Physiology & Behavior 114–115 (2013) 77–82

Contents lists available at SciVerse ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

A two-night comparison in the sleep laboratory as a tool to challenge the relationship between sleep initiation, cardiophysiological and thermoregulatory changes in women with difficulties initiating sleep and thermal discomfort

D. Anders, B. Gompper, K. Kräuchi *

Thermophysiological Chronobiology, Centre for Chronobiology, Psychiatric Hospital of the University of Basel, Switzerland

HIGHLIGHTS

- Faster build-up of delta power in the second night compared to the first.
- Distal skin vasculature is more dilated after lights out in the second night.
- Different dynamics between the 2 nights in skin temperature or sleep measures.
- Same dynamic between the 2 nights in heart rate variability measures.
- Therefore no direct causality between those functions suggested.

ARTICLE INFO

Article history:
Received 11 June 2012
Received in revised form 25 October 2012
Accepted 26 February 2013

Keywords:
Sleep onset episode
Biological rhythms
Vascular dysregulation

ABSTRACT

Cardiovascular and thermophysiological changes accompany the decision to fall asleep. A relationship between core body temperature and heart rate variability (HRV) especially during the sleep onset episode is suggested, but only few data are available, investigating a relationship between skin temperature and HRV at this time span. This study was aimed to elucidate the pattern of body temperature (i.e. distal and proximal skin temperature), heart rate and its variability in a specific population of ten healthy women having both, thermal discomfort from cold extremities and difficulties initiating sleep for two subsequent nights in the laboratory. Furthermore, changes in sleep, temperature or cardiac regulation were examined after 16-h of constant posture conditions.

Due to a faster decline of arousals, the build-up of sleep stage 2, slow wave sleep and hence delta power is promoted in the second night compared to the first. Both, proximal and distal skin temperatures show an increase after lights out. Distal skin temperature around lights out is already higher during the second night. Proximal skin temperature starts at the same temperature level for both nights but was significantly reduced in the second hour after lights out during the second night. The distal-proximal skin temperature gradient (DPG), as a measure for distal dilatation of the skin vasculature, starts with a lower level after lights out in the first night, compared to the second. Different dynamics and differences between the two nights in skin temperature or sleep variables, but not in heart rate and HRV variables were found during the sleep initiation episode. Thus, a direct causality between these functions seems rather unlikely in the present study sample. The described differences between both nights might occur from delayed relaxation, reflected in a slower decrease of arousals, prolonged sleep onset latency and a lower DPG at the first night. Especially the latter finding confirms nicely the statement that warm extremities promote a rapid onset of sleep.

1. Introduction

Large cardiovascular and thermophysiological processes occur around lights out, when sleep is initiated. Physical (lying down) and mental (relaxing), as well as physiological changes accompany the decision to fall asleep. The rapid decline of core body temperature (CBT) in the late evening has been suggested to increase the likelihood of sleep initiation [1,2]. CBT is the net result of heat production (well correlated with the heart rate (HR); [3]) and heat loss (foremost due to distal skin temperature vasodilatation; [4]), and from a circadian point of view, the latter is predominant in the evening. In that it is shown, that skin temperature changes, as well as the decline of HR are initiated already prior sleep onset (reviewed in: [5]). Especially

* Corresponding author at: Thermophysiological Chronobiology, Centre for Chronobiology, Psychiatric Hospital of the University of Basel, Wilhelm Klein-Strasse 27, CH-4012 Basel, Switzerland. Tel.: +41 61 325 5508; fax: +41 61 325 5577.
E-mail address: Kurt.Kraeuchi@upkbs.ch (K. Kräuchi).

0031-9384/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.physbeh.2013.02.020

distal heat loss and hence an increase of the distal-proximal skin temperature gradient (DPG) prior sleep is a much better predictor for a short onset of sleep, than CBT [4], at least in young adults [6]. Confirmatory studies found that the reverse is also true. A prolonged sleep onset episode was elucidated in healthy women suffering from thermal discomfort with cold extremities (TDCE, [4]).

Although skin temperature, especially the gradient between distal and proximal skin temperature, is known to be a measurement for distal vasodilatation, controlled by the autonomic nervous system, the relationship between skin temperature and cardiac autonomic control during sleep initiation was not investigated yet. One caveat in studying such relationships derives from the population normally examined for sleep studies. Good sleepers are often chosen, which are nearly completely vasodilated before lights out and fall asleep after few minutes. Therefore, the variance in these variables is low and bottom or ceiling effects are highly probable. To overcome this, the study was conducted in subjects with difficulties initiating sleep (DIS), hence prolonged sleep onset episode.

To our knowledge it has never been evaluated, whether changes in sleep, body temperature or cardiac regulation occur after constant posture conditions without prolonged wakefulness. Therefore, two subsequent nights were separated by controlled constant routine (CR) conditions in the laboratory, in which subjects remained awake for 16 h, according to their habitual sleep-wake cycle.

Due to the known relationship between DPG and sleep onset of women with TDCE, we were interested in comparing the sleep initiation episodes of both nights, in order to challenge the relationship between sleep initiation, cardiophysiological and thermoregulatory changes.

Thereby heart rate variability (HRV) measurement was used to determine changes in the cardiac autonomic control, in especially the low frequency power of heart rate variability (LF, reflecting both, sympathetic and vagal influence on the heart), the high frequency band (HF, reflecting the vagal influence on the heart), and the ratio of both (e.g. LFnu or LF/HF ratio, reflecting the balance of the sympathetic and vagal branch of the heart).

2. Methods

The following investigation was part of a larger study, involving 20 subjects with thermal discomfort from cold extremities associated with difficulties initiating sleep. The present investigation focused on two subsequent nights under controlled laboratory conditions, before a non-pharmacological intervention week started. Due to the balanced crossover design of the study ten participants had their non-interventional week prior the intervention week and their data were analyzed for the following examination.

2.1. Subjects

Ten healthy young women (26.0 ± 1.3 y; 20.5 ± 0.4 kg/m^2; mean ± SEM) were selected. None of them worked in shifts within 3 months or undertook transatlantic flights within 1 month prior to the study. Medication (excluding hormones) was prohibited. None of the participants had a history of drug abuse and smoking. Further exclusion criteria were extreme morning or evening chronotypes and amenorrhea or an irregular menstrual cycle. Chronotype was estimated using the Munich ChronoType Questionnaire (MCTQ). Five women took contraceptive medication and five conducted the study in the luteal phase of the menstrual cycle. Additionally women were screened for thermal discomfort from cold extremities and difficulties initiating sleep by subjective information about temperature sensation and sleep behavior (screening criteria see [7]). All volunteers were given questionnaires to determine physiological and psychological health. The data revealed that all women were physically and psychologically healthy.

The experimental protocol was approved by the Human Research Committee of the Department of Medicine, University of Basel. The main purpose and risks of the study were explained to the subjects before they gave their written consent. Subjects could stop the experiment at any time. All subjects completed the study without any complaints.

2.2. Study design and procedure

Within 4 weeks before initiation of the study, all subjects came for an adaptation night into the laboratory and completed an ambulatory screening week. Data based on actimetry data and sleep logs of the screening week were used to determine each subject's sleep times and confirm a habitual 8/16-h sleep–wake cycle. Volunteers had to ensure a regular sleep–wake schedule, moderate physical activity, and caffeine and alcohol abstinence during 4 days prior the study (compliance was checked via actimetry, sleep logs and questionnaires). Subjects came to the laboratory, 2 h before their habitual bedtime. They were instrumented for sleep with electrodes, as well as a rectal probe (polyoxymethylene probe: 2-mm diameter, copper-constantan, Interstar, Cham, Switzerland; Therm, type 5500-3, Ahlborn, Holzkirchen, Germany) and wireless thermosondes (iButtons®). They laid down 30 min prior lights out. Between the two 8-h nights (referred to as N1 and N2, respectively) a 16-h constant routine protocol was scheduled. Participants remained in dim-light conditions (<8 lx during wakefulness/0 lx during sleep) under constant semi-recumbent position in bed (head up not more than 45° during wakefulness/bed position 0° during sleep). Room temperature and relative humidity were kept constant at 22 °C and 55%, respectively. Subjects were studied singly and insulated from external sound or time cues. During the wake episode isocaloric sandwiches were administered at hourly intervals; water ad libitum.

3. Measurements

3.1. Electrocardiography (ECG)

Standard Ag–AgCl surface electrodes were placed on V2 and V5 (modified precordial lead). ECG was recorded with the Vitaport ambulatory system (Vitaport-3 digital recorder, TEMEC Instruments B.V., Kerkrade, the Netherlands) with a sampling rate of 256 Hz. The raw signals were stored online on a Flash RAM card (Viking) and later downloaded offline to a PC hard drive.

3.2. Polysomnography (PSG)

Sleep episodes were polysomnographically recorded using the Vitaport ambulatory system (Vitaport-3 digital recorder TEMEC® Instruments B.V., Kerkrade, the Netherlands). Six EEG derivations (frontal [Fz], central [Cz, C3, C4], parietal [Pz], occipital [Oz], referenced against linked mastoids, A1, A2), two electrooculograms (outer canthi), and one submental electromyogram (chin) were recorded. All EEG signals were filtered at 30 Hz (fourth-order Bessel-type anti-aliasing low-pass filter, total 24 dB/octave), and a time constant of 1.0 s was used prior to online digitization (range 610 μV, 12 bit analog-to-digital converter, 0.15 μV/bit; storage sampling rate at 128 Hz for the EEG). The raw signals were stored online on a Flash RAM Card (Viking) and downloaded offline to a personal computer hard drive.

3.3. Body temperatures

CBT data were continuously recorded by a computerized system (Ahlborn) in 30-sec intervals. Skin temperatures from the following 13 sites were measured: right and left side of the wrist at the radial artery above the os lunatum, left and right side above the calcaneus bone of the feet (together distal temperature), sternum, left and right infraclavicular, left and right groin (together proximal), left and right thigh and left and right calf. The distal-proximal skin temperature

gradient (DPG; distal-proximal) was calculated as an index for vasodilatation of the skin vasculature.

3.4. Melatonin and cortisol

Saliva collections (1–2 ml) were scheduled every 30 min, starting 4.5 h before habitual bedtime at home (two days prior the study). During the experiment, saliva was collected every 30 min during wakefulness and twice per night (2 h and 4 h after lights out each). The samples were immediately refrigerated at 5 °C, centrifuged within two days and stored at −20 °C. A direct double-antibody radioimmunoassay was used for the melatonin analysis (validated by gas chromatography–mass spectroscopy with an analytical least detectable dose of 0.65 pm/ml; Bühlmann Laboratories, Schönenbuch, Switzerland). The cortisol concentration was measured by an enzyme-linked immunosorbent assay (Cortisol—Direct Salivary EIA; ALPCO Diagnostics, Salem, MA, USA) with a least detectable value of 1 ng/ml.

3.5. Subjective ratings

During scheduled wakefulness, subjects were asked to complete questionnaires regarding to e.g. general discomfort (100 mm bipolar Visual Analog Scale [VAS]) at half hourly intervals.

3.6. Data analyses

3.6.1. ECG

A computerized system (System Hofstetter®, SHS Allschwil) was used to analyze the ECG signals and detect the length of all R–R intervals over the two nights. Each output was checked for plausibility by visual inspection. Obviously missing R-peak detections were replaced by interpolation of surrounding data. If the noise was low, this time duration was taken for further HRV analyses.

For time domain, as well as the frequency domain measures evaluating HRV the Kubios HRV 2.0 software ([8], Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland) was used.

In the time domain, the mean R–R interval, standard deviation of R–R intervals (STDRR) and root mean square of successive differences (RMSSD) were calculated for every 5-min R–R interval. HR was calculated as 1 / R–R interval * 60.

Before spectral analysis of 5-min sequences of R–R intervals, a cubic spline interpolation was used. Data were re-sampled at 4 Hz to provide equidistant time points. The fast Fourier transformation spectrum in the software was calculated using a Welch's periodogram [9].

The values for the bands of the HRV frequency-domain analysis were defined as follows: LF: 0–0.04 Hz, LF: 0.04–0.15 Hz and HF: 0.15–0.4 Hz. The LF/HF ratio, as well as LFnu (=normalized units: LF / (total power − VLF)) was taken as a measure for the balance of the autonomic nervous system.

3.6.2. PSG

All sleep episodes were visually scored (Vitaport paperless Sleep Scoring Software; TEMEC® Instruments) for consecutive 20-s epochs (C3-A2 derivation) according to standard criteria (Rechtschaffen and Kales, 1968). Sleep onset latency (SOL) was defined as the time interval between lights out and the occurrence of the first 20-s epoch of sleep stage 2. REM sleep latency (REML) was calculated from sleep onset. Total sleep time (TST) was defined as stage 2 + 3 + 4 + REM sleep. Sleep efficiency (SE) was defined as follows: SE = TST / time between lights out and lights on × 100. Arousals were defined as: wakefulness + sleep stage 1 + movement time (MT) and expressed as percentage of the time between lights out and lights on. Sleep stages [2–4] and rapid eye movement sleep (REMS) were calculated as percentage of total sleep time (TST) during the respective night for all participants.

EEGs were subjected to spectral analysis using a fast Fourier transform (10% cosine 4-s window; method described in detail in [10]), resulting in a 0.25 Hz bin resolution. EEG artifacts were detected by an automated artifact detection algorithm (Vitascore, CASA; 2000 Phy Vision B.V., Kerkrade, the Netherlands). For final data reduction, the artifact-free 4-s epochs were averaged over 20-s epochs and matched with the 20-s epochs of the visual sleep scoring. Especially the delta band (EEG power density in the range of 0.5–3.5 Hz) during NREMS of the frontal midline derivation (Fz) was calculated.

4. Statistics

To correct for a non-Gaussian distribution, spectral power indices, sleep onset latency and REM latency were logarithmically transformed. Additionally the times spent in different sleep stages were transformed by taking the square root. Data were averaged to 5-min bins. The statistical packages Statview™ 5.0 (SAS® Institute Inc., Cary, USA) and Statistica™ 6 for Windows (StatSoft Inc., Tulsa, USA) were used. Time-course analyses were performed using ANOVA for repeated-measures (rANOVA). The grouping factor was “night” (N1 vs. N2) and “time”. Huynh–Feldt analysis was used to correct for the violations of sphericity, all p-values were based on corrected degrees of freedom (reported are original degrees of freedom). The Duncan's multiple range test was conducted for post hoc comparison. Data were corrected for multiple statistical testing according to Curran-Everett [11]. SigmaPlot® (Systat Software, Inc., Chicago, USA) was used for graphics, whereby values are presented as means ± standard errors (SEM).

5. Results

Every subject had at least 7 h of sleep during night 1 and night 2, respectively. Thus 7-h-mean values for sleep variables and values of body temperature and HR of the entire night are displayed in Table 1. Melatonin concentration is shown as mean of both saliva collections each night.

Three subjects skipped their REM sleep either in N1 (two women) or in both nights (one woman) in the first sleep cycle. Thus their values were set to the duration of their NREMS in the first sleep cycle + 1epoch (20 s). Two subjects had very long sleep onset latencies and therefore were woken up too early for saliva collection to reach REM sleep. These two participants were excluded from statistics for REML.

If values for both nights are compared, only sleep onset latency is statistically significantly different, the gradient of distal and proximal skin temperature tends to show significant differences.

Table 1
Sleep variables of 7 h, temperature, heart rate and melatonin values per entire night are displayed. Data for CBT, DPG, HR and MEL were binned for every subject per night before repeated measure ANOVA was calculated. For SOL and REML original values are shown, but statistically analyzed with logarithmized values. Arousals are defined as wakefulness + sleep stage 1 + movement time and expressed as percentage of the time between lights out and lights on. The sum of sleep stages 2, 3, 4 and REM are amounted to 100%.

Variable	N1	N2	F(df)	p
SOL [min]	27.93 ± 5.93	13.13 ± 2.28	18.03(1,9)	0.002
REML [min]	96.42 ± 4.72	85.08 ± 8.72	2.12(1,7)	n.s.
Arousals [%]	27.61 ± 4.74	17.97 ± 1.66	2.85(1,9)	n.s.
S2 [%]	61.90 ± 1.83	60.97 ± 2.16	0.19(1,9)	n.s.
S3 [%]	12.76 ± 1.07	13.09 ± 1.04	0.07(1,9)	n.s.
S4 [%]	7.44 ± 2.21	7.96 ± 2.10	0.13(1,9)	n.s.
SWS [%]	20.20 ± 2.34	21.04 ± 2.41	0.40(1,9)	n.s.
REMS [%]	17.90 ± 2.10	17.99 ± 1.51	0.00 (1,9)	n.s.
SE [%]	72.39 ± 4.74	82.03 ± 1.66	2.85(1,9)	n.s.
CBT [°C]	36.79 ± 0.08	36.81 ± 0.10	0.07(1,9)	n.s.
DPG [°C]	−0.55 ± 0.07	−0.37 ± 0.09	3.27(1,9)	0.10
HR [bpm]	60.50 ± 2.08	59.45 ± 2.65	0.74(1,9)	n.s.
MEL [pg/ml]	1.82 ± 0.17	1.52 ± 0.18	0.80(1,9)	n.s.

Sleep onset latency (SOL); REM latency (REML); sleep stage 2–4 (S2–S4); slow wave sleep (SWS); REM sleep (REMS); sleep efficiency (SE); core body temperature (CBT); distal–proximal skin temperature gradient (DPG); heart rate (HR); melatonin (MEL).

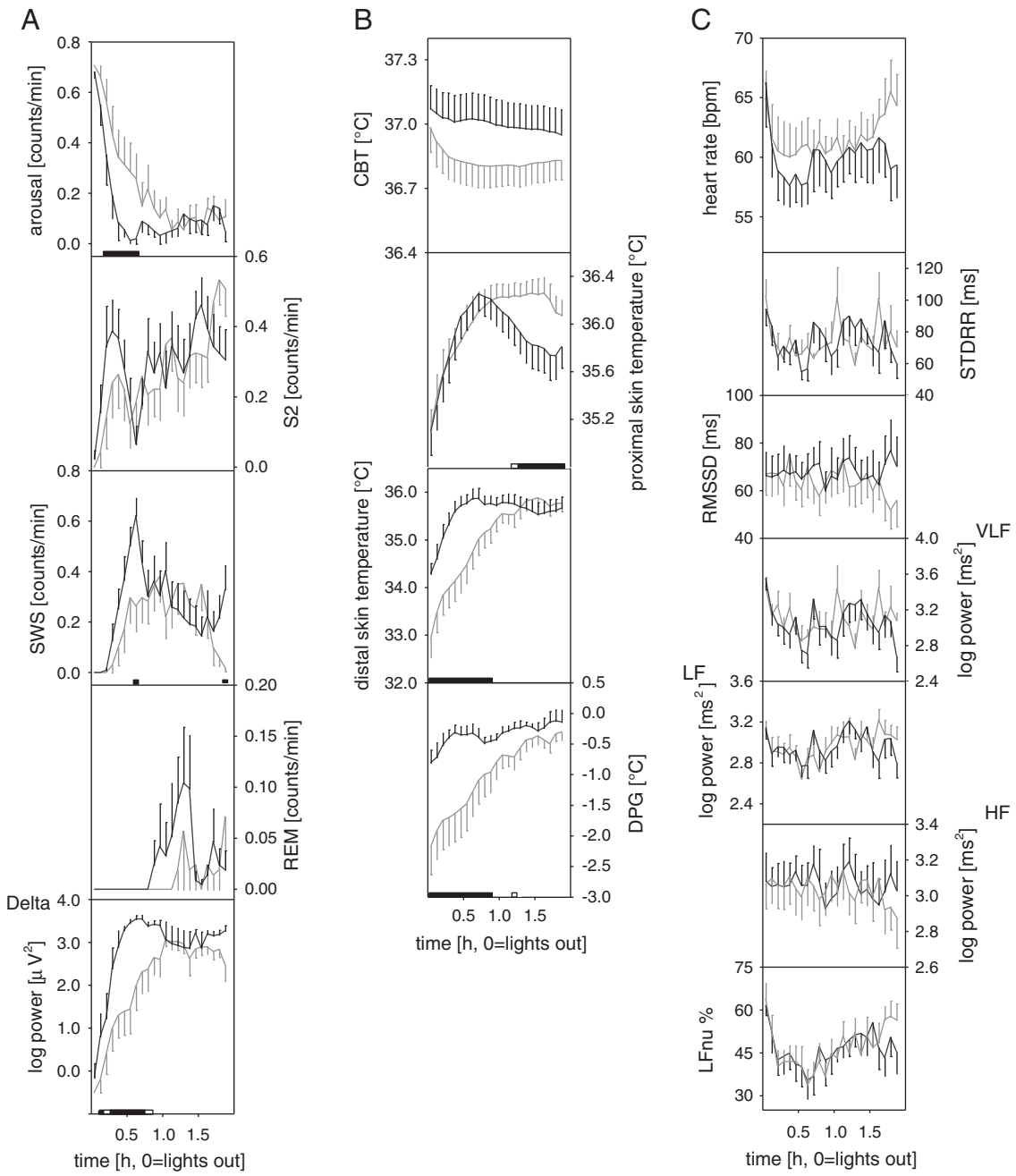

Fig. 1. A–C: Time course of physiological variables starting from lights out until 2 h after lights out. Grey line = night 1; black line = night 2. A: From top to bottom: Time course of arousal (awake + sleep stage1 + movement time), sleep stage 2, slow wave sleep (SWS; sleep stage 3 + 4), REM sleep (REMS) and delta power density in NREMS for the frontal deviation of the central EEG (Fz). B: From top to bottom: core body temperature (CBT), proximal skin temperature, distal skin temperature, distal–proximal skin temperature gradient (DPG). C: From top to bottom: heart rate, standard deviation of R–R intervals (STDRR), root means square of successive differences (RMSSD), spectral power of very low frequency (VLF), low frequency (LF) and high frequency (HF), as well as the ratio of LF and HF.

Time course of sleep variables, body temperature and HR and its variability for the first 2 h after lights out, are displayed in Fig. 1A–C.

Due to a faster decline of arousals, the build-up of S2, SWS and hence delta power is promoted in the second night compared to the first. Arousals revealed the significance for the factor night (N1 vs. N2: $F(1,9) = 6.22$, $p = 0.03$) and night × time ($F_{arousals}(22,198) = 2.17$, $p = 0.03$). SWS tended to be different for night × time ($F_{SWS}(22,198) = 1.87$, $p = 0.09$). Post hoc comparison showed a significant difference from the 15th until the 40th min after lights out for arousals and at the 40th and 115th min after lights out for SWS. For delta waves, rANOVA revealed a significant main effect (night: $F(1,9) = 19.81$, $p = 0.002$), and a tendency for the interaction (night × time: $F(22,198) = 2.33$, $p = 0.06$). After post hoc comparison, the times from 20 min until 45 min showed significant differences.

Although REM sleep seems to occur earlier and more often in N2 compared to N1 (Fig. 1A), it revealed neither a statistically significant main effect nor an interaction.

The CBT curve (Fig. 1B) seems to decline faster during the first 2 h of the first night, but rANOVA revealed no significant interaction term between night and time (night: $F(1,9) = 2.28$, $p = 0.17$; night × time: $F(22,198) = 1.56$, $p = 0.16$).

Both, proximal and distal skin temperatures increase after lights out. Distal skin temperature around light out is higher during the second night. Proximal skin temperature at sleep onset was similar in both nights. After rANOVA a significant interaction term between night and

time occurred for skin temperature (night × time: $F_{distal}(22,198) = 11.34$, $p < 0.001$; $F_{proximal}(22,198) = 4.49$, $p = 0.001$). Post hoc analysis showed a difference between N1 and N2 from minute 80 until 115 for proximal skin temperature while distal skin temperature show diverse developments immediately after lights out for 55 min.

The distal–proximal skin temperature gradient starts with a lower level after lights out in the first night, compared to the second. Factor night and night × time revealed statistical significance (night: $F(1,9) = 5.78$, $p = 0.04$; night × time: $F(22,198) = 4.44$, $p = 0.02$). Post hoc analysis revealed significant differences for the first 55 min.

Neither HR, nor any HRV variable showed a statistically significant difference between N1 and N2, after rANOVA. Nevertheless, the curves for HR, LF power and LFnu revealed significance for the factor time ($p < 0.05$). They start at a high level immediately after lights out and show a rapid decrease within 20 to 30 min (Fig. 1C).

6. Discussion

The present study aimed to compare the sleep initiation episodes of two nights in order to challenge the relationship between core body- and skin temperature, HR and its variability in women having both, TDCE and DIS. The study was conducted under highly controlled conditions, with controlled sleep–wake behavior before and during the investigated time span and a 16-h CR between the investigated nights.

Cold extremities; hence distal vasoconstriction is displayed by the low DPG at lights out of the first night. The vasoconstriction disappears and is not evident on the second night, confirming the data of diminished vasoconstriction during a CR study [12]. The low DPG is mainly caused by sympathetic innervation of the distal vascular muscles. A changed balance in the activity of the autonomic nervous system was previously found by measures of HRV (higher LF/HF ratio) in such a study population during 40-h of prolonged awakening under constant laboratory conditions [13]. However, the present results indicate that a direct link between skin temperature or sleep variables and HR or HRV variables seems unlikely at the sleep initiation episode. Not only the dynamics of the time courses are different (e.g. fast decrease in HR and LFnu immediately after lights out, but slow increase of skin temperature and SWS), but also marked differences in sleep and skin temperature variables are present between the two consecutive nights.

In early work ([14–16]) it was hypothesized that a rapid fall or even an active down driving of CBT is linked to increased sleep stage 3 or 4. The present results do not support these observations. Although not significant, CBT showed a slower decrease in the second night compared to the first, but an entire night comparison revealed no differences in SWS between both nights. Further analysis showed that values for SWS were significantly higher at 40 min after lights out in the second night. Thus the present data go in line with the observations of Dijk and Czeisler, who found higher CBT in the recovery night, accompanied by more SWS [17]. However, some studies suggest that skin temperature is a better predictor for delta power density and slow wave sleep than CBT. In detail, passive warming of the skin, without elevating CBT was linked to an increase in SWS [18]. An imaging study of the human brain revealed, that after skin warming the hypothalamus is partly activated [19], an anatomical site associated with sleep-promoting neurons. Although the time course of skin temperature, especially proximal skin temperature in the present study, is similar to that of SWS and delta power density, no differences were found between both nights.

At present, only one study has determined the changes in CBT regulation and autonomic control of the heart occurring especially at sleep onset [20]. In that, the authors concluded a relationship between CBT and measures for the sympathovagal balance especially during sleep initiation. This relationship cannot be confirmed by results of the present study, as patterns of LFnu (e.g. fast decline in the first minutes after lights out) do not match with patterns observed for CBT (slow decline during sleep initiation).

Not only the relationship between sleep variables, body temperature and HR or HRV, but also two different entrainment settings were elucidated. The first night includes the history of the entrained daily life (e.g. stress, light, large meals etc.), whereas the second night mirrors CR conditions, with constant dim light, supine posture and regular small food portions. Both nights have in common that they followed a 16-h wake phase, thus no difference in the homeostatic sleep pressure build-up should have been occurred.

Subjects remained in constant semi recumbent posture during the day in the laboratory and thus only minor posture changes occurred before lights out before the second night. Contrary, volunteers changed their posture from upright position to lying position before the first night. A “lying down” effect has been described and was found to affect CBT for around 2 h ([21,22]). Subjects in the present study laid down exactly 30 min before lights out in the first night, thus the trend of the CBT decrease during the first 90 min of the first night might be a result of the postural change. Heat redistribution from the core to the shell due to dilatation of the skin vasculature (seen e.g. by increasing DPG during the first night of the present data) has been suggested to promote these changes. Thereby heat distribution is linked to increased sleepiness, evaluated during times, when sleep pressure usually is very low (between 10 am and 1 pm; [22]). In the present examination, data suggest that subjects did not profit from the lying down effect (slower decrease of arousals in the first night compared to the second). Furthermore, a reduced sympathetic outflow as described in literature [23] has not been identified by LFnu spectral power measurements in the present study. Thus the lying down effect is unlikely to explain the observed data for HRV. This fact might be confirmed by another finding, derived using the same protocol apart from two additional laboratory nights one week prior. Data revealed no differences in arousals, SWS or delta activity between nights, but similar thermoregulatory effects (unpublished results).

An obvious further difference between the first and second night is given by its order. Studies investigating the “first night effect” in a sleep laboratory revealed a longer SOL [24,25]. Although longer SOL in the first night compared to the second was analyzed in the present study, effects due to the “first night effect” can be ruled out. Subjects underwent an adaptation night prior the study and additionally neither difference in SWS nor SE between the entire nights were found. Typically a decrease of SWS and less SE are found during sleep within the adaptation process to new environments [26,24,27]. Values of cortisol concentration revealed no statistical significance between nights (main effect “night”: $F(1,4) = 1.32$; $p = 0.32$), indicating that pronounced stress reaction effects in the first night, due to a new environment, can be excluded.

The relaxation process, a prerequisite for sleep initiation, has been shown to be reflected in heat redistribution from the core to the shell, a shift towards parasympathetic dominance and an increase in EEG delta power [5,28,29]. No differences in HRV measures between sleep initiation episodes of both nights occurred in the present study sample. However, a slower decrease in arousals, a slower increase in EEG delta power and a lower temperature level in DPG after lights out in the first night compared to the second were found. This suggests a delayed relaxation of subjects during sleep initiation on the first night without influencing HRV measures.

These data suggest that to shorten the sleep onset latency of the investigated subject population, psychobiological techniques with respect to HRV (e.g. biofeedback training) is less important than warming the extremities — thus confirming previous findings that warm extremities promote rapid onset of sleep [4].

6.1. Limitations

As with all studies, specific inclusion criteria might lead to difficulties when comparing populations. Nevertheless, subjects in the current study were physiologically and psychologically healthy, were representative of the overall population in respect to gender.

Leg movements may determine autonomic changes, but were not measured during the study. However, due to the careful analysis, episodes of noisy ECG signals (e.g. due to movements) were manually excluded from further evaluations.

The 16-h CR protocol itself could have led to different HRV findings between nights, e.g. due to discomfort. However, an analysis of self-rating questionnaires during the 16-h CR revealed no significant time course with respect to general discomfort (data not shown) indicating no support for such an explanation.

7. Conclusion

The results of the present study revealed different dynamics of the time course and differences between the sleep initiation episode of two consecutive nights in skin temperature and sleep variables, but not in HR and HRV variables in women having thermal discomfort from cold extremities and difficulties initiating sleep. A direct causality between these variables seems rather unlikely in the present study sample. Studies, which investigated gender effects on HRV during sleep elucidated that women show a less pronounced increase of the LF/HF ratio during REM [30,31] compared to men. Thus it might be concluded that in women, especially in the present study population, the central regulatory mechanisms of sleep, skin temperature and HR or HRV are rather weakly coupled.

However, observed night differences might not occur from the "lying down" effect, but from delayed relaxation, although this is only reflected in a slower decrease of arousals, a later rise in SWS and delta power and a lower DPG on the first night, but has no effect on autonomic cardiac control.

Further investigations with different genders, as well as a bigger study sample could give more hints about the underlying mechanism between sleep, body temperature and cardiac regulation during sleep initiation.

Acknowledgments

The authors are grateful to Sarah Chellappa for her consulting on analyzing the sleep EEG data, and Sylvia Frey and Doreen Hartwich for the comments on the manuscript. We thank Claudia Renz, Marie-France Dattler, and Giovanni Balestrieri for their help in data acquisition and the volunteers for participating. This work was supported by the Swiss National Science Foundation Grant # 3200B0-116504/1 and the Gottlieb Daimler and Karl Benz Foundation Consortium "ClockWork".

References

[1] Campbell SS, Broughton RJ. Rapid decline in body temperature before sleep: fluffing the physiological pillow? Chronobiol Int 1994;11:126–31.
[2] Murphy PJ, Campbell SS. Nighttime drop in body temperature: a physiological trigger for sleep onset? Sleep Jul 1997;20(7):505–11.
[3] Kräuchi K, Wirz-Justice A. Circadian rhythm of heat production, heart rate, and skin and core temperature under unmasking conditions in men. Am J Physiol Regul Integr Comp Physiol 1994;267:R819–29.
[4] Kräuchi K, Cajochen C, Werth E, Wirz-Justice A. Functional link between distal vasodilation and sleep-onset latency? Am J Physiol Regul Integr Comp Physiol 2000;278:R741–8.
[5] Krauchi K. The human sleep–wake cycle reconsidered from a thermoregulatory point of view. Physiol Behav Feb 28 2007;90(2–3):236–45.
[6] Raymann RJ, Swaab DF, Van Someren EJ. Skin temperature and sleep-onset latency: changes with age and insomnia. Physiol Behav Feb 28 2007;90(2–3):257–66.
[7] Krauchi K, Gasio PF, Vollenweider S, Von Arb M, Dubler B, Orgul S, et al. Cold extremities and difficulties initiating sleep: evidence of co-morbidity from a random sample of a Swiss urban population. J Sleep Res Dec 2008;17(4):420–6.
[8] http://kubios.uku.fi/.
[9] Welch PD. The use of fast Fourier transform for the estimation of power spectra: a method based on time averaging over short, modified periodograms. IEEE Trans Audio Electroacoust 1967;AU-15:70–3.
[10] Knoblauch V, Martens W, Wirz-Justice A, Krauchi K, Cajochen C. Regional differences in the circadian modulation of human sleep spindle characteristics. Eur J Neurosci Jul 2003;18(1):155–63.
[11] Curran-Everett D. Multiple comparisons: philosophies and illustrations. Am J Physiol Regul Integr Comp Physiol Jul 2000;279(1):R1–8.
[12] Vollenweider S, Wirz-Justice A, Flammer J, Orgül S, Kräuchi K. Chronobiological characterization of women with primary vasospastic syndrome: body heat loss capacity in relation to sleep initiation and phase of entrainment. Am J Physiol Regul Integr Comp Physiol 2008;294:R630–8.
[13] Anders D, Vollenweider S, Cann J, Hofstetter M, Flammer J, Orgül S, et al. Heart-Rate variability in women during 40-hour prolonged wakefulness. Chronobiol Int 2010;27(8):1609–28.
[14] Gillberg M, Akerstedt T. Body temperature and sleep at different times of day. Sleep 1982;5(4):378–88.
[15] Sewitch DE, Kittrell EM, Kupfer DJ, Reynolds III CF. Body temperature and sleep architecture in response to a mild cold stress in women. Physiol Behav 1986;36(5):951–7.
[16] McGinty D, Szymusiak R. Keeping cool: a hypothesis about the mechanisms and functions of slow-wave sleep. Trends Neurosci Dec 1990;13(12):480–7.
[17] Dijk DJ, Czeisler CA. Body temperature is elevated during the rebound of slow-wave sleep following 40-h of sleep deprivation on a constant routine. J Sleep Res Sep 1993;2(3):117–20.
[18] Raymann RJ, Swaab DF, Van Someren EJ. Skin deep: enhanced sleep depth by cutaneous temperature manipulation. Brain Feb 2008;131(Pt 2):500–13.
[19] Egan GF, Johnson J, Farrell M, McAllen R, Zamarripa F, McKinley MJ, et al. Cortical, thalamic, and hypothalamic responses to cooling and warming the skin in awake humans: a positron-emission tomography study. Proc Natl Acad Sci U S A Apr 5 2005;102(14):5262–7.
[20] Okamoto-Mizuno K, Yamashiro Y, Tanaka H, Komada Y, Mizuno K, Tamaki M, et al. Heart rate variability and body temperature during the sleep onset period. Sleep Biol Rhythms 2008;6(1):42–9.
[21] Kleitman N. Sleep and wakefulness. Chicago, IL: University of Chicago Press; 1963.
[22] Kräuchi K, Cajochen C, Wirz-Justice A. A relationship between heat loss and sleepiness: effects of postural change and melatonin administration. J Appl Physiol 1997;83:134–9.
[23] Sindrup JH, Kastrup J, Jorgensen B, Bulow J, Lassen NA. Nocturnal variations in subcutaneous blood flow rate in lower leg of normal human subjects. Am J Physiol Feb 1991;260(2 Pt 2):H480–5.
[24] Curcio G, Ferrara M, Piergianni A, Fratello F, De Gennaro L. Paradoxes of the first-night effect: a quantitative analysis of antero-posterior EEG topography. Clin Neurophysiol May 2004;115(5):1178–88.
[25] Agnew Jr HW, Webb WB, Williams RL. The first night effect: an EEG study of sleep. Psychophysiology Jan 1966;2(3):263–6.
[26] Le Bon O, Staner L, Hoffmann G, Dramaix M, San Sebastian I, Murphy JR, et al. The first-night effect may last more than one night. J Psychiatr Res May-Jun 2001;35(3):165–72.
[27] Marzec ML, Selwa LM, Malow BA. Analysis of the first night effect and sleep parameters in medically refractory epilepsy patients. Sleep Med May 2005;6(3):277–80.
[28] Krauchi K. The thermophysiological cascade leading to sleep initiation in relation to phase of entrainment. Sleep Med Rev Dec 2007;11(6):439–51.
[29] Boudreau P, Yeh WH, Dumont GA, Boivin DB. A circadian rhythm in heart rate variability contributes to the increased cardiac sympathovagal response to awakening in the morning. Chronobiol Int Jul 2012;29(6):757–68.
[30] Valladares EM, Eljammal SM, Motivala S, Ehlers CL, Irwin MR. Sex differences in cardiac sympathovagal balance and vagal tone during nocturnal sleep. Sleep Med Mar 2008;9(3):310–6.
[31] Elsenbruch S, Harnish MJ, Orr WC. Heart rate variability during waking and sleep in healthy males and females. Sleep Dec 15 1999;22(8):1067–71.