18	N.S.	1.83 ± 0.083	0.09	N.S.	1.90 ± 0.057
0430	2.25 ± 0.082	1.26	N.S.	1.74 ± 0.080	1.33	N.S.	2.21 ± 0.049
0500	2.65 ± 0.054	2.10 <	0.05	1.95 ± 0.076	0.67	N.S.	2.35 ± 0.077
0530	2.31 ± 0.056	0.99	N.S.	1.89 ± 0.092	2.05	N.S.	2.09 ± 0.083
0600	2.51 ± 0.099	1.76 <	0.05	1.61 ± 0.109	0.89	N.S.	1.80 ± 0.074
0630	2.54 ± 0.115	2.03 <	0.05	1.59 ± 0.089	1.47	N.S.	2.06 ± 0.087
0700	2.58 ± 0.099	2.62 <	0.0125	1.81 ± 0.075	0.68	N.S.	1.93 ± 0.087

N.S. = not significant

$P < 0.0125$) when cold nights were compared to baseline conditions. In 36°C nights no significant difference in TSH secretion could be detected.

The areas under the curve from 2300-0700 h were not significantly different in cold, hot, and baseline nights.

DISCUSSION

Our findings show that decreased body temperature may be associated with significantly increased plasma cortisol levels throughout the whole night, and activation of TSH release in the second part of the night without remarkable changes in EEG sleep parameters. The same trend, but to a lesser degree, was observed during relatively high ambient and body temperatures. In the latter situation, however, there was also a more abnormal sleep EEG, with a decrease in total sleep time and an abbreviation of paradoxical sleep. In contrast to cortisol and TSH, the plasma concentration of growth hormone tends to be diminished during abnormal ambient and body temperatures with lower peak values and smaller areas under the curves when individually compared to baseline conditions. This may indicate a possible inverse relation between ACTH and HGH secretion by the anterior pituitary and would correspond with the findings of Frantz et al. (1964) who described suppression of growth hormone release by corticosteroids. The delayed peak value in hot nights (see Fig. 2) correlated with the prolonged latency of slow-wave sleep stages 3 and 4.

Increased cortisol secretion was found in very restless sleep with frequent transitions of stage 0 and 1 sleep after drug withdrawal (Ogunremi et al., 1973). However, this situation has only been described with significant changes of sleep from baseline conditions. Our findings of TSH levels under baseline conditions are similar to those of Alford et al. (1973) with peak values at the onset of sleep followed by a fall in the morning. Since blood for TSH and cortisol assays was taken at 2-h intervals during the second part of the night, correlations between sleep stages and plasma hormone concentration cannot be reliable. The higher amount of mean TSH plasma concentrations is particularly pronounced in the second part of cold nights whereas the differences in cortisol plasma levels can be detected already at the beginning of night-sleep recording. This finding is of interest because it shows that the circadian pattern of TSH release may be abolished by exposure to cold (see Fig. 3).

The pronounced endocrinologic changes after a decrease in body temperature while electrophysiologic sleep criteria were unchanged provide evidence that EEG recordings of sleep do not correlate with metabolic activity during sleep.

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